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Obesity and Life-related Disorders

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Obesity has turned into a global public health emergency with its impact on millions and causing a mass increase in life-style diseases encompassing type 2 diabetes, cardiovascular diseases, hypertension and others cancers.

This pandemic is not only a personal health crisis, but also a societal issue that requires a holistic intervention that goes beyond effective cure and strong preventive strategies.

Managing obesity and the related disorders demands a multi-faceted strategy. For the most severe, medical therapies (e.g, bariatric surgery) can achieve great weight loss and result in improvements of conditions including diabetes. In fact, progress has been made in the area pharmacotherapy with drugs like GLP-1 receptor agonists providing hope to treat a weight and metabolic health derangements. But, these therapies are expensive and don't reach all especially in the low-income regions. At present, lifestyle interventions such as diet modifications and increased physical activity are the mainstays of obesity management. A few programs such as nutritional counseling integrated with exercise regimens have delivered sustainable results, although retention is a problem due to time constraints, loss of motivation, or socioeconomic disadvantages.

Treatment is important above all, and prevention should be the number one goal to stop this obesity epidemic. Awareness-driven public health campaigns may increase knowledge of healthy eating and active living, but they need to be combined with systemic shifts. The government should set some policies to for example tax sugar-sweetened beverages and mandate clear nutritional label, subsidize fresh produce. Schools have a critical role by embedding nutrition education and physical activity into curriculums that encourage lifelong habits. Walkable cities, and access to recreational spaces through improving urban planning can also facilitate movement.

Harmful social determinants of health are also addressed by community-based initiatives such as cooking or fitness groups that reach people who do not have the benefit of stronger support systems.

Addressing basic factors of health will attend to social determinants of obesity. Obesity, exacerbated by poverty stress and poor healthcare access. Targeted community-level interventions, such as providing free or reduced-cost health screenings, can bring attention to and alleviate the problem prior to full-blown disease. For example, technology such as wearables and remote patient monitoring are being used to track health indicators and wellness behaviors.

Obesity is a multifaceted problem that involves biology, environment and culture. Maybe treatments can, to some degree, decrease incidence but prevention driven policy and education with equitable access to resources has to be the answer if we want to stop this from dramatically increasing. Societies can reduce obesity and noncommunicable disease epidemics through health-promoting, empowering cultures that enable healthier lives.





Original Article



Association of Glycated Hemoglobin and Microalbuminuria with Renal Function Parameters in Type 2 Diabetic Patients

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ABSTRACT

One of the most serious complications of type 2 diabetes (T2DM) is diabetic nephropathy, which can eventually lead to kidney failure. While microalbuminuria is commonly used to detect early kidney damage, relying on it alone may not be enough. Additional markers could help improve early detection and timely treatment. **Objectives:** To look at how HbA1C levels, a key indicator of blood sugar control, relate to microalbuminuria in people with T2DM. Also, to explore how HbA1C correlates with other markers of kidney function, including the albumin-to-creatinine ratio (ACR), serum urea, creatinine, fasting blood sugar (FBS), and random blood sugar (RBS). **Methods:** The study included 250 participants: 200 patients with T2DM and 50 healthy individuals matched by age and sex. Those with hypertension, kidney disease, urinary tract infections, or other health issues were excluded. Blood and urine samples were collected. Hemoglobin A1C was measured using high-performance liquid chromatography (HPLC), and A1C was calculated. Data were analyzed using SPSS-20, and correlations were assessed with Pearson's coefficient. **Results:** Compared to healthy controls, diabetic patients had significantly higher levels of FBS, RBS, HbA1C, serum urea, creatinine, and microalbuminuria. Higher HbA1C levels were linked with worse kidney function, suggesting that poor blood sugar control may signal early kidney damage. **Conclusions:** It was concluded that monitoring both HbA1C and microalbuminuria offers a better chance of catching kidney problems early in T2DM patients. Adding both markers to routine screenings could help delay or prevent serious kidney issues.

INTRODUCTION

T2DM is a highly prevalent chronic metabolic disorder worldwide, and its prevalence is continuously increasing, so are its complications [1, 2]. The number of adult diabetic patients worldwide has exceeded more than 500 million, out of which 20% have end-stage renal damage, which is a major health issue [3]. Approximately 537 million persons worldwide were expected by the International Diabetes Federation (IDF) to have diabetes by 2021, with type 2 diabetes accounting for more than 90% of these cases [4]. The prevalence is particularly concerning in Pakistan, where, according to the IDF, 26.7% of people had diabetes

in 2022, ranking it third in the world behind China and India. "The News," one of the leading newspapers of Pakistan, published an article on diabetes, according to which Pakistan ranked third in the prevalence list of diabetes worldwide after India and China [5]. T2DM is the most common metabolic syndrome caused by disturbed carbohydrate metabolism, impaired insulin secretion, or, most of the time, insulin resistance due to blocking antibodies, resulting in hyperglycemia. In the absence of glucose, the tissue starts producing energy by lipolysis or proteolysis [6]. Simultaneous production of energy by



sources other than glucose in T2DM leads to an increased production of various dangerous byproducts like advanced glycation end products, ketones, and free radicals. The microvasculature of T2DM patients is the first organ to be affected by these byproducts, resulting in microvascular disorders, especially neuropathy, nephropathy, and retinopathy [7-9]. Diabetic nephropathy is one of the feared complications of T2DM, causing progressive damage to renal tissues resulting in end-stage renal disorder, and patients ultimately go for dialysis or renal transplant. Due to the high prevalence of DM, diabetic nephropathy cases have exceeded other causes of renal damage, e.g. immune immune-mediated renal disorders [10]. Diabetic kidney disease (DKD) is predicted to develop in 20-50% of persons with type 2 diabetes [11]. According to research, the prevalence of chronic kidney disease (CKD) in diabetic people in Pakistan ranges between 12.5% to 29.9% [12]. Furthermore, 88% of diabetic individuals in a Lahore research had albuminuria, suggesting a substantial burden of renal problems [13]. The diagnosis of diabetic nephropathy is mainly based on microalbuminuria and estimated glomerular filtration rate. But it has been observed that in those diabetic patients who have disturbed glucose metabolism for a long time, the detection of microalbuminuria alone does not reflect the true picture of renal damage. This group of patients must be advised to have their HbA1C along with microalbuminuria to better assess the extent of renal damage. HbA1c is a significant test for monitoring glycemic control, and it accurately provides a pattern of glucose control for the last couple of months. HbA1C is a steadfast measure of chronic hyperglycemia, and it is also well associated with the development of long-term complications of DM [14-16].

Microalbuminuria alone may not accurately reflect early renal damage in patients with long-standing type 2 diabetes, highlighting the need for additional markers. However, limited local evidence exists on the combined diagnostic value of HbA1c and microalbuminuria for early detection of diabetic nephropathy. This study aims to assess the diagnostic value of microalbuminuria and HbA1c in the early identification of nephropathy in patients with type 2 diabetes. In order to enable prompt interventions to stop the progression to end-stage renal disease (ESRD), we aim to correlate these indicators in order to identify patients at risk of developing DN at an earlier stage.

METHODS

This analytical case-control study was conducted at Life Care Molecular Lab, Karachi, from March 2023 to March 2024 in collaboration with Fazaia Ruth Pfau Medical College. Ethical approval was obtained from the Institutional Review Board of Fazaia Ruth Pfau Medical College (IRB Ref: FRPMC/003/IRB/23). The sample size of

250 participants was calculated using OpenEpi software, considering a correlation coefficient (r) of 0.2 between microalbuminuria and serum creatinine, with 80% power and 95% confidence level. A non-probability purposive sampling technique was employed. Among the 250 participants, 200 were diagnosed cases of type 2 diabetes mellitus (T2DM) for at least 10 years and aged above 30 years, while the remaining 50 were age-matched healthy individuals serving as controls with no history of diabetes or renal disease. Diabetic patients were further stratified into two groups based on the urine albumin/creatinine ratio (ACR): Group 1 with normal ACR (<30 mg/g) and Group 2 with microalbuminuria (30-299 mg/g), as per National Kidney Foundation (NKF) guidelines. In addition, T2DM patients were stratified based on HbA1C levels into well-controlled (HbA1C $<7.0\%$) and poorly controlled (HbA1C $\geq 7.0\%$), and by disease duration into two categories: 10-15 years and more than 15 years. This stratification was done to better understand the relationship between glycemic control, severity/duration of diabetes, microalbuminuria, and progression of nephropathy. The controls were selected based on normal fasting blood sugar (FBS), random blood sugar (RBS), and HbA1C levels, with no known renal or systemic illnesses. To ensure homogeneity of the sample, the following exclusion criteria were applied to diabetic patients: those with acute or chronic kidney disease from non-diabetic causes, hypertension, cardiovascular diseases, chronic infections, malignancies, autoimmune disorders, pregnancy, or use of nephrotoxic drugs were excluded. Patients with urinary tract infections or any systemic disease were also not included in the diabetic group. All participants were instructed to fast overnight for 12 hours before sample collection. A total of 7 mL of venous blood was collected under aseptic conditions. The samples were processed accordingly: 2 mL in EDTA tubes for HbA1C analysis using high-performance liquid chromatography (HPLC), which was chosen over immunoassay or enzymatic methods due to its superior analytical precision, reproducibility, and ability to detect hemoglobin variants, making it a gold-standard method for HbA1C measurement in clinical and research settings. Additionally, 2 mL in fluoride tubes was used for FBS measurement, 1 mL in a separate fluoride tube for RBS, and the remaining in gel tubes for estimation of serum urea and creatinine using chemiluminescence. Spot urine samples were collected for the assessment of microalbumin and creatinine, and the ACR was calculated by dividing albumin (mg) by creatinine (g). The primary outcome variables included microalbuminuria (defined by ACR 30-299 mg/g), HbA1C level, serum urea, and serum creatinine, while secondary variables included age, sex, duration of diabetes, FBS, and RBS. Microalbuminuria was considered an early marker of diabetic nephropathy. Data were recorded using a structured proforma and entered into Microsoft Excel. Statistical analysis was performed using SPSS version 20.

Mean and standard deviation (SD) were calculated for continuous variables. Independent sample t-tests and ANOVA were applied to compare means between diabetic and control groups. Pearson correlation analysis was performed among diabetic patients to explore relationships between HbA1C, ACR, and serum creatinine. A p-value of <0.050 was considered statistically significant throughout the study.

RESULTS

The study included 250 participants, divided into three

groups: Group A (Control group): 50 healthy individuals, Group B: 100 T2DM patients with normoalbuminuria, Group C: 100 T2DM patients with microalbuminuria. Results summarize the mean values $\pm$ SD of various biochemical parameters across the three groups and demonstrates statistically significant differences in all parameters as nephropathy progresses. The mean values of glycemic (HbA1C, FBS, RBS) and renal parameters (urea, creatinine) significantly increased with worsening albuminuria status among diabetic patients (Table 1).

Table 1: Comparison of Biochemical Parameters Among Study Groups

Parameter	Group A (Control)	Group B (Normoalbuminuria)	Group C (Microalbuminuria)	p-value (ANOVA)
FBS (mg/dL)	88.00 $\pm$ 10.00	165.00 $\pm$ 35.00	205.00 $\pm$ 40.00	<0.001
RBS (mg/dL)	130.00 $\pm$ 15.00	250.00 $\pm$ 45.00	300.00 $\pm$ 50.00	<0.001
Urea (mg/dL)	30.00 $\pm$ 5.00	48.00 $\pm$ 10.00	62.00 $\pm$ 15.00	<0.001
Creatinine (mg/dL)	1.00 $\pm$ 0.20	1.70 $\pm$ 0.80	2.50 $\pm$ 1.10	<0.001
HbA1C (%)	5.20 $\pm$ 0.40	7.20 $\pm$ 1.00	10.10 $\pm$ 2.00	<0.001
Microalbumin (mg/dL)	15.00 $\pm$ 5.00	25.00 $\pm$ 4.00	120.00 $\pm$ 50.00	<0.001

The following table presents the correlation coefficients of microalbuminuria with glycemic and renal markers in diabetic patients (Groups B and C combined). Findings show a strong correlation of microalbuminuria with serum creatinine, and a moderate correlation with HbA1C, confirming the relationship between poor glycemic control and progressive renal impairment in T2DM patients (Table 2).

Table 2: Correlation Between Microalbuminuria and Biochemical Markers in T2DM Patients

Parameter	Pearson's r	p-value	Interpretation
FBS	0.190	0.001	Mild positive correlation
RBS	0.240	0.001	Mild Positive Correlation
Urea	0.155	0.020	Weak But Significant
Creatinine	0.799	<0.001	Strong Positive Correlation
HbA1C	0.659	<0.001	Moderate Positive Correlation

DISCUSSION

Diabetic nephropathy is a serious and most feared complication of diabetes mellitus affecting the microvasculature of the kidneys, resulting in end-stage renal disease. Worldwide data from the International Diabetes Federation states that almost 30-40% of diabetic patients may develop chronic kidney damage, resulting in renal failure. Likewise, 80% of diabetics with hypertension lead to end-stage renal failure [17, 18]. Diabetic patients are ten times more prone to have chronic kidney disease, accompanied by increased morbidity and mortality among diabetic patients [19]. The prevalence of diabetic nephropathy is increasing as the diabetic pool is expanding worldwide, and it needs marked improvement in strategic plans for the prevention of diabetic nephropathy [20, 21]. Microalbuminuria is an early indicator of diabetic nephropathy. About 30-40% of diabetic patients may develop microalbuminuria-related nephropathy within ten years, and the majority of these patients develop end-stage renal disease. Estimation of HbA1C provides accurate and precise information about glycemic status,

and it accurately defines the cumulative glycemic history of the preceding two to three months. Besides, it is well correlated with the increasing risk of diabetic complications, especially nephropathy [22]. In our study, FBS, RBS in the control group are found to be 80 mg/dl and 120 mg/dl, respectively, with HbA1C below 6.0 %. While group 1 and group 2 have increased FBs and RBs levels with HbA1C more than 6.2 %. Similarly, urea and Creatinine were also found to be within normal range with normal HbA1C, while Group 1 and Group 2 showed increased levels of both urea and Creatinine with increased HbA1C. Microalbuminuria also showed a significant direct proportional relationship with HbA1C in both diabetic groups. These findings are by the results given by [23, 24]. The present study also showed a significant correlation of microalbuminuria with HbA1C (p-value=0.0001) and (r=0.65) as shown by [25]. Similar results were given by [26], which also showed a significant correlation between Microalbuminuria and HbA1C. The strong point of our study is the precise and accurate measurement of HbA1C and microalbuminuria, and it proves that good glycemic control by HbA1C can minimize microalbuminuria detection through resulting in the decreased progression of diabetic nephropathy. Even though our research shows a strong link between high HbA1C levels and microalbuminuria, it's crucial to take into account possible confounding factors like obesity, hypertension, dyslipidemia, and nephrotoxic medication use that could also play a role in the onset and progression of diabetic nephropathy. To reduce the impact of these confounders. According to our predetermined

exclusion criteria, patients with hypertension were not allowed to participate in the study. Because hypertension is a known risk factor for renal impairment and may have led to higher microalbuminuria levels on its own, skewing the correlation with HbA1C, this was crucial [1]. Another significant confounding factor is obesity, which can worsen kidney disease by encouraging glomerular hyperfiltration and insulin resistance. Although not specifically mentioned in our study, anthropometric measurements (waist circumference, BMI) should be used in future studies to account for the possible impact of obesity [27]. Our study's strength is the precise measurement of HbA1C using HPLC and the detection of microalbuminuria using chemiluminescence, both of which support the idea that strict glycaemic management helps prevent early renal involvement in diabetes patients. We recommend adding regular HbA1C and microalbuminuria tests to the routine clinical follow-up of all type 2 diabetic patients according to our results. Although annual or biennial microalbuminuria screening may help in early detection of renal impairment, HbA1C must be assessed every three months to monitor long-term glycaemic control. Ultimately, this holistic approach will reduce the burden of diabetic nephropathy by allowing for timely intervention and early detection of high-risk patients.

The study is limited by a relatively small sample size and the exclusion of key confounding factors such as obesity and dyslipidemia, which may influence the results. Additionally, its cross-sectional design restricts the ability to establish causal relationships between HbA1C and microalbuminuria. Future studies should include larger, multicenter populations and adopt longitudinal designs to better establish causal relationships. Additionally, incorporating confounding factors such as BMI, lipid profile, and medication use would provide a more comprehensive understanding of diabetic nephropathy progression.

CONCLUSIONS

It was concluded that the consequences of T2DM are becoming more sensitive in terms of healthcare expenditure in Pakistan, particularly concerning diabetic renal disease. The damage to kidney tissue must be identified early to avoid end-stage renal failure. This research proves that both urine microalbuminuria and glycosylated hemoglobin (HbA1C) are critical markers for the optimal control of diabetes and nephropathy detection in diabetes. Due to their interdependent relationship, the evaluation of these two parameters can be beneficial for both newly diagnosed and long-standing diabetic patients. The routine performance of these tests by healthcare providers will dramatically improve the management of advanced renal complications in diabetes patients.

Authors' Contribution

Conceptualization: AR

Methodology: NQ, SZ, I

Formal analysis: RFM

Writing and Drafting: SE, ZI, SS

Review and Editing: NQ, RFM, SE, ZI, SS, AR, SZ, I

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Operative Outcomes of Open Thyroidectomy with Electrothermal Bipolar Vessel Sealer versus Conventional Hemostasis for Benign Thyroid Swelling in Adults Population

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ABSTRACT

Precise dissection and effective hemostasis are crucial for safe thyroid surgery. The bipolar vessel sealer, a first-generation electrosurgical instrument, is widely used in thyroidectomies to improve hemostasis, reduce tissue trauma, shorten surgery time, and eliminate the need for sutures. **Objective:** To compare the operative outcomes of electrothermal bipolar vessel sealer in total thyroidectomy. **Methods:** At the Department of Surgery, Sir Ganga Ram Hospital, from August 2024 to January 2025, a quasi-experimental study was carried out, involving 80 patients undergoing total thyroidectomy. Exclusion criteria included patients with significant comorbidities, bleeding disorders, or renal and liver dysfunctions. The study participants were divided into two groups: Group A (bipolar vessel sealer) and Group B (clamp-and-tie technique). Primary outcomes included surgery duration, intraoperative blood loss, and hospital stay. Data were entered and analyzed by SPSS version 25.0. **Results:** The average age of patients was 35.5 ± 4.9 years. Group A had 70% female and 30% male, while Group B had 77.5% female and 22.5% male. Group A had significantly shorter hospital stays (3.8 ± 1.2 days) compared to Group B (5.2 ± 2.3 days, $p=0.000$). Intraoperative blood loss was significantly lower in Group A (109.7 ± 7.3 mL) compared to Group B (154.3 ± 6.7 mL, $p<0.000$). Surgery duration was longer in Group A (121.3 ± 13.1 minutes) than in Group B (94.3 ± 11.3 minutes, $p<0.05$). **Conclusions:** It was concluded that the bipolar vessel sealer in total thyroidectomy for benign thyroid swelling is effective, and results in shorter hospital stays without increasing complications or costs

INTRODUCTION

Thyroid disorders are among the most common conditions affecting the head and neck, with surgery being the definitive treatment for many cases. Thyroidectomy, the most common neck surgery, effectively addresses various thyroid disorders [1, 2]. Although advancements have lowered mortality rates to nearly 0% and complications to less than 3%, however, risks of hemorrhage, recurrent laryngeal nerve injury, and postoperative hypocalcemia persist as concerns [3]. Hemorrhage, although a rare but

serious complication of thyroid surgery, occurs in 0.3% to 4.2% of cases. It may lead to neck swelling, pain, and airway obstruction (dyspnea, stridor, hypoxia), with reoperation necessary if drainage fails to prevent obstruction [4]. Hypocalcemia, caused by postoperative hypoparathyroidism, affects 7% to 37% of total thyroidectomy patients [5], with rates varying due to differing diagnostic criteria. Most cases resolve within weeks, depending on the degree of parathyroid

devascularization or accidental removal [6]. However, Optimal outcomes rely on precise dissection, effective hemostasis, and preservation of vital structures, using techniques like knot-tying, electrocautery, and vessel-sealing devices [7]. The use of ultrasonic and bipolar energy devices has become increasingly common in surgery. Recently, integrated devices combining both energy types have gained popularity, particularly in laparoscopic and open surgeries [8]. Advances in hemostasis techniques have led to the growing use of energy-based devices in neck surgery [9]. These devices utilize different energy forms: Liga Sure™ relies on radiofrequency [10], the Harmonic Scalpel converts electrical energy into ultrasonic vibrations [11], and Thunder beat combines harmonic and radiofrequency technologies for efficient tissue dissection and coagulation [12]. These days, coagulation devices, metallic clips, staples, and suture ligation are used to stop bleeding. Nonabsorbable elements like staples and clips can occasionally induce irritation and impede wound healing, and ligation and sutures take time [13]. Electrocautery can cause thermal damage to the recurrent laryngeal nerve and parathyroid glands [14]. As an alternative, the electrothermal bipolar vessel-sealing system uses a combination of energy and pressure to denature collagen and elastin in vessel walls and adjacent tissues. The FDA approved Liga Sure (Tyco Int. Valley lab), which effectively seals vessels >7mm in diameter [15].

Despite the widespread application of the electrothermal bipolar vessel sealer in surgery, its precise advantage in total thyroidectomy for benign disorders, especially when pitted against standard techniques involving meticulous hemostasis, is still not well studied. With the growing sophistication of surgical technologies, consideration is needed regarding the effect of this approach on surgical time, blood volume loss, and complications. This study aims to evaluate the effectiveness of using a bipolar vessel sealer in total thyroidectomy in terms of operative outcome and complications and compare it to a traditional clamp-and-tie technique.

METHODS

At the Department of Surgery, Sir Ganga Ram Hospital, from August 2024 to January 2025, a quasi-experimental study was carried out from August 2024 to January 2025. A total of 80 patients undergoing total thyroidectomy were enrolled using a convenient sampling technique, following ethical approval (179-MS-Surgery/ERC). Taking a 5% margin of error and an 80% study power with 20% expected dropout, the sample of subjects by complication rate in the Bipolar Vessel Sealing group was 60.0%, and the traditional method was 24.0%. The sample size was 80 (40 in each group [16]. The study included patients aged 18-60, both genders, undergoing elective total thyroidectomy who

provided informed consent. Patients with an ASA grade of 3 or higher, significant comorbidities, bleeding disorders (INR >1.5), or renal (creatinine >2 mg/dl) or liver dysfunction (bilirubin >1.5 mg/dl) were excluded. The patients were divided into two groups. Group A (Bipolar Vessel Sealing): Liga Sure™ system was used for hemostasis. Group B (Clamp-and-Tie Technique): Hemostasis was achieved using suture ligation and electrocautery. Under aseptic conditions, patients underwent total thyroidectomy using the standard approach. After dissection of the thyroid gland, bleeding from the thyroid bed was observed. In Group A, the electrothermal bipolar vessel sealer was used for hemostasis. The middle thyroid vein, superior thyroid artery, vein, and terminal branches of the inferior thyroid artery and inferior pedicle were coagulated and divided with careful dissection to preserve the superior laryngeal nerve. The recurrent laryngeal nerve and parathyroid glands were identified and protected. Terminal branches of the inferior thyroid artery were coagulated near the gland, and the thyroid was retracted medially for vessel division at the ligament of Berry. Absorbable sutures (polyglactin 2-0) were used if vessels were encountered near vital structures. Intraoperative blood loss was calculated. In Group B, the conventional clamp-and-tie technique was employed. The middle thyroid vein, superior thyroid artery, vein, and terminal branches of the inferior thyroid artery and inferior pedicle were ligated and divided using absorbable sutures (polyglactin 2/0-3/0). Intraoperative blood loss was objectively measured by calculating the increase in the weight of surgical swabs and gauze used during the procedure, with each gram of weight gain considered equivalent to one milliliter of blood loss (i.e., 1 g = 1 mL). The effectiveness of the two methods was evaluated based on the cessation of bleeding from the thyroid bed within 10 minutes, indicating successful hemostasis. After securing hemostasis, drain placement was done if required, and the wound was closed in reverse fashion, and postoperative blood loss was calculated. All data, including demographic details, were recorded in the attached proforma. The same surgical team conducted all of the procedures, and the lead surgeon had five years of thyroid surgery experience. Numerical variables (e.g., age, hospital duration, and Intraoperative & Postoperative blood loss) were presented as mean $\pm$ SD. Categorical variables (e.g., gender, history of diabetes, history of hypertension, and complications) were presented as frequencies and percentages. Data were entered and analyzed using SPSS version 25.0, with independent sample t-tests and chi-square tests used for comparisons. A p-value of <0.05 was considered statistically significant.

RESULTS

The mean age was slightly higher in Group A (40.2 ± 5.3 years) compared to Group B (38.9 ± 4.5 years), though this difference may not be clinically significant. Group A had 70% females and 30% males, while Group B had 77.5%

females and 22.5% males, indicating a higher proportion of females in both groups. Regarding Body Mass Index (BMI), Group A had a higher proportion of obese individuals (47.5%) compared to Group B (37.5%), while both groups had a similar percentage of non-obese individuals (60% in Group A vs. 57.5% in Group B). Diabetes Mellitus was higher in Group A (47.5%) compared to Group B (30%), suggesting that Group A had a greater proportion of individuals with diabetes. The frequency of hypertension was slightly higher in Group A (57.5%) than in Group B (50%), with both groups showing a substantial percentage of individuals without hypertension (40% in Group A vs. 52.5% in Group B). There was no significant difference in baseline investigations between the two groups (p -value>0.050) (Table 1).

Table 1: Baseline Investigations of Patients

Variables	Group-A	Group-B	Total	p-value
Age (Years)	40.2 ± 5.3	38.9 ± 4.5	35.5 ± 4.9	0.311
Gender				
Male	12 (30.04%)	9 (22.5%)	21 (26.2%)	0.611
Female	28 (70.0%)	31 (77.5%)	59 (73.7%)	
Body Mass Index (BMI)				
Obese	19 (47.5%)	15 (37.5%)	33 (41.2%)	0.839
Non-Obese	24 (60.0%)	23 (57.5%)	47 (58.7%)	
Diabetes Mellitus				
Yes	19 (47.5%)	12 (30.0%)	31 (38.7%)	0.754
No	27 (67.5%)	22 (55.0%)	49 (61.3%)	

Table 2: Comparison of Intra- and Post-Operative Outcomes of Surgery Among Groups

Variables	Group A	Group B	p-value
Hospital Duration	3.8 ± 1.2	5.2 ± 2.3	<0.001
Duration of Surgery (In minutes)	94.3 ± 11.3	121.3 ± 13.1	<0.001
Intraoperative blood loss (mL)	109.7 ± 7.3	154.3 ± 6.7	<0.001
Postoperative blood loss (mL) by the amount of drain output at Day 1	32.03 ± 10.4	35.7 ± 10.3	0.110
Postoperative blood loss (mL) by the amount of drain output at Day 2	19.1 ± 5.72	19.2 ± 5.82	0.893
Postoperative blood loss (mL) by the amount of drain output at Day 3	16.8 ± 5.93	15.2 ± 6.68	0.269

Effectiveness was higher in Group A, with 47 participants showing positive outcomes compared to 23 in Group B. In contrast, fewer individuals in Group A reported ineffectiveness ("No"), with only 3 responses, compared to 7 responses in Group B. There was a significant association between the effectiveness of both groups (p -value<0.050) (Figure 1).

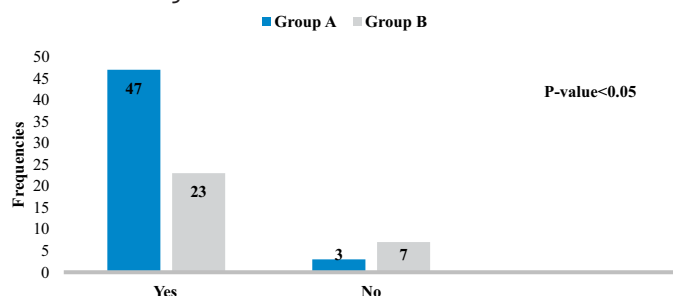


Figure 1: Comparison of Effectiveness among Groups

DISCUSSION

Precise dissection and efficient hemostasis are necessary for a safe surgical procedure to preserve important tissue. Although knot tying is the conventional technique for hemostasis, vessel sealing technologies save more time

Hypertension				
Yes	23 (57.5%)	20 (50.0%)	43 (5.7%)	0.490
No	16 (40.0%)	21 (52.5%)	37 (46.2%)	
Total	109	109	218	

The results demonstrated significant differences among groups across all measured variables. The mean hospital duration was shorter in Group A (3.8 ± 1.2 days) compared to Group B (5.2 ± 2.3 days), with a p -value of <0.001, indicating statistical significance. Moreover, the duration of surgery was notably longer in Group B (121.3 ± 13.1 minutes) compared to Group A (94.3 ± 11.3 minutes), with a p -value of <0.001. The mean intraoperative blood loss was significantly less in Group A (109.7 ± 7.3 mL) compared to Group B (154.3 ± 6.7 mL), with a p -value of 0.000. Moreover, the mean postoperative blood loss was similar in Group A (32.03 ± 10.4 mL) compared to Group B (35.7 ± 10.3 mL), with a p -value of 0.11. On Day 2, the mean blood loss was 19.1 ± 5.72 mL in Group A and 19.2 ± 5.82 mL in Group B (p =0.893), showing no significant difference. Similarly, on Day 3, the mean blood loss was 16.8 ± 5.93 mL in Group A and 15.2 ± 6.68 mL in Group B (p =0.269), with no statistical difference among study groups (Table 2).

but come at a higher cost. About 80 milliliters per 100 grams per minute is the rich blood supply to the thyroid gland, which increases in hyperthyroidism. Modern electrosurgical instruments reduce tissue reactivity, shorten the duration of the operation, and eliminate the need for sutures. The bipolar cautery, a common first-generation instrument for thyroidectomies, works with any standard electrosurgical unit that has a foot switch and monopolar cautery [17]. In the current study, the average age of patients was (35.5 ± 4.9 years), Group A had 70% female and 30% male, while Group B had 77.5% females and 22.5% males. The mean hospital duration was shorter in Group A (3.8 ± 1.2 days) compared to Group B (5.2 ± 2.3 days) (p -value<0.050). The comparison of intraoperative blood loss showed that Group A (109.7 ± 7.3mL) had less blood loss as compared to Group B (154.3 ± 6.7mL, p -value=<0.001).

However, the duration of surgery was notably longer in Group B (121.3 ± 13.1 minutes) compared to Group A (94.3 ± 11.3 minutes) (p -value <0.050). Bipolar cautery plays a crucial role in surgical procedures by significantly reducing blood loss, which improves the visibility of the surgical field. This enhanced clarity allows surgeons to work more effectively and accurately, making the procedure faster and more precise. By reducing or eliminating the need for conventional knot-tying techniques, bipolar cautery also contributes to better control of bleeding during surgery [18]. In research by Manouras et al. the efficacy of the bipolar vessel sealer and harmonic scalpel was compared to traditional methods. The findings showed a notable reduction in surgical time, with the advanced tools cutting the duration by approximately 20%. Specifically, surgeries using the bipolar vessel sealer or harmonic scalpel took 74.3 ± 14.2 and 73.8 ± 13.8 minutes, respectively, compared to 93.3 ± 12.5 minutes when the classic technique was employed. This reduction not only enhances procedural efficiency but also minimizes patient and surgical team strain [19]. These findings were also comparable to another study, which demonstrated notable differences in outcomes. Patients who underwent surgery with Liga Sure BDS had a significantly shorter postoperative hospital stay (2.3 ± 1.7 days) compared to those who had the conventional technique (2.8 ± 1.3 days), with a statistically significant difference ($p<0.050$). The results indicated that Liga Sure vessel sealer is an alternative, reducing the overall duration of surgery and being suitable for use through a narrow surgical incision [20]. However, another retrospective study comparing thyroid surgeries with traditional electric knives and bipolar electrocoagulation demonstrated that bipolar electrocoagulation reduced 50% of operation time and 80% of intraoperative bleeding, with no significant risk of complications [21]. A study was conducted to see the effectiveness of a bipolar electrosurgical device found that the bipolar vessel sealer reduced the surgical time. It also reduces the blood loss. It was demonstrated that these devices are time-efficient alternatives in low-resource settings [22]. Additionally, the study found that bipolar vessel sealer significantly reduces both total operation time and intraoperative bleeding compared to traditional methods. These results are consistent with existing literature, confirming that bipolar electrocoagulation allows for greater precision, reduces bleeding, and lowers the likelihood of complications [21, 23]. In the current study, it was demonstrated that the blood loss during the surgery was significantly less in Group A (109.7 ± 7.3 mL) compared to Group B (154.3 ± 6.7 mL). Moreover, the mean postoperative blood loss was similar in Group A (32.03 ± 10.4 mL) compared to Group B (35.7 ± 10.3 mL), which were comparable with literature, as the Electrothermal Bipolar Vessel Sealer (EBVS) offers significant advantages in thyroid surgery by reducing intraoperative and postoperative blood loss. It ensures precise hemostasis,

minimizing blood loss while protecting vital structures like the parathyroid glands and recurrent laryngeal nerve [24]. In another meta-analysis, it was found that EBVS reduced intraoperative blood loss by an average of 20.03 mL compared to conventional techniques [25]. Additionally, it shortens operative time, further enhancing surgical efficiency [15]. Postoperatively, EBVS promotes faster recovery by minimizing bleeding, enabling early drain removal, and reducing the risk of neck hematoma. This leads to shorter hospital stays, earlier discharge, and improved cost-effectiveness [19]. A meta-analysis confirmed that EBVS significantly lowers postoperative complications, reinforcing its value as a superior alternative to conventional methods [26]. Given these benefits, EBVS enhances both intraoperative safety and postoperative recovery, making it a preferred choice for thyroidectomy.

This study was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Additionally, cost-effectiveness analysis and long-term postoperative outcomes, including complications and recurrence rates, were not evaluated. Future multicenter studies with larger sample sizes and long-term follow-up should assess both clinical outcomes and cost-effectiveness of bipolar vessel sealing techniques.

CONCLUSIONS

It was concluded that the electrothermal bipolar vessel sealer is an effective hemostatic tool for total thyroidectomy in benign thyroid conditions. While it prolonged surgical duration, it significantly reduced intraoperative blood loss and hospital stay compared to the conventional clamp-and-tie technique. These benefits highlight its clinical value in enhancing recovery and reducing complications. The technique may be especially useful in resource-limited settings and for surgeons with varying experience, providing a sutureless, cost-effective option without increasing operative risks.

Authors' Contribution

Conceptualization: MI

Methodology: MI, AN, MTH, MR

Formal analysis: MTH, TJ, GB

Writing and Drafting: MI, MAJ, SA, SAZ

Review and Editing: MI, AN, MTU, TJ, GB, MR, MAJ, SA, SAZ

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Reliability of Mandibular Plane in Determining Gonial Angle on Lateral Cephalogram

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ABSTRACT

Gonial angle is an essential cephalometric indicator used in orthodontic diagnosis and treatment planning. The precise evaluation of the gonial angle is vital for understanding mandibular growth patterns and formulating efficient treatment strategies. **Objectives:** To assess the mean gonial angle according to the three mandibular planes, Tweed's, Steiner's, and Down's, on lateral Cephalogram and panoramic radiograph for Orthodontic Diagnosis and Treatment Planning. **Methods:** The Descriptive Cross-Sectional Survey was performed in the Orthodontics Department, Lahore Medical and Dental College (LMDC). Lateral Cephalogram and Ortho-pantomography (OPG) of 100 patients were used. The Gonial angle was assessed on the OPG by drawing a tangent to the lower border of the mandible and the most distal point of the ascending ramus and condyle. On the Lateral Cephalogram, however, the Gonial angle was measured by drawing a tangent to the posterior border of the ramus and making three mandibular planes according to Down, Tweed, and Steiner analysis. The Gonial angle assessed on the lateral Cephalogram was compared to that on OPG to evaluate which plane provides the gonial angle value closest to that obtained on OPG. All data were collected and recorded on a Performa. **Results:** The mean gonial angle on lateral Cephalogram was $123.06 \pm 6.80^\circ$, 121.5 ± 6.40 , and 123.77 ± 6.43 using Tweeds, Steiner's, and Downs mandibular planes, respectively, and on OPG, the mean gonial angle was 123.45 ± 6.89 . **Conclusions:** It was concluded that Down's mandibular plane provides the Gonial angle reading that is closest to that found on OPG.

INTRODUCTION

Radiographs play a crucial role in orthodontic diagnosis and treatment planning that ensures precise diagnosis, guides the development of personalized treatment plans, and monitors progress throughout orthodontic therapy. Understanding the importance of these diagnostic tools is key to achieving optimal outcomes in orthodontics. The two most commonly used radiographs in orthodontics are the Orthopantomogram (OPG) and lateral cephalogram [1]. Orthopantomography (OPG) is an important research and clinical tool for analyzing teeth, their axial inclinations, supporting bone levels, fractures, ankyloses, sinuses, and the shape of the condyles [1]. It provides the chance to evaluate the existence and non-existence of any pathology or the overall health of the surrounding teeth and oral tissues [2]. Absence superimposition of right and left side

structures with moderately reduced radiation exposure makes it a fundamental norm of care for Orthodontic diagnosis and treatment planning [3, 4]. A lateral cephalogram is another radiographic technique utilized for quantitative investigations and measurements [5]. Certain landmarks that can be anatomic or derived are used to assess the horizontal and vertical relationship of maxillary and mandibular dentition and their respective alveolar processes [6, 7]. The gonial angle is one of the main variables used to assess vertical growth patterns [8], mandibular steepness, mandibular asymmetry [9], and age determination in forensic medicine [10]. Patients with a downward and posterior rotation of the mandible tend to have an increased gonial angle, and these individuals are classified as having a "high-angle" profile. In contrast, the



angle is decreased in patients with forward and upward rotation and is termed "low angle" cases. The Gonial angle is formed at the convergance of mandibular and ramal plane. In the lateral Cephalogram, the Ramal plane is taken as a straight line at 90 degrees to the posterior aspect of the ramus. However, the mandibular plane can be defined in three different ways [3, 6], as proposed by various researchers: Tweed's method (using a tangent to the inferior margin of the mandible) [11], Steiner's method (drawing a line from Gonion to Gnathion) [12], and Down's method (drawing a line from Gonion to Menton) [13]. Irrespective of the method used for constructing the mandibular plane, Gonial angle measurement is questionable on lateral Cephalograms due to the overlapping of right and left sides [14]. However, the Gonial angle measurement on an OPG (Orthopantomogram) is relatively convenient as we can appreciate the right and left rami individually, avoiding any overlapping or superposing of anatomical landmarks that frequently occur in lateral cephalograms [15]. Several researchers have made the comparison between the two forms of radiographs for analyzing the Gonial angle [16]; some studies suggest that OPG is useful in providing a broad view of information on the dental and skeletal structures including the vertical aspect of craniofacial structure but it is less definitive for detailed and accurate analysis in comparison with lateral Cephalogram [13].

Although both OPG and lateral cephalogram are widely used for gonial angle assessment, inconsistency exists regarding which mandibular plane on cephalograms best correlates with OPG measurements. Additionally, limited evidence is available comparing different cephalometric methods with OPG for accurate and reliable gonial angle evaluation. This study aims to investigate which Mandibular plane intended for calculating the Gonial angle on the Lateral Cephalogram corresponds best with the Gonial angle evaluated on the OPG.

METHODS

A descriptive cross-sectional study was carried out from August 09 2021 to February 8, 2022, at Lahore Medical and Dental College. The study was approved by the ethical review board of Lahore Medical and Dental College (Reference number: LMDC/FD/ 2735/25). Before collecting pre-treatment radiographic records, patient consent was duly taken regarding the potential risks of radiation exposure. A non-probability, consecutive sampling technique was implemented to select 100 radiographs (lateral cephalograms and OPGs) [2] of 41 male and 59 female patients aged 13 to 29 years, from the Orthodontics Department at Lahore Medical and Dental College. The sample size was calculated by Open Epi software. One hundred radiographs are estimated using $\alpha=0.11$, 95% confidence level, and taking expected mean gonial angle as

125.3 ± 5.57 , 132.4 ± 5.74 , 128.37 ± 5.6 and 126.0 ± 7.13 on Steiner's, Tweed's, Downs and OPG, respectively [1]. The principal investigator thoroughly reviewed and verified all patients' clinical records. Radiographs from patients with a prior history of dento-facial surgery, disorders involving craniofacial structures, asymmetry, or a history of trauma were excluded. Lateral Cephalograms were taken while the teeth were in centric occlusion, using a Cephalostat. The x rays were acquired with the Villa Rotograph Evo D OPG system by Villa System Medical. The patients were exposed to a voltage range of 73kv-15ma to 84kv-13ma, following universal protocols while ensuring a natural head position. In the 100 chosen samples, the names were obscured on the radiographs. All lateral cephalometric radiographs were manually traced on acetate paper using a 3H pencil on a transilluminator. A geometrical protractor and a ruler were employed to determine the gonial angle. The gonial angle on the OPG was assessed by drawing a straight line to the base of the mandible and the most distal point of the condyle and ascending ramus [13] on both sides and then taking an average value of the two (Figure 1).



Figure 1: Gonial Angle Measurement on OPG

However, on Lateral Cephalogram, the Gonial angle was determined by depicting a straight line at a 90-degree angle to the posterior border of the ramus and drawing three mandibular planes according to Down [12], Tweed [11], and Steiner [17] analysis (Figure 2).

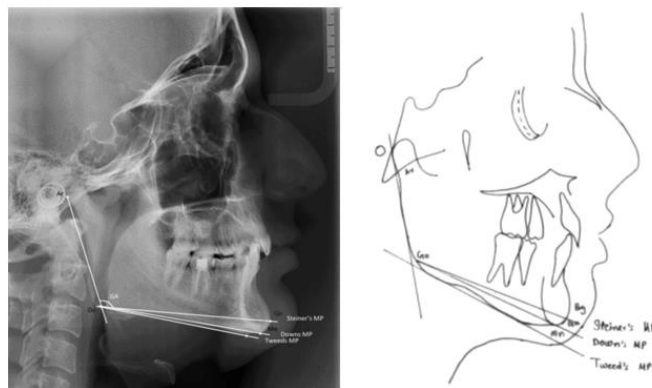


Figure 2: Gonial Angle Measurement on Lateral CEPH

All data were gathered and recorded on the Proforma. The mean and standard deviation (SD) were computed for the

Gonial angle measured on OPG and on lateral Cephalogram through Tweeds, Steiner, and Down's analysis. The statistical analysis was done utilizing SPSS software for Windows (IBM; SPSS, version 20.0). Numerical variables like age and gonial angle were calculated in terms of descriptive statistics. The mean gonial angle on lateral cephalogram using tweeds, steiners and the down mandibular plane and on OPG with standard deviations was calculated. The Kolmogorov-Smirnov and Shapiro-Wilk tests were applied to each variable (mean opg, Tweed, Steiner, and Down), which showed significant p-values ($p < 0.050$), indicating a significant deviation from normality. Non-parametric Spearman's rank correlation was used to measure the degree of correlation between three methods of gonial angle formation on cephalogram with the method on orthopantomogram.

RESULTS

A total of 100 individuals participated in the study, with 41 male and 59 female. The mean age of the individuals was 19.97 ± 4.23 years. Descriptive statistics of age and gender are presented (Table 1).

Table 1: Descriptive Statistics for Age and Gender

Variables	Minimum	Maximum	Mean $\pm$ SD
Age	13.00	29.00	19.97 ± 4.23
Gender Frequency (%)	Male	41%	—
	Female	59%	—

The mean of the gonial angle on lateral cephalogram using Tweeds, Steiner's, and Downs mandibular plane was $123.06 \pm 6.80^\circ$, $121.52^\circ \pm 6.40^\circ$ and $123.77^\circ \pm 6.43^\circ$, respectively. The mean value of the Gonial angle on Orthopantomogram among participants was $123.45^\circ \pm 6.89^\circ$ (Table 2).

Table 2: Descriptive Statistics of Gonial Angle on Lateral Cephalometric Radiograph and Orthopantomogram

Radiograph		Mean $\pm$ SD
Gender Frequency (%)	Tweed	$123.06 \pm 6.80^\circ$
	Steiner	$121.52^\circ \pm 6.40^\circ$
	Down's	$123.77^\circ \pm 6.43^\circ$
OPG	Mean OPG	$123.45^\circ \pm 6.89^\circ$

Spearman's rank correlation values for gonial angles on OPG and lateral cephalogram using the three different mandibular planes revealed a very strong positive correlation between mean OPG and Down's method ($p = 0.924$, $p < 0.001$) (Table 3).

Table 3: Spearman's Correlation Between Mean Gonial Angle On OPG and Lateral Cephalogram (Tweed, Steiner's and Down)

Comparison	Spearman's ρ	Sig. (2-tailed) p-value
Mean OPG vs. Down	0.924	0.000
Mean OPG vs. Tweed	0.685	0.000
Mean OPG vs. Steiner	0.285	0.004

**Correlation was significant at the 0.010 level (2-tailed).

*Correlation was significant at the 0.050 level (2-tailed)

DISCUSSION

Implant research on jaw rotations conducted by Bjork and coworkers in 1960 suggested that the rotation of the mandible during the growth period results in different vertical facial patterns, including normal, short, and long faces [1]. Gonial angle is one of the most significant cephalometric parameters indicating the facial skeleton's vertical growth pattern and symmetry [2]. The structure and form of the mandible are depicted by the gonial angle, and its numerical value suggests the mandibular growth direction. It also strongly affects the facial profile, lip seal and competence, and angulation of the lower incisors [8]. Moreover, re-evaluating the gonial angle after orthodontic treatment has been completed can provide important information about post-treatment results and stability [5]. Panoramic radiographs, when utilized in orthodontic practice, offer insightful information regarding the gonial angle and have the advantage of visualizing both the right and left angles without superimposition [9]. Upadhyay et al., [14], Hardin et al., [16] and Nadkerny et al., [9] examined the use of panoramic radiography for assessing the gonial angle, and the findings indicated that gonial angle measurements on panoramic radiographs are both accurate and consistent. However, the gonial angle on the lateral Cephalogram is assessed by convergence of a straight line 90 degrees to the Mandible's lower border and posterior ramus [18]. Because of the superimposition of structures in the lateral Cephalogram, it's sometimes hard to identify and determine the gonial angle. Lateral cephalograms provide a distorted view of the gonial angle, making it difficult to obtain accurate measurements for each angle, and are typically considered as a median angle between the right and left gonial angles [14]. The mandibular plane, used for analysing the gonial angle through lateral cephalometry, is horizontal, and three ways to assess the mandibular plane as described by different orthodontists are Tweed's, Steiner's and Down's. Due to the different mandibular planes (Tweed, Steiner's, and Down), there is significant variation in the gonial angle associated with each specific plane used [11]. This study evaluated which gonial angle (obtained from Tweed, Steiner, or Downs mandibular planes) on a lateral cephalogram had a value closest to that obtained on a panoramic radiograph. According to the results of our study, the Down's method showed a very strong positive correlation with the OPG measurement ($p = 0.924$, $p < 0.001$), followed by the Tweed method ($p = 0.685$, $p < 0.001$) and the Steiner method showed the weakest correlation ($p = 0.285$, $p = 0.004$). This concluded that the Down's mandibular plane provides the best correspondence with the gonial angle as measured on the OPG compared to the other two mandibular planes, Steiner's and Tweed's. Our study's result is in contrast with Bibi T's survey [15], which reported an important link between the cephalometric and panoramic values using Tweed's mandibular plane and the gonial angle is defined as

the intersection of two tangents: One tangent along the inferior border of the mandible and the other along the posterior ramus. The disparity in the results with our study could be because in Bibi T's survey, no other mandibular plane was assessed, and the results were based only on Tweed's mandibular plane. Another research carried out by Kundi I, also found a statistically significant mean gonial angle value, measured using the Tweeds mandibular plane on lateral Cephalogram compared with that on an OPG in Class I, Class II, and Class III patients [7]. The research concluded that both lateral cephalometric and panoramic radiographs are reliable methods for measuring the gonial angle in orthodontic patients. However, among the three mandibular planes assessed for determining gonial angles on lateral cephalograms, Tweed's mandibular plane relates better with OPG than Steiner's and Downs' planes. According to Natasha et al., Tweed, as it considers the straight line at 90 degrees to the lower margin of the mandible, is independent of the anatomic variation of the chin and hence corresponds accurately with the gonial angle obtained on the OPG [19]. However, as per our study results Downs mandibular plane is the most reliable one, and we assume that since it uses the menton, i-e the lowest point on the chin, it is least affected by the anatomical differences, and most of the chin variations are usually depicted at the pogonion. The difference in our results compared to the Thilagarani study might also be because they stratified different types of malocclusion and had a larger sample size. In contrast to our findings, several studies reported a major disparity in the measurement of the gonial angle by lateral cephalometric and panoramic radiographs. Adil et al., in their survey conducted in the hospital of 80 patients, outlined the gonial angle on radiographs (OPG and lateral Cephalogram) and found an important discrepancy in the measurement of the gonial angle between the two radiographs [15]. This may be because of the difference in malocclusions as our study incorporates all types of malocclusions, whereas only Class I malocclusion patients were included in Adil's study. Therefore, orthodontists should exercise caution when analyzing skeletal cephalometric variables from radiographs due to their lower predictability percentages. The difference in the outcomes from other studies could be due to the selection of various malocclusion types and the age of the patients. The differences in results could be due to our small sample size, and the precision and strength of our study would have been improved if this study had been conducted on a larger sample size [20].

This study had a relatively small sample size and included mixed malocclusion types, which may have influenced the variability and limited the generalizability of the findings. Additionally, inherent differences between radiographic techniques and potential measurement bias may have affected the accuracy of gonial angle assessment. Future studies with larger, stratified samples and standardized imaging protocols are recommended to validate the most

reliable method for gonial angle measurement.

CONCLUSIONS

It was concluded that the gonial angle serves as a crucial indicator for assessing facial growth patterns in patients. Both lateral cephalometric and panoramic X-rays are reliable methods for quantifying the gonial angle in orthodontic patients. The lateral cephalogram showed the mean value of the gonial angle as $123.06 \pm 6.80^\circ$, $121.5 \pm 6.40^\circ$, and $123.77 \pm 6.43^\circ$ using Tweeds, Steiner's, and Downs mandibular planes, respectively, while on OPG, the mean Gonial angle was 123.45 ± 6.89 . As per our study, Down's mandibular plane provides the value of the Gonial angle that is closest to that found on OPG.

Authors' Contribution

Conceptualization: MM

Methodology: MM, AS, AAS

Formal analysis: MM, AS, AAS

Writing and Drafting: MM, AS

Review and Editing: MM, AS, AAS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency of Diabetic Nephropathy among Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Diabetic Nephropathy (DN) is a predominant consequence of Type 2 Diabetes Mellitus (T2DM), contributing to chronic renal disease. **Objective:** To determine the frequency of diabetic nephropathy and its correlation with glycemic control. **Methods:** A cross-sectional study was conducted at the Nephrology and Diabetic OPD of Lahore General Hospital from July to November 2024. A total of 282 type 2 diabetic patients were enrolled. Clinical evaluation, fundoscopy, neurological examination, and laboratory tests were performed. Diabetic nephropathy was diagnosed based on albuminuria and eGFR. Statistical significance was set at $p < 0.050$. **Results:** Out of 282 patients, 150 (53.2%) were males and 132 (46.8%) females. The majority (43.3%) were aged 50-59 years. Microalbuminuria and macroalbuminuria were present in 20.9% and 32.3%, respectively. Mean serum creatinine and eGFR were 1.16 ± 0.53 mg/dL and 68.15 ± 24.58 mL/min/1.73m². Mean HbA1c and FBS levels were 8.40 ± 1.84 % and 137.03 ± 19.19 mg/dL. Hypertension was noted in 41.5%. Diabetic nephropathy was significantly more prevalent in those with FBS >140 mg/dL (29.1%) and HbA1c >7.5 % (32.6%) compared to those with lower values ($p < 0.050$). Declining eGFR was also significantly associated with nephropathy, with most cases found in those with eGFR <60 mL/min/1.73m² ($p < 0.001$). **Conclusion:** The study revealed a high frequency of diabetic nephropathy in type 2 diabetes, linked to poor glycemic control, declining eGFR and complications.

INTRODUCTION

Diabetic Nephropathy (DN) is the most common sequela of type 2 diabetes mellitus and a predominant cause of chronic renal disease and end-stage renal disease worldwide [1]. DN is defined by a rise in albumin excretion, a decrease in GFR or both. It impairs kidney function and changes the normal process of eliminating waste and extra fluid from the body (Neild, 2004). The global burden of DN continues to rise due to the increasing prevalence of T2DM, with approximately 30-40% of diabetic patients developing renal impairment over time [2]. T2DM patients are more prone to develop DN (40%) compared to Type 1 Diabetes Mellitus (T1DM) (30%) [3]. The pathophysiology of DN is multifactorial, involving hyperglycemia-induced

glomerular injury, oxidative stress, inflammation and endothelial dysfunction, leading to progressive albuminuria and dropping Glomerular Filtration Rate (GFR) [4]. Ali et al., in (2023) documented that hypertension, dyslipidemia and prolonged diabetes were strong determinants of DN, with smoking and obesity further worsening renal dysfunction [5]. Microalbuminuria, an early indicator of renal dysfunction, presents before nephropathy becomes evident and serves as a predictive factor for CKD progression. Consequently, early detection of albuminuria and estimation of GFR are essential for risk stratification and timely intervention to prevent renal deterioration [6, 7]. Alongside the global prevalence of DM,



the incidence of DN has been on the rise. According to risk assessment management program in China, the prevalence of CKD in 15856 diabetic patients was 38.8% [8]. Sana et al., in (2020) documented a DN prevalence of 30.1%, with 25.6% of T2DM patients demonstrating microalbuminuria and 4.5% progressing macroalbuminuria [9]. Similarly, Ullah et al., in (2024) noted that 54% of T2DM patients had DN, with 31% presenting microalbuminuria and 19% having macroalbuminuria [10]. According to the analysis of third national health and nutrition assessment survey, prevalence of DN in United States (US) population was observed to be 2.2% [11]. Diabetic kidney disease increases the mortality risk by 31.1% in Diabetic patients [12]. The American Diabetes Association (ADA) endorses once-a-year screening for albuminuria and eGFR assessments in diabetic patients to facilitate early detection and intervention [13]. Despite these guidelines, DN remains underdiagnosed in many regions, specifically in low- and middle-income areas, where resources are limited. This research aims to evaluate frequency of DN among patients with T2DM and assess its association with key clinical and biochemical parameters. These findings will contribute in the making of national health policies, counselling and treatment planning.

Despite established screening guidelines, diabetic nephropathy remains underdiagnosed in many low- and middle-income settings, including Pakistan. Moreover, limited local data exist on its frequency and association with clinical and biochemical parameters in T2DM patients. This study aims to determine the frequency of diabetic nephropathy among patients with type 2 diabetes mellitus and evaluate its association with key clinical and biochemical parameters.

METHODS

A cross-sectional study was executed at Lahore General Hospital, Lahore, in the Nephrology Department and the Diabetic Outpatient Department (OPD) from July to November 2024. Ethical approval for the study was obtained from the Institutional Review Board of Postgraduate Medical Institute/Ameer-ud-Din Medical College, Lahore General Hospital, Lahore (Approval Reference No. 00/168/2023), and informed consent was taken from all patients before enrollment. A non-probability consecutive sampling technique was utilized for participant enrollment. A sample size of 282 patients was calculated using the following formula, based on an expected prevalence of diabetic nephropathy of 24.2%, with a 95% confidence level ($Z = 1.96$), 5% margin of error ($d = 0.05$), population size of 1,000,000, and design effect (DEFF)=1 [14].

$$n = \frac{DEFF \times N \times p(1-p)}{[Z^2 \times (N-1) + p(1-p)]}$$

All patients diagnosed with T2DM aged over 18 years and

willing to participate were recruited in study after taking consent. Patients who had T1DM, obstructive uropathy, congestive heart failure, liver diseases, autoimmune diseases, neoplasm, UTI or taking medications that could affect insulin sensitivity such as corticosteroids and hormone replacement therapy were not enrolled in the study. Patients who were taking medications that affect kidney function or had experienced an acute kidney injury in the last 6 months were also excluded. A proforma was utilized to gather demographic, clinical and laboratory data, including age, sex, body mass index, duration of DM, history of HTN, ischemic heart disease and medication use such as oral hypoglycemic drugs, insulin, antihypertensives, and lipid-lowering agents. All the patients were examined for other microvascular complication of diabetes e.g., diabetic retinopathy and neuropathy with fundoscopy and nervous system examination respectively. BP was quantified by standardized sphygmomanometer after five minutes of rest, with two readings 3–4 min apart taken and averaged. After an overnight fasting of at least eight to ten hours blood samples were gathered to evaluate fasting blood sugar using an automated chemistry analyzer, glycosylated haemoglobin (HbA1c) by high-performance liquid chromatography, a gold-standard method approved by the National Glycohemoglobin Standardization Program (NGSP) and serum creatinine was measured using the Jaffe kinetic method, a widely accepted, cost-effective, and reproducible photometric technique based on creatinine's reaction with alkaline picrate [15, 16]. A mid-stream urine sample was obtained to evaluate urinary albumin-to-creatinine ratio using an automated immunoturbidimetric assay, with albuminuria grouped as normal (<30 mg/g), microalbuminuria (30–299 mg/g) or macroalbuminuria (≥ 300 mg/g). Immediately, urine samples were stored at 2–4°C. To stop bacterial overgrowth, sodium azide (0.02%) was added to the urine sample [17]. All samples before the assay were mixed well. Estimated glomerular filtration rate (eGFR) was measured using the CKD-EPI formula and patients were categorized into CKD stages ranging from stage 1 to stage 5 [18]. Diabetic nephropathy was characterized as a decline in eGFR <60 mL/min/1.73 m², prolonged macroalbuminuria confirmed on at least two occasions three to six months apart, provided that other causes of CKD are ruled out. Secondary outcomes included associations between diabetic nephropathy and glycemic control (HbA1c levels), blood pressure status and diabetes duration. Statistical analysis was performed using IBM SPSS Statistics, Version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were demonstrated in the form of frequency and percentages and descriptive variables were mentioned as mean and standard deviation. The Chi-Square test was employed to examine associations between categorical variables such as age group, gender, glycemic control (HbA1c and FBS levels), eGFR categories, and albuminuria stages. A confidence level of 95% was

used for all statistical analyses. Results were considered statistically significant at a p -value ≤ 0.05 .

RESULTS

The study included 282 patients diagnosed with T2DM. The average age of study participants was 56.39 ± 9.89 years. The mean body mass index and duration of DM were 29.59 ± 5.20 kg/m² and 8.02 ± 4.57 years respectively. The mean Fasting Blood Sugar (FBS) level was 137.03 ± 19.19 mg/dL. The average serum creatinine level was 1.16 ± 0.53 mg/dL and the mean eGFR was 68.15 ± 24.58 mL/min/1.73m². The mean glycated hemoglobin (HbA1c) level was $8.40 \pm 1.84\%$. The most of patients was categorized under 50-59 years age group (43.26%), followed by the 40-49 years group (21.99%), with a male predominance of 53.19%. Overweight and obesity (BMI ≥ 25 kg/m²) were prevalent, with 32.62% overweight and 44.68% obese. Renal function assessment revealed that 53.19% of patients had albuminuria, with 20.92% having microalbuminuria and 32.27% having macroalbuminuria. A drop in renal function was noted, with 43.61% of patients having an eGFR < 60 . Glycemic control was suboptimal, with 66.31% of patients having HbA1c $> 7.5\%$. The prevalence of diabetic complications was notable, with 51.06% having retinopathy and 62.77% having neuropathy. Poor fasting glucose control (> 140 mg/dL) was observed in 40.07%, and 41.49% of patients had hypertension. For further details see table 1.

Table 1: Baseline Characteristics of Study Patients

Variables	Mean $\pm$ SD
Age Groups (Years)	
30-39	10 (3.55)
40-49	62 (21.99)
50-59	122 (43.26)
60-69	45 (15.96)
≥ 70	43 (15.25)
BMI (kg/m²)	
18-24	64 (22.70)
25-30	92 (32.62)
31-35	84 (29.79)
≥ 36	42 (14.89)
Gender	
Male	150 (53.19)
Female	132 (46.81)
Urinary Albumin to Creatinine Ratio (UACR)	
< 30 mg/g	132 (46.81)
30-299 mg/g	59 (20.92)
≥ 300 mg/g	91 (32.27)
Estimated Glomerular Filtration Rate (eGFR) (mL/min/1.73m²)	
G1 (≥ 90)	94 (33.33)
G2 (60-89)	65 (23.05)
G3a (45-59)	52 (18.44)
G3b (30-44)	55 (19.50)
G4 (15-29)	16 (5.67)
Glycated Hemoglobin (HbA1c)	
$\leq 7.5\%$	95 (33.69)

$> 7.5\%$	187 (66.31)
Retinopathy	
Yes	144 (51.06)
No	138 (48.94)
Neuropathy	
Yes	177 (62.77)
No	105 (37.23)
Fasting Blood Sugar (FBS, mg/dL)	
≤ 140	169 (59.93)
> 140	113 (40.07)
Hypertension (HTN, mmHg)	
Yes	117 (41.49)
No	165 (58.51)

Nephropathy was diagnosed in 42.60% of patients (Figure 1).

Diabetic Nephropathy

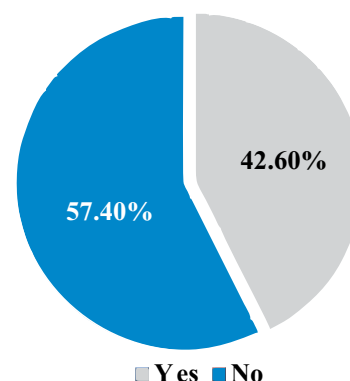


Figure 1: Frequency of Diabetic nephropathy in studied Cohort (n=282)

A statistically significant association was found between eGFR stages and albuminuria levels ($\chi^2 = 276.48$, $p < 0.001$), with worsening eGFR showing higher proportions of macroalbuminuria. Among patients with eGFR ≥ 90 (G1), 71.21% had normal UACR, while no cases of microalbuminuria or macroalbuminuria were found. In contrast, in eGFR 60-89 (G2), 44.38% had albuminuria and in eGFR 45-59 (G3a), 72.23% had albuminuria. UACR abnormalities became more pronounced in eGFR 30-44 (G3b), where 65.80% had macroalbuminuria and in eGFR 15-29 (G4), where all patients had macroalbuminuria (Table 2). The Pearson Chi-Square test was used to assess the association between eGFR categories and UACR levels. The p -value obtained was ≤ 0.05 , indicating a statistically significant relationship ($p \leq 0.05$). The percentages within each cell represent the proportion within each UACR classification. Nephropathy was significantly associated with age ($*p = 0.018$), with the highest prevalence in 50-59 years group (52.50%), while gender showed no significant correlation ($p = 0.967$). Poor glycemic control was strongly linked to nephropathy, with HbA1c $> 7.5\%$ (76.70%, $*p = 0.002$) and fasting blood sugar > 140 mg/dL (68.30%, $*p < 0.001$) being major risk factors. Diabetic complications were significantly associated, as 72.50% of nephropathy cases had retinopathy ($*p < 0.001$) and 75.01% had neuropathy ($*p < 0.001$).

Table 2: Association Between eGFR Categories and Urinary Albumin-to-Creatinine Ratio(UACR) Levels(n=282)

CKD Stages		Albuminuria			Total Frequency (%)	p-Value
eGFR (mL/min/1.73m ²)		< 30 Frequency (%)	30-299 Frequency (%)	30-299 Frequency (%)		
	Stage 1	94 (71.21)	0 (0.00)	0 (0.00)	94 (33.33)	<0.001*
	Stage 2	36 (27.27)	21 (35.59)	8 (8.79)	65 (23.05)	
	Stage 3a	2 (1.52)	29 (49.15)	21 (23.08)	52 (18.44)	
	Stage 3b	0 (0.00)	9 (15.25)	46 (50.55)	55 (19.50)	
	Stage 4	0 (0.00)	0 (0.00)	16 (17.58)	16 (5.67)	

DISCUSSION

This study assessed the frequency and baseline characteristics of diabetic nephropathy in type 2 DM patients. The mean age of participants in present researchs was 56.39 ± 9.89 years, which is parallel with studies conducted by Jeerasuwannakul et al., in (2021) (56.36 ± 13.88 years) and Wan et al., in (2024) (mean age 61.4 years) [19, 20]. Age was significantly associated with nephropathy ($p=0.018$), with highest prevalence seen in the 50-59 years age group (52.5%). This observation is parallel with studies by Merid et al., in (2024) and Farah et al., in (2021) which reported a significant correlation between older age and nephropathy progression [21, 22]. The mean BMI in this study was 29.59 ± 5.20 kg/m², with overweight and obesity present in 32.6% and 44.7% of patients, respectively. This consistent with the findings of Farah et al., in (2021), where 66% of patients had BMI >30 kg/m², and Ali et al., in (2023), who reported obesity in 51.4% of nephropathy patients [5, 22]. Obesity is a well-established risk factor for nephropathy, contributing to glomerular hyperfiltration and renal injury. HTN was noted in 41.5% of patients, comparable to Elhefnawy and Elsayed., in (2019) (28.5%) and Aboelnasr et al., in (2020) (48.4%) [23, 24]. The significant correlation between systolic blood pressure and nephropathy progression has been observed in many studies, including Hussain et al., in (2021), which recorded an odds ratio of 1.67 for nephropathy in hypertensive patients and Merid et al., in (2024), where hypertension significantly decreased survival in nephropathy patients ($p < 0.001$) [21, 25]. The correlation between eGFR decline and albuminuria was significant ($p < 0.001$), validating previous findings from Kebede et al., in (2021), where progressive eGFR decline was a measure of nephropathy [26]. Glycemic control was an important predictor of nephropathy in this study, with HbA1c >7.5% noted in 66.3% of patients and significantly correlated with nephropathy ($p=0.002$). This finding is parallel with Jeerasuwannakul et al., in (2021), which observed a mean HbA1c of $8.57 \pm 2.31\%$ in proteinuric patients and Wan et al., in (2024), where HbA1c >8% was correlated with high risk of CKD (OR 1.29, 95% CI 1.24-1.34) [19, 20]. Analogously, Ali et al., in (2023) noted that 100% of nephropathy patients had HbA1c >7%, compared to 40.5% in non-nephropathy patients ($p < 0.05$) [5]. Renal function assessment showed that 42.6% of patients had nephropathy, with microalbuminuria in 20.9% and

macroalbuminuria in 32.3%. These results match those reported by Ullah et al., in (2024), where nephropathy was noted in 54% of patients (31% microalbuminuria and 19% macroalbuminuria) and Elhefnawy and Elsayed, in (2019), which recorded microalbuminuria in 31.8% and macroalbuminuria in 7.9% of patients [10, 23]. Prevalence of albuminuria was similar to that documented by Wan et al., (2024), where 48.1% of T2DM patients had albuminuria and Farah et al., in (2021), where 44.7% of patients had albuminuria, indicating significant renal involvement [20, 22]. The mean eGFR in this research was 68.15 ± 24.58 mL/min/1.73m², with 43.6% of patients having eGFR <60, reflecting dropping renal function. This matches well with Wan et al., in (2024), where 22.4% of T2DM patients had eGFR <60 and Farah et al., in (2021), where 19.17% had CKD with eGFR <60 [20, 22]. Similarly, Ali et al., in (2023) documented that nephropathy patients had lower eGFR than those without nephropathy [5]. This study showed a clear trend of increasing albuminuria with declining eGFR, with all patients in the G4 eGFR category demonstrating macroalbuminuria (>300 mg/g) [15]. This trend corresponds with findings from Fenta et al., in (2023), which observed albuminuria as a strong predictor of CKD and Hussain et al., in (2021), which highlighted albuminuria as early indicator of diabetic nephropathy [25, 27]. These results emphasize the need for routine renal function assessment, particularly albuminuria and eGFR monitoring, to detect nephropathy early and slow CKD progression. Diabetic complications such as retinopathy and neuropathy were associated with nephropathy ($p < 0.001$). Retinopathy was noted in 51.1% of patients, in consistent with Farah et al., in (2021), which documented retinopathy in 34.12% of diabetic nephropathy patients and Wan et al., in (2024), which reorted an OR of 1.19 (95% CI 1.13-1.26) for retinopathy forecasting CKD [20, 22]. Similarly, neuropathy was found in 62.8% of patients, with a significant correlation with nephropathy, consistent with findings from Merid et al., in (2024), where diabetic neuropathy significantly reduced survival probability ($p=0.039$) [21]. Fasting blood sugar was significantly correlated with nephropathy ($p < 0.001$), with 68.3% of patients having FBS >140 mg/dL. This is supported by Jeerasuwannakul et al., in (2021), which found an independent association between fasting plasma glucose and proteinuria (aOR 1.009, $p < 0.050$) [19]. Similarly,

Ali et al., in (2023) reported that 64.8% of nephropathy patients had fasting blood sugar >200 mg/dL, compared to 29.7% in non-nephropathy patients [5]. This research provides valuable insights into the frequency of diabetic nephropathy among T2DM patients, utilizing a comprehensive analysis of renal function parameters, glycemic control, and associated microvascular complications. The strengths include a well-defined study population, standardized diagnostic criteria and robust statistical analysis. However, limitations include its cross-sectional design, which limits causality assessment and single-center data, reducing generalizability.

The strengths include a well-defined study population, standardized diagnostic criteria and robust statistical analysis. However, limitations include its cross-sectional design, which limits causality assessment and single-center data, reducing generalizability. Future researches should embed longitudinal follow-ups, multicenter studies and interventional strategies to assess nephropathy progression and evaluate targeted preventive measures for high-risk diabetic populations.

CONCLUSIONS

This study demonstrated a high frequency of diabetic nephropathy among patients with type 2 diabetes mellitus. Significant associations were observed between nephropathy and indicators of poor glycemic control, including elevated fasting blood sugar and HbA1c levels. Furthermore, nephropathy was more frequently noted in patients with coexisting microvascular complications such as retinopathy and neuropathy. Declining eGFR corresponded with increasing albuminuria, indicating progressive renal impairment. These findings emphasize the importance of early detection and routine monitoring to mitigate disease progression.

Authors' Contribution

Conceptualization: MIJ

Methodology: YH, AS, AA, IN

Formal analysis: MIJ, MSNK, AS, AI, AA, IN

Writing and Drafting: MIJ, YH, MSNK, AS, AI, AA, IN

Review and Editing: MIJ, YH, MSNK, AS, AI, AA, IN

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Identification of Genetic Polymorphism of Centrosomal Protein 290 to Assess Its Role as A Novel Diagnostic and Prognostic Biomarker for Ovarian Cancer

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ABSTRACT

Ovarian cancer (OC) is one of the most lethal gynecological malignancies, with the dilemma of diagnosing at an advanced stage due to the lack of sensitive early detection markers. Centrosomal protein 290 (CEP290) is important for various functions within cellular processes, and its genetic changes may contribute to tumor development and progression. Identifying polymorphisms in the CEP290 gene could provide valuable insights into its potential as a novel diagnostic and prognostic biomarker for OC. **Objective:** To identify genetic polymorphism of CEP 290 in ovarian cancer and to determine its role as a novel prognostic and diagnostic biomarker for OC. **Methods:** A genetic profiling methodology was utilized to detect single-nucleotide polymorphisms (SNPs) within the CEP290 gene in patients diagnosed with ovarian cancer. Techniques such as polymerase chain reaction (PCR) and DNA sequencing were implemented to ascertain these genetic variations, followed by statistical analysis to evaluate their association with disease susceptibility and prognosis. **Results:** Two potential SNPs, CXCR2 C+785T and VEGF C+936T, were identified in the CEP290 gene. These polymorphisms may be linked to ovarian cancer pathogenesis, influencing tumor growth, angiogenesis, and immune response mechanisms. **Conclusions:** It was concluded that this study highlights CXCR2 C+785T and VEGF C+936T as potential SNPs within the CEP290 gene, suggesting their role in ovarian cancer diagnosis and prognosis. Further research with larger cohorts is necessary to validate these findings and discover their clinical utility as predictive biomarkers.

INTRODUCTION

Ovarian cancer, often referred to as a silent killer, ranks as the fifth most prevalent cancer among women globally. In Pakistan, it is classified among the top three most common malignancies affecting females, with a rising incidence rate [1]. The challenge posed by OC lies in its detection, as over 70% of ovarian cancer cases are identified at their later stages, leading to a high mortality rate. This underscores the urgent necessity for specific biomarkers to facilitate early and accurate diagnosis. CA-125, though currently accepted and widely used serum biomarker, it is

nonspecific in advanced stages and neither sensitive nor specific in early-stage OC diagnosis [2]. In our previous study, by employing 2-DE and Matrix Assisted Laser Desorption Ionization-Time of Flight (MALDI-TOF) Mass spectrometry, comparison of proteomic maps and profiles of differential proteins of human OC and healthy ovarian tissues was conducted to explore the potential proteomic biomarker of OC [3]. In this regard, an upregulated expression of a novel protein, Centrosomal protein of 290 kDa (CEP290), was identified and validated by ELISA as a



potential candidate biomarker for early diagnosis of OC. This protein is involved as an integral part of the centrosome and cilia and cellular signal transduction, but its genetic role in OC was not elucidated before. It has been shown that CEP290 controls the molecular maintenance of the primary cilium and results in various multi-organ disorders known as ciliopathies (like Leber congenital amaurosis and Joubert syndrome), if a mutation occurs via disruption of key cellular processes. Moreover, the genetic mutations related to renal and retinal diseases have been linked to the presence of antibodies targeting this protein, showing an association with different types of cancer. While CEP290 mutations have been implicated in various ciliopathies, their role in tumorigenesis, including ovarian cancer, remains underexplored [4]. Centrosomes and centrioles play a role in cell polarity, migration, proliferation, signalling in cell transition phases and in all processes which may affect tumorigenesis. Since cancer is a condition where unchecked cell proliferation occurs [5, 6]. So, CEP290 may have a crucial involvement in the unregulated growth of cells, which can lead to the onset of cancer. Previous studies determined its role in pancreatic ductal adenocarcinoma by suppression of ciliogenesis for centrosome amplification in cancer [7]. It was also suggested that genome instability and centrosomal alterations are significant characteristics in developing cancer. Moreover, it was proposed that the amplification of centrosomes has been identified as a potential initiator of cancer. Following this groundbreaking study, centrosomal proteins have once more garnered significant interest in the context of carcinogenesis. Single-nucleotide polymorphisms (SNPs) are germline genetic variations present from birth and detectable before the onset of malignancy. Identifying SNPs associated with elevated CEP290 expression can genetically validate proteomic observations, thereby reinforcing the biological significance of CEP290 as a biomarker in ovarian cancer. This genotype-phenotype correlation supports its involvement in tumorigenesis and its potential utility in early detection and prognostication. Protein markers that reflect dynamic tumor states, SNPs are stable and constitutive throughout life, rendering them ideal for assessing cancer susceptibility in asymptomatic individuals [8]. Currently, there is no specific and sensitive marker which can detect OC at the preliminary stage to reduce the high mortality and morbidity associated with this disease. CEP290 will be used as a minimally invasive novel biomarker for early diagnosis in OC. This tool can serve as an effective screening method for the early detection of OC in high-risk populations, particularly those with a positive family history of breast and ovarian cancer. Early and prompt disease diagnosis leads to the development of more targeted diagnostic tests, better

prognosis and ultimately a healthy outcome by decreasing mortality and morbidity of OC patients. Early detection of this deadly disease will be highly beneficial in reducing the financial burden of chemotherapy on individuals and the government, which is otherwise given in the advanced stages only. Keeping in view the unexplored genetic role of CEP290 in OC, the present study is a continuation of the previous study to identify the genetic mutation of CEP290 in OC predisposition and its further validation as a potential novel biomarker for early diagnosis and prognosis of OC [3]. Despite identification of CEP290 as a potential proteomic biomarker in ovarian cancer, its underlying genetic polymorphisms and role in tumor predisposition remain largely unexplored. Furthermore, there is a lack of validated genetic evidence supporting CEP290 as an early diagnostic and prognostic marker for ovarian cancer. This study aims to identify genetic polymorphism of CEP 290 in ovarian cancer and to determine its role as a novel prognostic and diagnostic biomarker for OC.

METHODS

This study was carried out for one year, starting from 23 March 2023 to 23 March 2024, following the approval from the institutional Ethical Review Board (Case# 999/ERC/CMH/LMC). Ovarian tissue samples (n=40), including both malignant and healthy, were collected by using a purposive sampling technique, after getting their informed consent and recording of all demographic data on a predesigned proforma. Similarly, the study population was divided into two distinct groups, with Group 1 comprising patients who had been diagnosed with ovarian cancer, aged between 40 and 65 years. Group 2 included women within the same age range who were scheduled to undergo a hysterectomy accompanied by bilateral salpingo-oophorectomy for indications other than OC. The sample size was calculated by the World Health Organization (WHO) calculator using the following formula: $n = 2\sigma^2 (z_{1-\alpha/2} + z_{1-\beta})^2 (\mu_1 - \mu_2)^2$. Where: μ_1 is the anticipated mean in the population, μ_2 is the anticipated mean in cases, $1-\beta$ is the desired power of the study = 90 %, $1-\alpha/2$ was the desired level of significance = 1.96 41, and n is the calculated sample size. Therefore, sample size is calculated by taking the difference between 2 means of expressed proteins in each group (control and ovarian cancer). Population standard deviation = 6.5. Population variance = 42.25. Difference between the two population means = 6.9. Sample size (n) = 20 for each group. The histopathological analysis for each malignant ovarian tissue sample had been compiled, confirming the cancer staging and the presence of 80-90% cancer cells within the resected tissues. Similarly, the analysis for each healthy ovarian tissue sample confirmed the absence of tumor cells. DNA was extracted from ovarian tissues for each of the 40 patients (malignant & healthy). Samples were thawed on ice before extraction to prevent DNA

degradation. Tissue lysis was done by mincing approximately 20-30 mg of tissue and homogenized manually in a sterile mortar and pestle to increase surface area for efficient lysis. Transferred the homogenized tissue to a micro-centrifuge tube and added 300 µL of tissue lysis buffer. Proteinase K (20 mg/ml) was added to the sample to aid in protein digestion, followed by RNA removal. Added 150 µL of protein precipitation solution to the lysate after cooling the lysate and mixing, as it clears digested RNA fragments and proteins together, leaving behind purer DNA. Centrifuged at 12,000 x g for 10 minutes at 4°C and transferred the clear supernatant to a new tube, avoiding the protein pellet. For DNA precipitation, added 500 µL of cold isopropanol was added to the supernatant, and the tube was gently centrifuged 5-10 times until DNA appeared as visible threads, leaving the DNA pellet intact. Finally, the DNA pellet was re-suspended in 30-50 µL of nuclease-free water to protect the DNA from degradation. DNA concentration was quantified by using a spectrophotometer (260/280 nm) to confirm adequate yield and purity for PCR. Following extraction, all DNA samples were stored at -20°C. The quality and concentration of the DNA were assessed using photometric methods, with an optical density ratio (OD260/OD280). Nucleotide sequence of the CEP290 gene (GenBank accession no DQ109808.1) was retrieved from the

NCBI database. Primers of the CEP290 genes were designed using Primer 3 software. Properties of primers such as melting temperature, GC content, and self-complementarity were checked by using Oligo-Calculator software. The sequence of primers is given in the table below. Primer Name Sequence Length(bp). Forward primer 5' ATG CCA CCT AAT ATA AAC TGG AAA 3' 24 bp. Reverse primer 5' TTA ACA GGA CTT TCT TCT TCA TCT TCA 3' 27bp. The PCR tubes were placed on a 96-well plate. Allowing 0.2 ml of cold water to be added with PCR reagents. In a PCR tube, pipette the PCR reagents like MgCl₂, primers, template DNA, sterile water, 10xPCR buffer, master mix and dNTPs. On completion of the procedure, the tubes were taken out, followed by loading of aliquots into the wells of an agarose gel, and after electrophoresis, DNA that had migrated into the gel was stained with ethidium bromide, enabling bands to be seen using a UV illuminator. PCR was conducted by using 20 µM of primers, and the amplification was carried out under specific thermal cycling parameters. An initial denaturation step was followed by denaturation, annealing and extension. The PCR products were then analyzed by electrophoresis on a 1.0% agarose gel, with visualization performed under UV light. The resulting gels were documented using a UV gel imaging system. This was followed by DNA sequencing to identify any single-nucleotide polymorphism related to the CEP 290 gene.

RESULTS

DNA sequencing revealed two potential single-nucleotide polymorphisms, i.e. CXCR2 C+785T, VEGF C+936T (Table 1).

Table 1: Ovarian Cancer Polymorphism

Gene	Properties	Location of Polymorphism	Role in OC
VEGF	Blood and Lymphatic Vessel Regulation and Control	5'UTR C+405G/C-634G3'UTR C+936T	Over-expresses and potential role in the facilitation the progression of OC
CXCR2 C+785T	Facilitates Angiogenic Potential of IL-8	C+785T	Strong expression in OC cells was found

Whereas the association of identified SNPs with developing ovarian cancer risk was found to be statistically significant (Table 2).

Table 2: Association of SNPs with Ovarian Cancer Risk

SNP	Allele	Ovarian Cancer (n=20)	Control (n=20)	OR (95% CI)	χ ²	p-value
CXCR2 C+785T	T	18	8	3.27 (1.21-8.84)	4.615	0.031*
	C	22	32			
VEGF C+936T	T	15	5	4.20 (1.35-13.06)	5.400	0.020*
	C	25	35			

OR: Odds Ratio; CI: Confidence Interval. *Statistical significance considered at p<0.050. χ²: Chi-square test for allele frequency differences between groups

The PCR products were then analyzed by electrophoresis on a 1.0% agarose gel, with visualization performed under UV light. The resulting gels were documented using a UV gel imaging system (Figure 1).

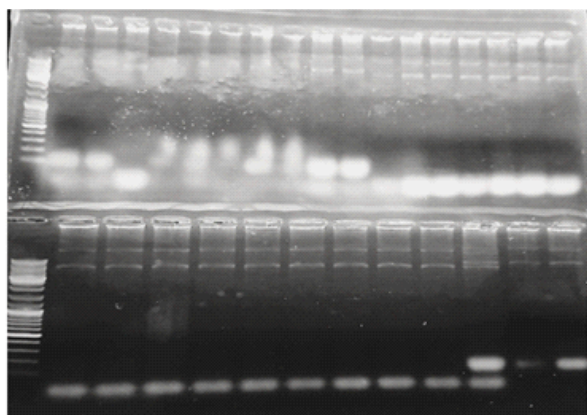


Figure 1: 1% Agarose Gel Electrophoresis Showing Isolated DNA in Healthy and Ovarian Cancer Groups

DISCUSSION

Ovarian cancer has one of the worst stages among gynecologic oncological diseases, owing to the stage of diagnosis and life expectancy after treatment [9]. There is an urgent need for reliable prognosis and diagnostic biomarkers to enhance detection as well as the overall outcomes for patients. CEP290, a critical player in centrosomal and ciliary function, has emerged as a candidate for genetic polymorphism studies in cancer. As a result, it was found that CXCR2 C+785T and VEGF C+936T SNPs were found, which are putative markers for disease susceptibility and progression [10]. A few studies have pointed towards the relevance of CEP290 with cellular maintenance and the consequences of its mutations in some disease conditions like ciliopathies and cancers. The presence of the CXCR2 C+785T SNP in our study corroborates the previous work of some researchers who indicated that it is involved in inflammation and tumorigenesis. High-grade serous ovarian carcinomas with CXCR2 overexpression are poor prognostic factors for early disease recurrence. It has been reported that CXCR2 markedly facilitated cell cycle advancement by influencing several regulatory proteins of the cell cycle [11]. It promotes apoptosis along with elevating p53 phosphorylation and stimulating multiple pro-angiogenic factors, which may collectively explain the enhanced cell death. This phenomenon is likely brought about by increased p53 phosphorylation and elevated stimuli of pro-apoptotic factors like Puma and Bcl-xs, plus weakened anti-apoptotic factors Bcl-xl and Bcl-2. These observations suggest that CXCR2 enhances the mitotic activity of cells by influencing several proteins which control the cell cycle, including D1 cyclin and its enzyme, CDK-6. If CXCR2 is inhibited in xenograft tumor tissues from ovarian cancer models, there is a decrease in the overall density of vascular structures in addition to increased quantities of VEGF and diminished TSP-1. This evidence serves to underline a role for CXCR2 in angiogenesis in ovarian tumor

[12]. Research has suggested that the activation of these pathways could be significant in the CXCR2 signalling network among various cell types [13, 14]. VEGF plays a significant part in the development of blood and lymphatic vessels. In a nonmalignant state, it is mainly synthesized by endothelial, hematopoietic, and stromal cells when there is a lack of oxygen or are stimulated by some growth factors like TGF, interleukin, and PDGF. The isoform VEGF165, for instance, is a prominent mediator of angiogenesis in the tumors, enhancing growth, invasiveness, and metastatic spread of the tumors [15]. In solid and hematological cancers, the expression of VEGF in cancer cells relates directly to tumor tissue quantity, metastases, and negative prognostic factors [16]. Likewise, the C+936T polymorphism in VEGF was suggested to modify the angiogenic potential and, therefore, have an impact on the tumors' microenvironment and progression. These polymorphisms overall are predisposed to ovarian cancer by altering pathways of cell proliferation, migration, and angiogenesis [17]. On the contrary, some studies could not find an explicit link between these SNPs and their subsequent risk of ovarian cancer. For example, one study found a large cohort study with no significant correlation between susceptibility to ovarian cancer and the polymorphisms of VEGF C+936 T. Similarly, there have been studies with CXCR2 polymorphisms in various ethnic groups, which cannot consistently support the existence of a genetic risk for ovarian cancer. Such differences could stem from the combination of environmental, genetic diversity, and changes in sample sizes [17-19]. Current results imply that CEP290 polymorphisms, along with CXCR2 and VEGF variations, may function as potential biomarkers for ovarian cancer [20]. To clarify the molecular involvement of these SNPs in the pathophysiology of ovarian cancer and their therapeutic value in risk stratification and individualized therapy, further extensive, multi-ethnic investigations with functional validation are required. Comprehending the genetic terrain of ovarian cancer will aid in the creation of focused therapies, ultimately enhancing therapy results and patient prognosis.

The study is limited by a relatively small sample size and lack of functional validation of the identified polymorphisms, which restricts the ability to establish a direct mechanistic link. Additionally, the single-population design may limit the generalizability of the findings across different ethnic groups. Future research should include larger, multi-ethnic cohorts with functional and molecular studies to validate the role of CEP290, CXCR2, and VEGF polymorphisms in ovarian cancer. Prospective studies are also needed to assess their potential as reliable diagnostic and prognostic biomarkers.

CONCLUSIONS

It was concluded that this study explores two single-nucleotide polymorphisms, CXCR2 C+785T and VEGF C+936T, in association with CEP290, to evaluate their potential as prognostic and diagnostic biomarkers for ovarian cancer. This helps uncover the underlying molecular mechanisms of OC progression and the identification of CEP290 mutations linked to therapeutic resistance. This could also support the development of targeted therapies and improve early diagnosis, treatment outcomes, and overall survival, while reducing healthcare costs.

Authors' Contribution

Conceptualization: AT

Methodology: AT, SB

Formal analysis: ZA, UZ

Writing and Drafting: AT

Review and Editing: AT, SB, ZA, UZ

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Role of Foley's Catheter as Intra-Uterine Balloon Tamponade in Controlling Primary Post-Partum Hemorrhage after Vaginal Delivery

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ABSTRACT

One of the leading causes of maternal morbidity and mortality is primary post-partum hemorrhage (PPH). The utilization of intrauterine balloon tamponade has drastically reduced this deadly complication. In low-resource areas, the balloon of a 24-French Foley catheter is used for the same purpose. **Objectives:** To determine the safety and success rate of 24 Fr Foley's catheter as intra-uterine balloon tamponade in controlling Primary Post-Partum Hemorrhage after vaginal delivery. To determine the amount of bleeding at 15 and 30 minutes after the Foleys insertion to predict failure. **Methods:** This cross-sectional study included 140 consecutive women with PPH after failed medical treatment. A 24-French Foley catheter was placed in the uterine cavity, and the balloon was filled with 100 ml of normal saline. Bleeding was observed for the next 15 and 30 minutes. **Results:** The Foley Balloon tamponade was successful in controlling hemorrhage in 125 (89.2%) patients. While 15 (9.8%) patients had failed balloon tamponade. Patients with failed balloon tamponade had a higher rate of anemia, coagulopathy, and more bleeding after delivery, after 15 minutes, and after 30 minutes of Foley balloon placement. The positive predictive value for 150 ml and 200 ml was 0.60 and 0.80, respectively. **Conclusions:** It was concluded that the 24 Fr Foley is effective in controlling primary post-partum hemorrhage. A blood loss of ≥ 200 ml after 15 minutes of Foley balloon placement should alert the physician to adopt a more aggressive approach to control bleeding.

INTRODUCTION

One of the most dangerous obstetric complications is postpartum hemorrhage (PPH). Globally, it is among the leading causes of maternal morbidity and mortality. It complicates up to 10% of all deliveries. It impacts 6% of cesarean deliveries and 4 % of vaginal deliveries [1]. The World Health Organization (WHO) defines it as blood loss of more than 500 milliliters following vaginal delivery or 1,000 milliliters following cesarean section. A 10% decrease in hemoglobin from the baseline or altered vital signs upon

delivery are alternative definitions. Primary PPH is defined as PPH that appears within 24 hours of delivery. Up to 60% of mortality in underdeveloped nations is caused by primary PPH [2]. Uterine atony (failed uterine contraction after delivery) occurs in up to 70% of cases of primary PPH. Other causes include genital tract trauma, retained products of conception, and coagulopathy [3]. Premature or prolonged labor, excessive oxytocin use, multiple gestations, fetal macrosomia, grand multiparity,



chorioamnionitis, and numerous other conditions are risk factors for uterine atony. In South Asia, these variables are frequently present in expectant mothers. The bulk of the population lives in rural areas, where there are disparities in the health care system, inadequate prenatal care, frequent short-spaced childbirths, lack of contraception, and unskilled birth attendants [4]. The management of primary PPH includes exclusion of genital tract trauma, coagulopathy, evacuation of retained conception products, and administration of uterotonic agents. Other measures like Uterine compression, intrauterine balloon tamponade, or surgical intervention are used in primary PPH that is refractory to uterotonic agents [5]. The utility of the Foley catheter for intrauterine balloon tamponade was initially reported by Goldrath [6]. The WHO, International Federation of Gynaecology and Obstetrics (FIGO), and American College of Obstetricians and Gynaecologists (ACOG) advocate that uterine balloon tamponade is useful in low-resource settings when uterotonics fail to control PPH. It can reduce bleeding and allow resuscitation before shifting the patient to the operating theatre [7]. The success rate of intrauterine balloon tamponade in uterine atony is reported to be up to 87% by Suarez *et al.*, [8]. For uterine tamponade, there are several different catheter options, including the Sengstaken-Blackmore tube, condom, Rusch urology catheter, and Bakri balloon. Still, the Foley catheter is less intrusive, less expensive, more widely available, and useful in low-resource environments. It functions by physically closing the orifices of the bleeding venous sinuses in the placental bed and applying mechanical pressure on them. Other processes could be the contraction of the uterine muscles and the hydrostatic pressure of the balloon, which reduces the flow of blood through the uterus. This results in blood clot formation and stops bleeding [9, 10]. The primary objective of our study is to determine the safety and success rate of uterine balloon tamponade using a 24 Fr Foley catheter for treating postpartum hemorrhage in an atonic uterus.

To anticipate the device's failure, it is crucial to estimate the amount of bleeding following the placement of the Foley catheter. No literature from the region has addressed this problem. The secondary objective is to determine the amount of bleeding at 15 and 30 minutes following the Foley's insertion to forecast failure. This study aims to provide valuable insights into the effectiveness of this intervention and potentially influence obstetric emergency protocols to improve maternal outcomes in low-resource settings where such emergencies are more prevalent. Also, it will provide evidence to intervene on time in case the Foley balloon tamponade fails.

METHODS

This cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Bacha Khan Medical Complex, Swabi, from June 2023 to May 2024. Ethical clearance was taken from the institutional ethical review board (ID No: IREB/GKMCS/022411). A non-probability consecutive sampling technique was used. A sample size of 139 was calculated using a confidence interval of 90%, margin of error of 5%, and population proportion of 85% [11]. The study included 140 consecutive women with primary PPH. The inclusion criteria included all patients with PPH following failed medical therapy after vaginal delivery or cesarean section, stable hemodynamic status, patients desiring for preservation of reproductive potential, patients consenting for surgery in case balloon tamponade fails. Patients with unstable hemodynamic status, suspected uterine rupture, traumatic PPH, retained placenta, bleeding tendency, and chorioamnionitis were excluded. All patients had detailed history, clinical examination, clotting profile, baseline investigations, blood grouping, and antenatal ultrasound as a routine protocol. Patients were included in the study after written informed consent and after discussing the study protocol. The patients with PPH due to uterine atony were monitored hemodynamically in labor room by recording their blood pressure, pulse, and oxygen saturation via a standard monitor. Before insertion of the Foley catheter, the blood loss was assessed visually by using suction, mops, and a collection bag. The instruments used for 24 Fr Foley catheter placement included a speculum, sponge forceps, 24 Fr Foley catheter, normal saline, a 20 milliliters syringe, gauze, urine bag. The balloon of a 24 Fr Foley catheter can withstand up to 150 mL of normal saline efficiently. The Patients were put in the lithotomy position. The cervix was examined under aseptic technique for tears. Then 24-French Foley catheter was placed in the uterine cavity with the help of sponge holding forceps. The catheter balloon was initially inflated up to 100 mL of normal saline and observed for bleeding for the next 15 minutes. When the bleeding stopped within 15 minutes or there was only a small loss <150 milliliters of blood, the procedure was deemed effective. When bleeding (>150 ml) persisted 15 minutes after the correct placement of the balloon catheter and surgical intervention was required to control the bleeding, we deemed the balloon tamponade to have failed. It was followed by resuscitation and surgical intervention in the form of compression suture, triple ligation, or hysterectomy. A roller gauze was used to pack vagina to maximize mechanical compression and prevent the expulsion of the Foley catheter. A moderate traction was applied to the catheter by tying it to the thigh with tape. The Foley catheter was connected to a urine bag for estimation of blood loss. The limit of the uterine fundus was marked with a marker. Subsequent uterine enlargement was noted from this marker line. The Bladder

Catheterization was also done for estimation of urine output. The Foley catheter was left in the uterus for 24 hours, and the vitals of patients were monitored continuously with the help of standard monitors. Coagulopathy was defined by the appearance of clinical signs (bruising, bleeding from mucosal surfaces, petechiae) coagulation profile (prolongation of a partial thromboplastin time (APTT), decrease in prothrombin time (PT) or fibrinogen, thrombocytopenia) from blood samples sent just before or at the time of 24 Fr Foley balloon placement. After 24 hours, vaginal pack was removed and the balloon was gradually deflated and removed. The patient was observed for 30 minutes. When bleeding had stopped and no further intervention was required, the balloon tamponade was deemed effective. The patients were kept on intravenous antibiotics and oxytocin infusion during the balloon tamponade. Data were collected using a proforma. All data were analyzed using SPSS version 23.0 (SPSS Inc., Chicago, Illinois, USA). Numbers and percentages were used to express categorical data. Chi-square test or Fisher's exact test was used to compare categorical data between successful and failed balloon tamponade groups. Mean and standard deviation (SD) or

medians and interquartile intervals with p-value were used for quantitative data. The normality of distributions was assessed using the Shapiro-Wilk test. Quantitative variables were compared using Student's t-test or ANOVA test. A p-value ≤ 0.050 was considered significant. An ROC curve analysis was performed for estimated blood loss after 15 min of Foley balloon placement to determine the maximum positive predictive value for various cut-offs.

RESULTS

During the study duration, 296 patients with PPH secondary to uterine atony were managed. 140 patients had failed medical treatment and were managed with a 24 Fr Foley catheter balloon tamponade. Balloon tamponade was successful in controlling hemorrhage in 125 (89.2%) patients. While 15 (9.8%) patients had failed balloon tamponade and needed further surgical intervention, 11 patients were treated with compression suture and ligation. 4 patients needed emergency hysterectomy. Patients with successful Foley balloon tamponade and failed balloon tamponade had similar characteristics (p-value > 0.050) (Table 1).

Table 1: Characteristics of enrolled Patients

Variables		Successful n (%)	Failed n (%)	p-value
Foley Catheter Balloon Tamponade		125 (89.2)	15 (9.8)	-
Maternal Age (Years)		29.1 $\pm$ 4.8	30.3 $\pm$ 6.1	0.600*
Body Mass Index (kg/m ²)		22.2 (20.0%; 26.0%)	23 (20.4%; 27.0%)	0.780*
Gestational age	≥ 37 Weeks	93 (74.4%)	10 (66.6%)	0.520 †
	< 37 Weeks	32 (25.6%)	5 (33.3%)	
Parity	Primigravida	43 (34.4%)	5 (33.3%)	1.000 †
	Multigravida	82 (65.6%)	10 (66.6%)	
Mode of Delivery	Vaginal	93 (74.4%)	9 (60%)	0.470 †
	Instrumental Vaginal	23 (18.4%)	4 (26.6%)	
	Cesarean Section	9 (7.2%)	2 (13.3%)	
History of PPH	Yes	13 (10.4%)	4 (26.6%)	0.800 †
	No	112 (89.6%)	11 (73.3%)	
Booking Status	Booked	47 (37.6%)	2 (13.3%)	0.140 †
	Un-Booked	37 (29.6%)	5 (33.3%)	
	Referral	41 (32.8%)	8 (53.3%)	
Mode of Labor	Spontaneous	103 (82.4%)	11 (73.3%)	0.480 †
	Induced	22 (17.6%)	4 (26.6%)	

Means, standard deviations, or medians (1st quartile; 3rd quartile) for quantitative data. Numbers (n) and percentages (%) for qualitative data.

*Student-t - t test for continuous variables. † Chi-square test/Fisher's exact test for categorical variables

Results show a statistically higher rate of anemia, coagulopathy, higher volume of blood loss after delivery, shorter duration from birth to Foley balloon placement, and higher volume of blood loss after 15 minutes and 30 minutes of Foley balloon placement in the failed balloon tamponade group as compared to the successful balloon tamponade group. ICU admissions were statistically more common and hospital stay was longer in the failed Foley balloon tamponade group in comparison to successful balloon tamponade patients (Table 2).

Table 2: Prognostic Factors for 24 Fr Foley Balloon Failure

Variables		Successful Tamponade n=125 (%)	95% CI	Failed Tamponade n=15 (%)	95% CI	p-value
Foley Catheter Balloon Tamponade		10.2 ± 0.4	10.1-10.2	9.2 ± 0.3	9.0-9.4	<0.005*
Maternal Age (Years)	Yes	4 (3.2%)	—	9 (60%)	—	<0.005 †
	No	121 (96.8%)		6 (40%)		
Blood Loss After Delivery/ C-Section to Balloon Placement (ml)		816.9 ± 112.3	797.0-836.8	906.0 ± 124.5	837-975	0.005*
Duration from Birth to Foley Balloon Placement (min)		33.4 ± 2.8	32.9-33.9	30.5 ± 2.3	29.2-31.8	<0.005*
Blood Loss at 15 min (ml)		45.4 ± 18.7	42.1-48.7	186.3 ± 33.7	167.6-205.1	<0.005*
Blood Loss at 30 min (ml)		71.2 ± 21.8	67.4-75.1	346.6 ± 46.7	320.8-372.5	<0.005*
ICU admission		25 (20%)	—	12 (80%)	—	<0.005 †
Mean Hospital Stay		3.7 ± 0.7	3.6-3.9	5.9 ± 0.7	5.4-6.3	<0.005*

Numbers (n) and percentages (%) for qualitative data. † Chi square or Fisher's exact test for qualitative variables. Means, standard deviations for quantitative data. * Student t-test or one-way ANOVA test for quantitative data

Further study shows the threshold of blood loss after 15 minutes of Foley balloon placement. The positive predictive value for 150 ml and 200 ml was 0.60 and 0.80, respectively.

Table 3: Prediction of 24 Fr Foley Balloon Failure at 15 Minutes of Placement

Blood Loss at 15 minutes (ml)	Area Under Curve	Standard Error	95% CI	p-value	Sensitivity	Specificity	PPV	NPV
150	0.95	0.02	0.90-1.0	0.020	0.25	99.1	0.60	95.2
200	0.98	0.008	0.97-1.0	<0.001	0.75	97.5	0.80	96.8

PPV: Positive Predictive Value, NPV: Negative Predictive Value

DISCUSSION

Previously, sterile gauze was used to pack the uterine cavity to control PPH. Recently, the use of an intrauterine balloon for PPH has streamlined this deadly complication. The Bakri Balloon is most commonly used. It is noninvasive and preserves fertility. It also provides a window to resuscitate the patient and reduce blood loss before moving to more invasive treatments like arterial embolization, internal iliac artery ligation, uterine compression sutures, and hysterectomy [12]. Now it is possible to avoid multiple blood transfusions, decrease surgical interventions, and minimize related maternal morbidity and mortality. Various studies have reported success rates of Bakri balloon tamponade after vaginal delivery. A meta-analysis by Suarez *et al.*, reported a 87.1 % success rate of balloon tamponade in uterine atony [8]. A meta-analysis by Abul *et al.*, concluded that intrauterine balloon tamponade is superior to uterine gauze packing for PPH [13]. Dorkham *et al.*, reported a success rate of 90% in a retrospective study [14]. A Randomized controlled trial by Rozenberg *et al.*, compared a combination of second-line uterotonic (sulprostone) and ebb balloon tamponade with second-line uterotonic alone (sulprostone) and reported success rates of 67.2% and 74.3%, respectively [15]. However, in low-resource areas, the balloon of a Foley catheter has been used to control PPH. The uterine tamponade was successful in effectively controlling bleeding in atonic uterus in 125 (89.2%) patients in our study. This corresponds to the success rate reported by other prospective observational studies. A study by

Bukhari *et al.*, reported a success rate of 98% utilizing a 16 Fr Foley catheter in the atonic uterus with PPH [16]. Similarly, a prospective study by Nipanal and Talawar, found 24 Fr Foley catheter to be 95.7% effective in controlling PPH in atonic uterus after vaginal delivery [17]. Variations in success rate are attributed to various factors like preoperative hemoglobin, history of PPH, previous cesarean section scars, placenta accreta and increta, gestational hypertension, placenta previa, and intrapartum or antepartum bleeding, timing of balloon insertion, heterogeneity of the subjects including indications and context for balloon tamponade and the inconsistency in clinical practice [18]. Randomized trials that directly compare the Bakri balloon and 24 Fr Foley catheter for uterine tamponade are lacking. Similarly, angioembolization is another option for such patients in developed health care systems. A recent study compared intrauterine balloon tamponade and uterine artery embolization in PPH and found no difference in the risk of peripartum hysterectomy and/or maternal death. The small size of the sample did not allow for the determination of whether intrauterine balloon tamponade is equivalent or superior [19]. However, the hemodynamic status of the patient, cost, expertise, prompt availability of an interventional radiologist, and radiology suite are limitations in low-resource healthcare. While insertion of an intrauterine 24 Fr Foley to tamponade the uterus is easier and cheaper. Our study also showed that coagulopathy increases the failure rate of intrauterine

balloon tamponade. The time for Foley balloon insertion in the failure group was shorter, but the volume of blood loss was higher. Although serum fibrinogen <2 g/L can serve as a predictor for progression to severe PPH, it does not help clinicians during the management of PPH due to the delay of blood results [20]. In addition, some patients may have more than one cause of PPH, and uterine atony may be secondary to abnormalities of the placenta. However, the risk of coagulopathy increases with larger blood loss and leads to more bleeding as reported in the literature. Liu *et al.*, reported that multiple gestations, blood loss, and placenta accreta spectrum were independent risk factors for Bakri balloon tamponade failure [21]. Also, Intrauterine balloon tamponade was only 54.8% successful in cases with previa abnormalities. A retrospective cohort study found that higher antenatal hemoglobin values were negatively correlated with the incidence of transfusion, uterine artery embolization, or hysterectomy. Similarly, uterine balloon tamponade performed in the placental site bleeding group was more likely to have adverse PPH outcomes compared to the uterine atony group [22]. Antenatal anemia was common in our patients with PPH. Antenatal anemia needs to be investigated and treated in such patients. More than half of our patients with PPH were unbooked, referred cases, or multigravidas with no antenatal screening at all. Low or lower limit of normal hemoglobin in such patients is not uncommon. A lower prenatal hemoglobin value means that the mother has a lower reserve capacity for blood loss, which is an important parameter in managing PPH. Our study showed that failure of an intrauterine Foley balloon can be predicted within 15 minutes, thus avoiding delay in further surgical interventions. Our results showed that 200 ml blood loss has a positive predictive value of 0.97 for Foley balloon tamponade failure. In a retrospective cohort study by Leleu *et al.*, the predictive positive value of 250 ml blood loss was 0.94 at 10 minutes [23]. Current results also match these findings. One may suspect that balloon tamponade may delay surgical intervention in case of failure. However, this is merely an assumption. Intrauterine Balloon tamponade's utilization improves the hemodynamic status of patients undergoing interventional angioembolization. No complications were found in our patients, although intrauterine balloon tamponade may cause fever, endometritis, uterine necrosis, cervical tears, scar dehiscence, or uterine perforation [24]. The strengths of our study are utilizing a cheap alternative for uterine balloon tamponade, highlighting the need for early intrauterine placement of a 24Fr Foley in PPH and early recognition of failure of balloon tamponade after 15 minutes with estimated blood loss of 200 ml. This finding can help trigger more invasive treatment and reduce blood loss.

The study is limited by a relatively small sample size and lack of randomization, which may affect the

generalizability of the findings. Additionally, being a single-center study, the results may not be applicable to broader populations or different healthcare settings. Multicenter, larger-sized randomized control trials in the future will address the limitations and biases inherent to this study.

CONCLUSIONS

It was concluded that the placement of a 24 Fr Foley catheter in the uterine cavity effectively controls PPH in low-resource settings. A blood loss of ≥ 200 ml after 15 minutes of Foley balloon placement should alert the clinician to adopt a more aggressive approach to control bleeding. However, the results should be interpreted with caution due to the observational nature of the study.

Authors' Contribution

Conceptualization: AK¹

Methodology: BR, AR, SAR

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Writing and Drafting: NK, AK², MFH

Review and Editing: AK¹, NK, AK², BR, SAR, MFH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

Awareness and Knowledge for Risk Factors, Screening, Control of GDM and its Effect among Pregnant Women Visiting Gynae Outpatient Department at Tertiary Care Hospital Bahawalpur

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ABSTRACT

This study explores the disparities observed in knowledge and awareness of Gestational Diabetes Mellitus (GDM) among pregnant women attending a military hospital. **Objective:** To determine the awareness and knowledge on GDM among pregnant mothers during antenatal visit, to identify factors that can influence such knowledge (demographics) population. **Methods:** This cross-sectional study was carried out in the Department of Obstetrics and Gynaecology, Tertiary Care Hospital Bahawalpur during November 24, 2022 till June 23, 2023. The data were collected via face to face interview employing a pretested structured questionnaire and it aimed the risk factors of GDM, history and lifestyle with regard to GDM screening/management. Statistical analysis involved the chi-square tests and ANOVA to investigate associations among demographic variables with knowledge of GDM. **Results:** Total 196 pregnant women were selected. The pre-pregnancy, mean BMI was 25.00 ± 4.384 , mean age was 31.42 ± 8.215 years, and the average fasting glucose level was 96.71 mg/dL ($SD = 15.588$). Significant associations were found between family history and GDM knowledge ($p = 0.004$), as well as previous history of GDM and screening awareness ($p < 0.001$). **Conclusions:** There was a notable gap in GDM knowledge among pregnant females, influenced by demographic factors. Enhanced targeted educational programs are necessary to improve awareness and management of GDM.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is one of the most common metabolic disorders identified during pregnancy, characterized by glucose intolerance first diagnosed during gestation. Typically, GDM is diagnosed between 24 and 28 weeks of pregnancy due to increased insulin resistance occurring in the second trimester. Its prevalence has significantly increased globally, paralleling the rise in obesity and Type 2 Diabetes Mellitus (T2DM) [1]. GDM has profound implications for maternal and fetal health, significantly increasing risks for adverse outcomes such as hypertensive disorders of pregnancy, preeclampsia, fetal macrosomia, neonatal hypoglycemia,

birth trauma, respiratory distress syndrome, and long-term metabolic complications in offspring, including increased risk of obesity and diabetes later in life [2, 3]. Early identification and effective management of GDM are crucial in reducing these adverse outcomes. Current guidelines from the American Diabetes Association recommend universal screening for GDM between 24-28 weeks of gestation; however, earlier screening may be beneficial for high-risk populations, enabling earlier intervention and potentially improved pregnancy outcomes [3, 4]. Nonetheless, there remains debate regarding the optimal timing of screening, as some studies



suggest limited benefits from early screening compared to the standard mid-pregnancy screening approach [4]. Risk factors strongly associated with the development of GDM include advanced maternal age (≥ 35 years), elevated pre-pregnancy body mass index ($\text{BMI} \geq 25 \text{ kg/m}^2$), and excessive gestational weight gain. Guidelines from the World Health Organization (WHO) and American College of Obstetricians and Gynecologists (ACOG) support these BMI thresholds, associating higher BMI with increased insulin resistance and consequently higher risk of GDM [4-6]. Maternal hyperglycemia directly affects fetal health through mechanisms such as increased transplacental glucose transfer, leading to fetal hyperinsulinemia and excessive fetal growth (macrosomia). Additionally, maternal hyperglycemia induces placental alterations, such as villous immaturity and increased placental-to-fetal weight ratios, negatively impacting placental function and fetal nutrient and gas exchange, thus exacerbating neonatal risks [7, 8]. Women diagnosed with GDM also face increased postpartum risk of developing T2DM. Research indicates that even mild cases of GDM significantly contribute to the global burden of T2DM, highlighting the importance of postpartum glucose monitoring and targeted interventions aimed at lifestyle modification [9, 10]. Selective screening based on specific risk factors has been proposed as an efficient alternative to universal screening; however, universal screening remains widely recommended to prevent missing at-risk individuals [4]. Recent evidence also suggests potential advantages in utilizing first-trimester HbA1c measurements as an additional screening method, although definitive guidelines for this practice are yet to be standardized [10]. Considering the escalating incidence and significant public health implications of GDM, comprehensive educational programs targeting healthcare providers and pregnant women, alongside evidence-based screening and intervention strategies, are essential. Effective management through dietary modifications, increased physical activity, and consistent antenatal care is vital in mitigating the short- and long-term impacts of GDM, reinforcing the importance of an integrated approach to managing this growing global health concern.

Despite the widespread use of removable partial dentures, limited local evidence exists on patient satisfaction and compliance with mandibular RPDs. Moreover, factors influencing short-term satisfaction using standardized tools like SAPS have not been adequately explored in the local population. This study aims to assess patient satisfaction with mandibular removable partial dentures over a period of 2 months using the SAPS scale.

METHODS

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Tertiary Care

Hospital Bahawalpur, from November 24, 2022, to June 23, 2023. Pregnant women aged 18 years or older who visited the antenatal clinic and consented to participate were included. Women with pre-existing Type 1 or Type 2 diabetes or those unable to participate due to severe medical illness or language barriers were excluded. A convenience sampling technique was used. Potential participants were identified through hospital visitation logs and approached in the waiting area before their appointments. Informed written consent was obtained from all participants. The sample size was calculated using a reported GDM awareness prevalence of 16.7% among pregnant women in Pakistan, as reported by Adnan and Aasim, (2024) conducted a systematic review and meta-analysis revealing a high and variable prevalence of gestational diabetes mellitus across different regions of Pakistan [11]. Furthermore, a post-hoc power analysis based on one of the key outcome comparisons awareness of GDM screening between women with and without a previous history of GDM (86.5% vs. 51.1%) confirmed that the study had over 95% power to detect statistically significant differences with an alpha level of 0.05. These findings support that the sample size was sufficient not only for prevalence estimation but also for subgroup comparisons, providing robust evidence to address the study objectives. Data were collected through face-to-face interviews conducted by trained healthcare staff in a private clinic setting to ensure confidentiality. A structured questionnaire (available in Urdu and English) was used to evaluate participants' awareness of GDM risk factors, screening, management, and complications. The questionnaire included both open- and closed-ended items. Key variables included maternal age (years), pre-pregnancy BMI (kg/m^2 , categorized), family history of diabetes, previous history of GDM, and fasting glucose levels (mg/dL). Knowledge about GDM risk factors was scored and categorized as: Low (0), Moderate (1), High (2) and Very High (3). All data were analyzed using SPSS version 25.0. Descriptive statistics (mean $\pm$ standard deviation for continuous variables; frequencies and percentages for categorical variables) were used to summarize demographic and clinical characteristics. Chi-square tests were used to explore associations between categorical variables. Where significant, odds ratios (ORs) with 95% confidence intervals (CIs) were computed to quantify effect sizes. One-way ANOVA was used to assess differences in continuous variables (age and BMI) across GDM knowledge groups, and meta squared (η^2) was calculated to estimate effect sizes. The internal consistency of the knowledge assessment section of the questionnaire was evaluated using Cronbach's alpha, which yielded a value of $\alpha = 0.82$, indicating good reliability. The study was approved by the Ethical Review Committee of Tertiary Care Hospital Bahawalpur (1516/Tig/2022). Ethical

guidelines, including voluntary participation, informed consent, and confidentiality of participant data, were strictly followed throughout the study.

RESULTS

A total of 196 pregnant women were enrolled in the study. The average age was 31.42 ± 8.21 years, and the mean pre-pregnancy BMI was 25.00 ± 4.38 kg/m². The average fasting blood glucose level was 96.71 ± 15.59 mg/dL. Among participants without a family history of diabetes ($n = 96$), 4 (4.2%) had low, 32 (33.3%) moderate, 42 (43.8%) high, and 18 (18.8%) very high knowledge of GDM risk factors. Among those with a positive family history ($n = 100$), 10 (10.0%) had low, 30 (30.0%) moderate, 24 (24.0%) high, and 36 (36.0%) very high knowledge. This association was statistically significant ($\chi^2 = 13.469$, $p = 0.004$). Participants with a family history of diabetes were more likely to have very high knowledge (36.0%) compared to those without such history (18.8%), indicating that family exposure may increase GDM awareness (Table 1).

Table 1: Distribution of GDM Risk Factor Knowledge Levels by Family History of Diabetes

Family History	Low	Moderate	High	Very High	Total
No ($n = 96$)	4 (4.2%)	32 (33.3%)	42 (43.8%)	18 (18.8%)	96 (49.0%)
Yes ($n = 100$)	10 (10.0%)	30 (30.0%)	24 (24.0%)	36 (36.0%)	100 (51.0%)

Among participants without a previous history of GDM ($n = 92$), 4 (4.3%) had low, 34 (37.0%) moderate, 38 (41.3%) high, and 16 (17.4%) very high knowledge. In contrast, among those with a previous history of GDM ($n = 104$), 10 (9.6%) had low, 28 (26.9%) moderate, 28 (26.9%) high, and 38 (36.5%) very high knowledge. This association was statistically significant ($\chi^2 = 12.944$, $p = 0.005$). Women with prior GDM were more than twice as likely to have very high knowledge (36.5%) compared to those without GDM history (17.4%) (Table 2).

Table 2: Distribution of GDM Risk Factor Knowledge Levels by Previous History of GDM

GDM History	Low	Moderate	High	Very High	Total
No ($n = 92$)	4 (4.3%)	34 (37.0%)	38 (41.3%)	16 (17.4%)	92 (46.9%)
Yes ($n = 104$)	10 (9.6%)	28 (26.9%)	28 (26.9%)	38 (36.5%)	104 (53.1%)

Among participants without a family history ($n = 96$), 75 (78.1%) were aware and 21 (21.9%) were not. Among those with a family history ($n = 100$), 62 (62.0%) were aware and 38 (38.0%) were not. This association was significant ($\chi^2 = 6.053$, $p = 0.014$). The adjusted odds ratio showed that those with a family history of diabetes had 2.19 times higher odds of being unaware (aOR = 2.19, 95% CI: 1.17–4.11, $p = 0.037$), after controlling for confounders. Despite having a family history, participants were less likely to be aware of screening methods, which may indicate a knowledge gap in early detection protocols (Table 3).

Table 3: Awareness of GDM Screening Methods by Family History of Diabetes with Adjusted Odds Ratios

Family History	Not Aware	Aware	Total	aOR (95% CI)
No ($n = 96$)	21 (21.9%)	75 (78.1%)	96 (49.0%)	Reference
Yes ($n = 100$)	38 (38.0%)	62 (62.0%)	100 (51.0%)	2.19 (1.17–4.11)

Among participants without a previous history of GDM ($n = 92$), 47 (51.1%) were aware and 45 (48.9%) were not. Among those with previous GDM ($n = 104$), 90 (86.5%) were aware and 14 (13.5%) were not. This difference was statistically significant ($\chi^2 = 29.159$, $p < 0.001$). Multivariate analysis revealed that participants with prior GDM had 84% lower odds of being unaware of screening methods (aOR = 0.16, 95% CI: 0.08–0.33, $p < 0.001$). Previous experience with GDM greatly improved screening awareness, reinforcing the role of patient education during and after diagnosis (Table 4).

Table 4: Awareness of GDM Screening Methods by Previous History of GDM with Adjusted Odds Ratios

GDM History	Not Aware	Aware	Total	aOR (95% CI)
No ($n = 96$)	45 (48.9%)	47 (51.1%)	92 (46.9%)	Reference
Yes ($n = 104$)	14 (13.5%)	90 (86.5%)	104 (53.1%)	0.16 (0.08–0.33)

One-way ANOVA showed significant differences in age and BMI across GDM knowledge levels. Women with very high knowledge had the youngest mean age (29.63 ± 6.18 years) and highest BMI (26.89 ± 4.27 kg/m²). Eta squared (η^2) = 0.096 for both age and BMI, indicating a moderate effect size (9.6% variance explained). Post-hoc comparisons confirmed significant differences between very high knowledge and all other groups ($p < 0.050$).

Table 5: Comparison of Age and Prepregnancy BMI across GDM Risk Factor Knowledge Levels

Knowledge Level	N	Age (Mean $\pm$ SD)	BMI (Mean $\pm$ SD)
Low	14	34.71 ± 5.93	26.84 ± 4.52
Moderate	62	31.18 ± 4.34	25.80 ± 4.09
High	66	32.32 ± 7.23	25.30 ± 4.50
Very High	54	29.63 ± 6.18	26.89 ± 4.27

Using "Low knowledge" as the reference, we found that, Age remained a significant inverse predictor for both moderate (aOR = 0.80, $p = 0.006$) and very high knowledge levels (aOR = 0.73, $p < 0.001$). Previous GDM significantly predicted moderate (aOR = 0.12, $p = 0.007$) and high knowledge (aOR = 0.13, $p = 0.011$). Family history was inversely related to moderate and high knowledge levels but not to very high knowledge. This adjusted model confirms that age and prior GDM experience are robust predictors of GDM knowledge, even when accounting for other variables (Table 6).

Table 6: Multinomial Logistic Regression for Predictors of GDM Risk Factor Knowledge (Reference: Low Knowledge)

Predictor	Moderate OR (95% CI)	p	High OR (95% CI)	p	High OR (95% CI)	p
Age	0.80 (0.68–0.94)	0.006	0.89 (0.76–1.05)	0.172	0.73 (0.62–0.86)	<0.001
BMI	0.90 (0.62–1.41)	0.581	0.71 (0.48–1.39)	0.081	1.19 (0.83–1.71)	0.344
Family History	0.17 (0.04–0.78)	0.022	0.08 (0.02–0.36)	0.001	0.68 (0.30–2.07)	0.616
Previous GDM	0.12 (0.03–0.56)	0.007	0.13 (0.03–0.63)	0.011	0.32 (0.07–1.55)	0.158

In addition to overall group differences, a post-hoc analysis using Tukey's HSD test revealed that participants with very high knowledge were significantly younger than those in the low (mean difference = -5.08, $p = 0.002$), moderate (-1.55, $p = 0.045$), and high knowledge groups (-2.69, $p = 0.001$). With respect to BMI, women in the very high knowledge group had significantly higher BMI than those in the moderate (mean difference = -1.09, $p = 0.031$) and high knowledge groups (-1.59, $p = 0.001$). These findings suggest that younger and overweight or obese women may receive more targeted antenatal education or may be more proactive in learning about GDM.

Table 7: Tukey's HSD Post-Hoc Comparisons for Age and BMI across GDM Knowledge Levels

Comparison	Age Mean Diff (Years)	Age p-value	Age Interpretation	BMI Mean Diff (kg/m ²)	BMI p-value	BMI Interpretation
Low vs. Very High	-5.08	0.002	Very High group significantly younger	—	—	—
Moderate vs. Very High	-1.55	0.045	Very High group younger	-1.09	0.031	Very High group had higher BMI
High vs. Very High	-2.69	0.001	Very High group younger	-1.59	0.001	Very High group had significantly higher BMI

DISCUSSION

This study conducted at a Tertiary Care Hospital in Bahawalpur highlights considerable variability in the understanding of Gestational Diabetes Mellitus (GDM) among pregnant women, mirroring trends observed globally. A key finding was the significant association between having a family history of diabetes and enhanced awareness of GDM risk factors, suggesting that personal or familial experiences with diabetes may serve as a driver for better understanding and vigilance. These observations align with the results of Adnan and Aasim, who in their systematic review and meta-analysis reported a high and regionally diverse prevalence of GDM across Pakistan, indicating not only clinical but also educational disparities [11]. Notably, these findings on the inadequate awareness regarding GDM screening methods resonate with the study conducted by Alharthi *et al.*, who reported a marked deficiency in knowledge of GDM diagnostic practices among Saudi women despite general awareness about the disease itself [12]. Thomas *et al.*, further support these findings, noting that demographic factors, particularly maternal age, significantly influence GDM awareness [13]. Younger pregnant women in this study exhibited greater awareness, suggesting targeted educational strategies could effectively address knowledge disparities among older age groups. Wafa *et al.*, have also highlighted that comprehensive educational interventions significantly elevate awareness levels among women in Saudi Arabia [14]. Similarly, Bhavadharini *et al.*, emphasize the critical need for culturally tailored public health initiatives to address regional disparities in GDM knowledge across India, suggesting the potential effectiveness of localized educational approaches [15]. Kondamuri *et al.*, further

advocate for targeted health education campaigns tailored to semi-urban and rural communities, underscoring their necessity in regions with limited healthcare access [16]. Their findings regarding these observations were the urgent requirement for focused interventions aimed at enhancing GDM screening awareness, especially in populations with limited prior exposure or knowledge. The influential role of personal experience with GDM, as noted by Byakwaga *et al.*, highlights how experiential learning substantially enhances women's readiness and awareness regarding GDM management [17]. These findings corroborate this perspective, with significantly higher awareness levels among women with previous GDM histories, indicating the value of integrating personal experiences into educational frameworks. Chikeme, and Bada both emphasize the effectiveness of culturally adapted educational interventions tailored specifically to local demographic characteristics [18, 19]. They argue that culturally sensitive health education significantly enhances both engagement and understanding, effectively improving outcomes related to GDM screening and management. Recent studies further validate these insights, emphasizing critical gaps in GDM awareness due to persistent misconceptions about screening methods, particularly the Oral Glucose Tolerance Test (OGTT). Tan and Bayyigit identified prevalent misconceptions among Turkish women regarding OGTT safety, resulting in higher refusal rates and reinforcing the need for focused educational interventions addressing such specific misconceptions [20]. Moreover, recent findings highlight significant socioeconomic disparities in GDM knowledge, with rural, less-educated, and lower socioeconomic groups

exhibiting notably lower awareness [21]. This underscores the necessity of educational programs specifically designed to bridge these disparities, ensuring equitable knowledge distribution and improved health outcomes across diverse population segments. Additionally, demographic influences such as maternal age, gestational age, and parity significantly affect GDM awareness, according to recent research by Gari *et al* [22]. These demographic factors must be considered in the design and implementation of educational programs, further enhancing their efficacy and relevance. In line with these international observations, studies from Pakistan have reported similarly low levels of GDM awareness among pregnant women. For instance, a cross-sectional study conducted at Niazi Medical and Dental College, Sargodha, involving 150 pregnant women diagnosed with GDM, revealed that 60% lacked knowledge about GDM risk factors and symptoms, and 67.3% had poor knowledge about glucose monitoring [23]. Another study conducted at Shifa College of Medicine and Shifa Foundation Community Health Centre, Islamabad, assessed the perception and knowledge of women regarding GDM and identified barriers faced in acquiring healthcare and lifestyle modifications [24]. These findings support the results and emphasize the urgent need for targeted awareness programs tailored to local communities to enhance GDM knowledge and screening adherence in Pakistan. While this study provides valuable insights, it is important to acknowledge that the current dataset did not include stratification by socioeconomic status, educational background, or parity factors known to influence health literacy and maternal health outcomes. Despite these associations, overall understanding of GDM remained limited, underscoring the need for targeted antenatal education programs. Implementing structured counseling and awareness initiatives during routine antenatal visits may play a pivotal role in improving early detection, management, and outcomes related to GDM in similar healthcare settings. Future studies should incorporate these variables to explore more nuanced associations and to better guide the design of targeted, demographically sensitive educational interventions. In conclusion, these findings combined with recent literature emphasize the critical need for culturally tailored, targeted educational interventions addressing demographic-specific knowledge gaps and misconceptions surrounding GDM. Such tailored strategies are essential for improving awareness, screening adherence, and overall pregnancy outcomes related to GDM.

CONCLUSIONS

This study identified significant gaps in knowledge and awareness of Gestational Diabetes Mellitus (GDM) among pregnant women attending a military hospital in Bahawalpur. The findings emphasize that demographic

factors, particularly a family history of diabetes and previous GDM experience, are strongly associated with increased awareness.

Authors' Contribution

Conceptualization: NS

Methodology: NH

Formal analysis: RS

Writing and Drafting: NS, VA, SU, NH

Review and Editing: NS, RS, VA, SU, NH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article



Level of Patient Satisfaction with Mandibular Acrylic Removable Partial Dentures (RPDS) for Different Kennedy Classes

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ABSTRACT

Tooth loss affects facial profile, speech, and mastication, limiting social activities. Maintaining oral health involves using prostheses like implants, bridges, and partial dentures, with acrylic polymers being widely used. Various classifications are used for partially edentulous arches, among them Edward Kennedy's classification being the most often accepted. **Objective:** To assesses patient satisfaction for two months about mandibular Removable Partial Dentures (RPDs) utilizing the Short Assessment of Patient Satisfaction (SAPS) scale from the University of Wollongong's Centre for Health Service Development. **Methods:** A Cross-sectional observational study was conducted at Outpatient Department (OPD) of prosthodontics, Institute of Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad. Fifty three patients were selected on Non-probability convenient sampling. Data on comfort, speech, chewing ability, and prosthesis aesthetics were collected at insertion and after two months. The outcomes were categorized using the 5-point rating scale, The Short Assessment of Patient Satisfaction (SAPS). **Results:** SAPS was significantly differentiated among Kennedy Classifications at the time of insertion, out of 53 patients who were categorized into class 1 to class 4. The mean age of the patients was 39.6 years, 22 patients were very satisfied, 16 satisfied, and 15 not satisfied, with 25 males and 28 females this studies revealed that female patients are more likely to suffer from tooth loss and manage with partial dentures. **Conclusion:** The majority of patients were satisfied with Mandibular Removable Partial Dentures, with significant differences in SAPS among Kennedy Classifications at insertion and after two months.

INTRODUCTION

Tooth loss can negatively impact facial appearance, communication, and social activities. Prosthetics can preserve oral health and quality of life using alternative methods, like implant-supported prostheses and bridges [1]. Acrylic polymers are economical and suitable for RPD frameworks [2]. Kennedy's classification was created by Edward Kennedy, it comprises four categories, specifically Class I, Class II, Class III, and Class IV Denture satisfaction is influenced by several key factors, including comfort,

chewing ability, appearance, and how well the denture stays in place [3]. Comfort affects how easily a patient can wear the denture without discomfort, while good chewing function allows them to eat properly [4]. Aesthetics play a role in confidence and social interactions, and proper retention helps keep the denture stable during daily activities. These factors are associated with the relationship between the missing teeth and the remaining natural ones, as the position and condition of the existing



teeth affect how well the denture fits and functions [5]. RPD, implant-supported prostheses, and resin-bonded bridges, are widely recommended for the replacement of missing teeth. The selection of an appropriate prosthetic option is influenced by several factors, including the patient's systemic health, anatomical structure, psychological adaptability, and financial limitations [6]. Moreover, these treatment modalities provide flexibility for adjustments in response to potential future tooth loss, supporting long-term functionality and patient satisfaction [6]. Kennedy classification Dr. Edward by introduced a simple system in 1923 for classifying partial edentulism into four classes. Class 1 edentulous regions cause premature molar or premolar loss, Class 2 have absent posterior teeth, Class 3 have both anterior and posterior teeth, and Class 4 has a singular bilateral edentulous space [7]. This classification helps in diagnosis and treatment for prosthodontic rehabilitation, as well as in communication between clinicians [7]. Patient satisfaction with prosthesis is crucial for therapeutic efficacy, with factors like age, edentulous location, occluding teeth, pain, and aesthetic appearance significantly influencing satisfaction [8]. The Short Assessment of Patient Satisfaction (SAPS) is a reliable tool for measuring patient satisfaction with RPD treatment. In RPD, SAPS score range is from 0 (extremely dissatisfied) to 28 (extremely satisfied) [9]. It is important to understand why some patients stop wearing Removable Partial Dentures (RPDs) to improve their overall effectiveness. Discomfort, poor fit, difficulty chewing, dissatisfaction with appearance, and challenges in cleaning the dentures are common reasons for discontinuation. Long term studies on patient satisfaction and compliance can provide valuable insights into these issues. Additionally, analyzing multiple factors such as oral health, personal preferences, and financial constraints can help uncover the key influences on a patient's experience with RPDs. This knowledge can lead to better treatment approaches, improved patient education, and higher long term success rates for RPD therapy [10, 11]. To the knowledge there is no local study on this topic in this population. Due to genetic and educational reasons the result can be different. Despite the widespread use of removable partial dentures, limited local evidence exists on patient satisfaction and compliance with mandibular RPDs. Moreover, factors influencing short-term satisfaction using standardized tools like SAPS have not been adequately explored in the local population. The objective of this research was to assess the patient satisfaction for 2 months about mandibular RPDs using the SAPS scale.

METHODS

This observational study was conducted at Outpatient Department (OPD) of prosthodontics, Institute of

Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad using non-probability convenience sampling. The study was conducted from 1-11-2021 to 31-10-2022 after ethical approval from Research Ethics Committee via letter no: LUMS/REC-181. The sample size was determined using the OpenEpi software, yielding a sample of 50 participants with a 95% confidence interval and a 12% margin of error, based on a patient satisfaction rate with RPDs of 73.6% [12]. Patients classified as Kennedy's Class I, II, III, and IV, who were not medically compromised and had been using acrylic mandibular RPDs fabricated by post graduate students for two months were included after obtaining written consent. Patients' satisfaction, along with age and gender, was recorded at the time of insertion and after two months using a validated questionnaire. The questionnaire consists of three sections: the first includes the patient's personal biodata, while the second assesses satisfaction through the evaluation of comfort, mastication, prosthesis design, speech and aesthetics over a two-month period [13]. The third section of the questionnaire was classified, the Short Assessment of Patient Satisfaction (SAPS) was created by the University of Wollongong. SAPS scores are categorised into four groups: In general, SAPS scores can be interpreted as follows: 0 to 10 = Very Dissatisfied: Indicates significant dissatisfaction, with the individual reporting dissatisfaction or strong dissatisfaction in at least four aspects of their healthcare. Suggests a highly inadequate healthcare experience requiring urgent intervention. 11 to 18 = Dissatisfied: Reflects dissatisfaction in at least two areas of healthcare or an absence of a "very satisfied" response in any aspect. Highlight major shortcomings in healthcare that require attention. 19 to 26 = Satisfied: Represents satisfaction, with the individual rating more than half of the SAPS items (4 out of 7) as satisfied or very satisfied. Identifying and addressing any areas of dissatisfaction is essential to enhance their healthcare experience. 27 to 28 = Very Satisfied: Indicates high satisfaction, with the individual expressing satisfaction or strong satisfaction across all seven SAPS items. Suggests that their healthcare experience has met or exceeded their expectations [14]. The overall written response rate was 90 percent. The data were analyzed in SPSS (Statistical Package for Social Sciences) version 22.0. Frequency and percentages were calculated for qualitative variables such as gender, age and Kennedy Classes. Satisfaction was compared at insertion and after two months using Chi-square/Fisher exact test. $P < 0.050$ was set to be significant threshold.

RESULTS

Among the 53 patients, there were 25 male patients (47.2%) and 28 female patients (52.8%) (Figure 1).

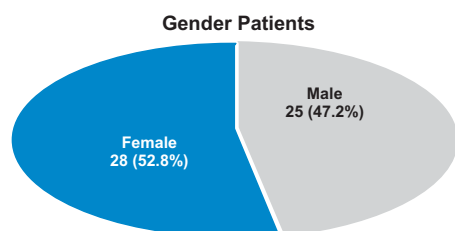


Figure 1: Graphical Presentation of Patients Distribution According to Gender

In this study enrolled patients were grouped as; 20-30 years having 3 (5.7%) patients, 31-40 years having 20 (37.7%) patients and > 40 years having 30 (56.6%) patients (Figure 2).

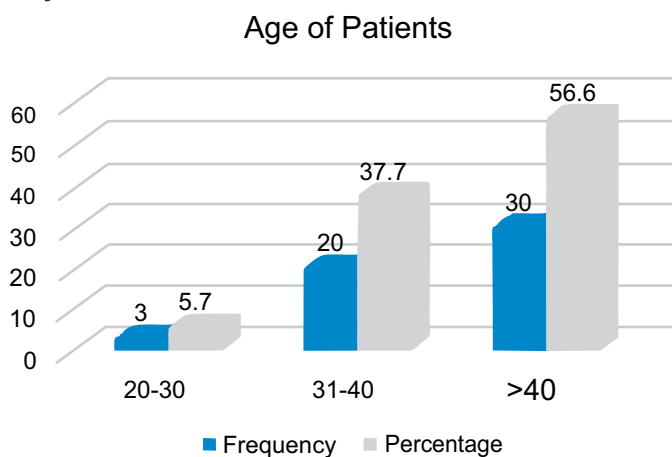


Figure 2: Graphical presentation of Patients Distribution According to Age

Table 2: Patients' distribution according to design of prosthesis level of comfort, aesthetics, speech, mastication, and SAPS

Patients Distribution According to Design of Prosthesis				Patients Distribution According to Comfort			Patients Distribution According to Speech		
Comfort	Baseline Frequency (%)	2 Months Frequency (%)	p-Value	Baseline Frequency (%)	2 Months Frequency (%)	p-Value	Baseline Frequency (%)	2 Months Frequency (%)	p-Value
Prosthesis									
V.Satisfied	22 (41.5)	13 (24.5)	0.123	23 (43.4)	23 (43.4)	0.965	4 (7.5)	4 (7.5)	0.965
Satisfied	17 (32.1)	26 (49.1)		18 (34.0)	19 (35.8)		37 (69.8)	36 (67.9)	
Not Satisfied	4 (26.4)	14 (26.4)		12 (22.6)	11 (20.8)		12 (22.6)	13 (24.5)	
Total	53 (100%)	53 (100%)		53 (100%)	53 (100%)		53 (100%)	53 (100%)	
Aesthetics									
V.Satisfied	11 (20.8)	19 (35.8)	0.218	3 (5.7)	2 (3.8)	0.899	22 (41.5)	21 (39.6)	0.974
Satisfied	32 (60.4)	25 (47.2)		36 (67.9)	37 (69.8)		16 (30.2)	17 (32.1)	
Not Satisfied	10 (18.9)	9 (17.0)		14 (26.4)	14 (26.4)		15 (28.3)	15 (28.3)	
Total	53 (100.0)	53 (100.0)		53 (100.0)	53 (100.0)		53 (100.0)	53 (100.0)	

The SAPS showed significant differentiation among the Kennedy classifications both at the moment of insertion (P value <0.001) and after two months (P-value <0.001).

At the time of insertion, the satisfaction rate for SAPS was 41.5% and 39.6% in 22 and 21 patients, respectively. After two months, the satisfaction rate was 30.2% and 32.1% in 16 and 17 patients, respectively. Fifteen patients (28.3%) were not satisfied (Table 3).

According to Kennedy classification, Class 1 included 15 patients, accounting for 28.3% of the total. Class 2 had 10 patients, representing 18.9% of the total. Class 3 consisted of 23 patients, making up 43.4% of the total. Class 4 had 5 patients, accounting for 9.4% of the total (Table 1).

Table 1: Patients Distribution According to Kennedy Classification (n=53)

Classification	Frequency (%)
Class 1	15 (28.3)
Class 2	10 (18.9)
Class 3	23 (43.4)
Class 4	5 (9.4)
Total	53 (100.0)

Patient's distribution was done according to design of prosthesis, comfort, aesthetics speech, mastication and SAPS at base line and after 2 months is shown in table 2.

Table 3: Stratification of Patients According to SAPS with Kennedy Classification at Baseline (n=53)

Kennedy Classification	Successful Tamponade n=125 (%)			p-value
	Very Satisfied Frequency (%)	Satisfied Frequency (%)	Not Satisfied Frequency (%)	
Class 1	0 (0.0)	0 (0.0)	15 (100.0)	<0.001
Class 2	0 (0.0)	10 (62.5)	0 (0.0)	
Class 3	22 (100.0)	1 (6.3)	0 (0.0)	
Class 4	0 (0.0)	5 (31.3)	0 (0.0)	
Total	22 (100.0)	16 (100.0)	15 (100.0)	

DISCUSSION

The study evaluated 53 patients with removable partial dentures, with 25 males and 28 females. Studies show that female patients are more likely to suffer from tooth loss and manage with partial dentures, with varying satisfaction rates across different studies, such as Ibrahim LM, reports the 55.9% female patients and 44.1% male patients, Salih HA, et al., reported the 68.6% female patients and 31.4% male patients. Zlatarić DK, et al reported the 63.6% female patients and 36.4% male patients [2, 3, 14]. This research shows a significant impact of prosthetic treatments on patient satisfaction and quality of life. The study found that the majority of patients with removable partial dentures were over 40 years old (56.6%), followed by those aged 31-40 years (37.5%), and only 5.7% were in the 20-30 age group corresponding to studies by Salih HA 45.42 ± 0.682 years, Aljabri MK 51.18 ± 13.06 years, Almohsen & Mahmoud 52.25 ± 1.8 years 10 and Cosme et al., reports the 96.0% patients having age > 40 years [3, 11, 15, 16]. The study analyzed patients with removable partial dentures based on Kennedy Classification, with the majority in Kennedy Class 3 (43.4%) patients, followed by Kennedy class 1 having 15 (28.3%) patients, Kennedy class 2 having 10 (18.9%) patients and Kennedy class 4 having 5 (9.4%) patients. A study by Cosme et al., reports the Kennedy class 1 in 40.0% patients followed by Kennedy class 4 in 4.0% patients and Kennedy class 2 in 2.0% patients [16]. Removable partial dentures (RPDs) offer advantages like easy manufacturing and minimally invasive treatment, but they still cause oral issues like mastication, speaking, pain, and aesthetic concerns. Research shows a significant impact of prosthetic treatments on patient satisfaction and quality of life [17]. The study found that patients with removable partial dentures had a mean SAPS score of 9.98 ± 2.79 at baseline and 10.0 ± 2.79 after two months. Most patients (41.5%) and 39.6% were very satisfied, followed by satisfied (30.2%) and not satisfied (28.1%) patients. SAPS was significantly different among Kennedy Classifications at the time of insertion and after two months this aligns with study by Aljabri MK and Almohsen & Mahmoud [11, 15]. Removable partial dentures are a cost-effective, reversible treatment for partial tooth loss, aiming to improve aesthetics, speech, chewing, self-assurance, and psychological well-being [18]. Acrylic resin-based RPDs are preferred in poorer areas due to cost and ease of fabrication [19]. Removable Partial Dentures (RPDs) offer

advantages like easy manufacturing and minimally invasive treatment, but they still cause oral issues like mastication, speaking, pain, and aesthetic concerns [20, 21]. This study was conducting for short duration. Further observation is required. This is Single institute based study with small sample size and high margin of errors.

This study was conducted over a short duration and at a single institution with a relatively small sample size, which may limit the generalizability of the findings. Additionally, the small cohort may introduce a higher margin of error in the results. Future studies should be conducted on larger, multicenter populations with longer follow-up periods to better assess long-term patient satisfaction and prosthetic outcomes. Inclusion of broader demographic and clinical variables would further strengthen the evidence.

CONCLUSIONS

This study concluded that the majority of patients expressed satisfaction with Mandibular Removable Partial Dentures; nonetheless, a notable disparity existed in the Subjective Assessment of Prosthesis Satisfaction across various Kennedy classifications.

Authors' Contribution

Conceptualization: SB

Methodology: SB, A

Formal analysis: IQ, FJ

Writing and Drafting: SZ, UBS, IQ, FJ

Review and Editing: SB, SZ, UBS, A, IQ, FJ

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article


Analytical Study of Beneficial Effects of Magnesium Sulfate for the Neuroprotection in Pre-Term Babies in Tertiary Care Hospital Bahawalpur

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ABSTRACT

Neonatal morbidity and mortality are greatly influenced by preterm birth. Magnesium sulfate (MgSO₄) has been suggested as a neuroprotective therapy to reduce the negative consequences on neurodevelopment in preterm infants. **Objective:** To investigate how MgSO₄ works to reduce the incidence of cerebral palsy as well as other neurodevelopmental impairments in preterm infants. **Methods:** This quasi experimental study was conducted at Tertiary Care Hospital Bahawalpur in the Department of Obstetrics and Gynecology from September 30, 2022 to March 29, 2023. This research involved 312 preterm infants. The infants were divided to a group of treatment with MgSO₄ or compared with a group without MgSO₄ exposure. The incidence of intraventricular hemorrhage (IVH), need for mechanical ventilation, neonatal mortality, as well as cerebral palsy were also measured and compared between the groups using Chi-square and T-tests. **Results:** The administration of MgSO₄, dramatically reduced the rate of IVH (6.4%, 16%, $p = 0.007$ respectively treatment and control group) and neonatal mortality (3.2%, 10.3%, $p = .013$). It did not significantly affect the need for mechanical ventilation. This proved to be effective in reducing cerebral palsy by 21.8 percentage points (4.5% vs 26.3%, $p < 0.001$). **Conclusion:** MgSO₄ administration antenatally greatly decreases the risks of IVH and neonatal mortality while decreasing the incidence of cerebral palsy in preterm infants, thereby resulting more to be a 'gold standard' neuroprotective strategy in prenatal care.

INTRODUCTION

Preterm birth, defined as delivery prior to 37 weeks of gestation, remains a significant global health challenge, accounting for a considerable proportion of neonatal morbidity and mortality. It is closely associated with long-term neurodevelopmental impairments, including cerebral palsy (CP), cognitive deficits, and sensory dysfunction. These outcomes impose a profound burden on healthcare systems and families, particularly in low- and middle-income countries where neonatal intensive care resources are limited [1]. Among the strategies employed to mitigate these adverse outcomes, antenatal administration of

magnesium sulfate (MgSO₄) has emerged as a widely recommended and evidence-based neuroprotective intervention for fetuses at risk of preterm birth [2]. Its protective role is primarily mediated through multiple biochemical and physiological mechanisms. These include blockade of N-methyl-D-aspartate (NMDA) receptors, antagonism of calcium influx into neurons, attenuation of oxidative stress, and modulation of excitatory neurotransmission all of which serve to prevent hypoxic-ischemic injury and stabilize the immature brain environment [3]. The efficacy of MgSO₄ in reducing the

incidence of CP and enhancing survival without major neurological impairment has been consistently demonstrated. For example, Gupta et al., (2021) found that antenatal MgSO₄ significantly lowered the risk of cerebral palsy in preterm infants when administered before early delivery [4]. Similarly, Oddie in (2015) evaluated the use of antenatal magnesium sulfate for neuroprotection in preterm infants, highlighting its potential to reduce the risk of cerebral palsy. [5]. Hurion in (2023) declared that the SuPreme Study outlined a protocol to investigate whether sulfate is the key neuroprotective component in antenatal magnesium sulfate therapy for very/extremely preterm infants [6]. These findings have reinforced guideline recommendations from bodies such as the American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO), which advocate MgSO₄ use in women at risk of imminent preterm delivery before 34 weeks [7, 8]. Despite this, clinical implementation in low-resource settings remains inconsistent. The majority of existing studies have focused on high-income populations, with a lack of regional data from South Asia—particularly Pakistan—limiting the generalizability of these findings. Furthermore, the literature remains underdeveloped in terms of subgroup analysis based on maternal comorbidities, fetal sex, and gestational age [9, 10]. Emerging pharmacokinetic data suggest that treatment success depends on achieving adequate serum magnesium concentrations, balanced against potential risks such as neonatal electrolyte disturbances [11]. While adverse effects like transient hyperkalemia or hypocalcemia have been observed, they are usually self-limiting and manageable within neonatal care settings [12, 13]. Although the neuroprotective benefits of antenatal magnesium sulfate are well-established in high-income countries, there remains a significant gap in the literature from low- and middle-income regions, particularly South Asia. Current evidence is largely derived from Western populations with advanced neonatal intensive care systems, which may not reflect the realities of resource-constrained settings like Pakistan. Furthermore, there is limited data analyzing the stratified effects of MgSO₄ across different maternal comorbidities, fetal sexes, and degrees of prematurity factors that may influence outcomes but are often underreported. Given the high burden of preterm birth in Pakistan and the scarcity of local, context-specific evidence, this study was undertaken to evaluate the effectiveness of antenatal MgSO₄ for fetal neuroprotection in a tertiary care setting. By addressing this critical gap, the study aims to generate actionable insights tailored to the unique demographic, clinical, and infrastructural realities of developing countries. The findings of this study have the potential to inform national perinatal care guidelines, encourage

standardized use of MgSO₄ for neuroprotection in preterm labor, and improve neonatal outcomes by preventing cerebral palsy and other severe neurological complications. If proven effective within the local context, MgSO₄ administration could serve as a cost-effective, scalable intervention to reduce long-term disability and neonatal mortality in Pakistani healthcare settings.

METHODS

This quasi experimental was conducted at the Department of Obstetrics and Gynecology, Tertiary Care Hospital Bahawalpur, from September 30, 2022, to March 29, 2023. The primary objective was to evaluate the effectiveness of antenatal magnesium sulfate (MgSO₄) administration for fetal neuroprotection in women at risk of preterm delivery, with key neonatal outcomes including intraventricular hemorrhage (IVH), need for mechanical ventilation, neonatal mortality, and the incidence of cerebral palsy (CP). Based on the findings by Bansal and Desai who observed a reduction in IVH from 16% in the non-treated group to 8% in the MgSO₄-treated group, a total sample size of 312 participants (156 per group) was calculated to achieve a statistical power of 70% and an alpha of 0.10 [14]. Participants were recruited using a non-probability consecutive sampling technique. Women who met the eligibility criteria were divided into the treatment or control group using the lottery method. The study received ethical approval from the Ethical Committee of Combined Military Hospital Bahawalpur (Ref: EC-18-2022). Written informed consent was obtained from all participants after a thorough explanation of the study's aims, procedures, and potential risks. Confidentiality was strictly maintained. Inclusion criteria required participants to be pregnant women aged 18 to 45 years, with a gestational age between 26 weeks and 36 weeks + 6 days, confirmed by early ultrasound or reliable last menstrual period. Participants had to be at risk of imminent preterm delivery, defined by clinical evidence of spontaneous preterm labor (regular contractions and cervical dilation ≥ 3 cm), preterm premature rupture of membranes (PPROM), or medically indicated preterm delivery due to maternal or fetal complications such as preeclampsia or intrauterine growth restriction. Both singleton and twin pregnancies were included, provided the mother was hemodynamically stable and capable of receiving intravenous treatment. Exclusion criteria included known allergy or hypersensitivity to MgSO₄, severe renal dysfunction (serum creatinine >1.5 mg/dL or oliguria <30 mL/h), neuromuscular disorders such as myasthenia gravis, cardiac conduction abnormalities, recent MgSO₄ use for other obstetric indications, intrauterine fetal demise, and any major fetal congenital anomalies identified antenatally. Women with urgent medical or surgical conditions requiring immediate delivery were also excluded, as were those unable or unwilling to provide informed consent. Women in the

intervention group received a 4 g IV bolus of MgSO₄ administered over 20–30 minutes, followed by a 1 g/hour maintenance infusion for up to 12 hours or until delivery. The control group received a matched volume of normal saline placebo, administered in an identical manner. Both groups received standard obstetric and neonatal care throughout. Data collection was carried out using a structured and pre-tested proforma, including demographic details such as maternal age, gestational age at delivery, birth weight, and infant sex. Clinical outcomes were assessed based on standardized definitions. Cerebral palsy was diagnosed during follow-up visits using criteria established by the Surveillance of Cerebral Palsy in Europe (SCPE), which includes the presence of abnormal muscle tone, delayed developmental milestones, and persistent motor dysfunction at or after 6 months of age [15]. Intraventricular hemorrhage was diagnosed and graded using cranial ultrasonography based on the Papile classification system [16], and all scans were interpreted by neonatologists blinded to group assignment. Neonatal mortality was defined as death within the first 28 days of life, while the need for mechanical ventilation was recorded from NICU records and defined as the requirement for invasive respiratory support within the first 72 hours after birth. All data were analyzed using SPSS version 25.0. Descriptive statistics were computed for demographic variables. Categorical variables such as IVH, CP, mechanical ventilation, and mortality were analyzed using Chi-square tests, while continuous variables like birth weight and maternal age were assessed using independent-sample t-tests. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The descriptive statistics for the study population (n = 312) are as follows: The mean gestational age was 30.00 ± 1.95 weeks, and the average birth weight was 1500.26 ± 196.81 grams. The mean maternal age was 30.75 ± 4.76 years.

These baseline characteristics provide a demographic overview of the preterm cohort enrolled in the study. The comparison of key neonatal outcomes between the magnesium sulfate (MgSO₄) treatment and control groups demonstrated a significant benefit of antenatal MgSO₄ administration in reducing several critical complications associated with preterm birth. A notable reduction in intraventricular hemorrhage (IVH) was observed in the treatment group (6.4%) compared to the control group (16.0%), with a statistically significant risk difference of 9.6% (95% CI: 2.7% to 16.5%), confirming a protective neurological effect. Similarly, the incidence of neonatal mortality was significantly lower in the MgSO₄ group (3.2%) versus controls (10.3%), corresponding to a risk difference of 7.1% (95% CI: 1.5% to 12.6%), indicating a meaningful improvement in survival among preterm neonates receiving neuroprotective therapy. The most pronounced benefit was seen in the reduction of cerebral palsy, where the treatment group had only 4.5% affected compared to 26.3% in the control group. This yielded a risk difference of 21.8% (95% CI: 14.2% to 29.4%), strongly supporting MgSO₄'s role in preventing long-term neuromotor impairment. In contrast, the need for mechanical ventilation was slightly higher in the treatment group (22.4%) than in controls (16.0%). This resulted in a negative risk difference of -6.4% (95% CI: -15.1% to 2.3%), suggesting that more neonates in the MgSO₄ group required respiratory support. However, this difference was not statistically significant (p = 0.151), and the confidence interval includes zero, indicating the observed increase may be due to chance rather than a treatment-related effect. Overall, the risk difference estimates and corresponding confidence intervals reinforce the conclusion that antenatal MgSO₄ confers substantial neuroprotective benefits particularly in reducing IVH, neonatal mortality, and cerebral palsy – with no conclusive evidence of harm in terms of respiratory outcomes. (Table 1).

Table 1: Comparison of Neonatal Outcomes between Treatment and Control Groups

Outcome	Group	Yes Frequency (%)	No Frequency (%)	p-Value	Risk Difference (%)	95% Confidence Interval
IVH	Treatment	10 (6.4%)	146 (93.6%)	0.007	9.6	2.7 to 16.5
	Control	25 (16.0%)	131 (84.0%)			
Mechanical Ventilation	Treatment	35 (22.4%)	121 (77.6%)	0.151	-6.4	-15.1 to 2.3
	Control	25 (16.0%)	131 (84.0%)			
Neonatal Mortality	Treatment	5 (3.2%)	151 (96.8%)	0.013	7.1	1.5 to 12.6
	Control	16 (10.3%)	140 (89.7%)			
Cerebral Palsy	Treatment	7 (4.5%)	149 (95.5%)	0.001	21.8	14.2 to 29.4
	Control	41 (26.3%)	115 (73.7%)			

Gender-based stratification of outcomes is detailed in table 2.

Table 2: Outcome Variables Stratified by Gender of Preterm Baby

Gender	Study Group	IVH Yes Frequency (%)	IVH No Frequency (%)	Total	P-value
Male	Treatment Group	4 (4.65%)	82 (95.35%)	86	0.018
Male	Control Group	12 (15.79%)	64 (84.21%)	76	

Female	Treatment Group	6 (8.57%)	64 (91.43%)	70	0.158
Female	Control Group	13 (16.25%)	67 (83.75%)	80	
Male	Treatment Group	14 (16.28%)	72 (83.72%)	86	0.932
Male	Control Group	12 (15.79%)	64 (84.21%)	76	
Female	Treatment Group	21 (30.00%)	49 (70.00%)	70	0.045
Female	Control Group	13 (16.25%)	67 (83.75%)	80	
Male	Treatment Group	3 (3.49%)	83 (96.51%)	86	0.043
Male	Control Group	9 (11.84%)	67 (88.16%)	76	-
Female	Treatment Group	2 (2.86%)	68 (97.14%)	70	0.129
Female	Control Group	7 (8.75%)	73 (91.25%)	80	-
Male	Treatment Group	3 (3.49%)	83 (96.51%)	86	<0.001
Male	Control Group	25 (32.89%)	51 (67.11%)	76	-
Female	Treatment Group	4 (5.71%)	66 (94.29%)	70	0.010
Female	Control Group	16 (20.00%)	64 (80.00%)	80	-

Among male preterm infants, MgSO₄ treatment was associated with significant reductions in IVH (4.65% vs. 15.79%, $p = 0.018$), neonatal mortality (3.49% vs. 11.84%, $p = 0.043$), and cerebral palsy (3.49% vs. 32.89%, $p < 0.001$). No significant difference was observed in mechanical ventilation need ($p = 0.932$). Among female infants, a significant reduction in cerebral palsy was also observed in the treatment group (5.71% vs. 20.00%, $p = 0.010$). However, the requirement for mechanical ventilation was significantly higher in treated females (30.00% vs. 16.25%, $p = 0.045$). This observation, although statistically significant, warrants cautious interpretation due to the narrow margin of significance. IVH and neonatal mortality rates in female infants did not differ significantly between groups ($p = 0.158$ and $p = 0.129$, respectively). Outcomes stratified by maternal health conditions are shown in Table 3. A statistically significant reduction in IVH was observed in neonates born to mothers with diabetes mellitus (4.17% vs. 26.09%, $p = 0.035$). While neonates of mothers with no disease also showed lower IVH rates in the MgSO₄ group (6.96% vs. 14.68%), the difference was not statistically significant ($p = 0.062$). No meaningful differences were found in mechanical ventilation need across maternal subgroups: no disease ($p = 0.430$), diabetes ($p = 0.477$), or preeclampsia ($p = 0.175$). Neonatal mortality also did not differ significantly by maternal health status, although the “no disease” group trended toward lower mortality in the treatment arm ($p = 0.061$). Significant reductions in cerebral palsy were seen among neonates of mothers with no disease ($p < 0.001$) and those with preeclampsia ($p = 0.014$), indicating subgroup-specific neuroprotective effects of MgSO₄.

Table 3: Outcome Variables Stratified By Maternal Health Conditions

Maternal Health Condition	Study Group	IVH Yes Frequency (%)	IVH No Frequency (%)	Total	P-value
No Disease	Treatment Group	8 (6.96%)	107 (93.04%)	115	0.062
	Control Group	16 (14.68%)	93 (85.32%)	109	
Diabetes Mellitus	Treatment Group	1 (4.17%)	23 (95.83%)	24	0.035
	Control Group	6 (26.09%)	17 (73.91%)	23	
Preeclampsia	Treatment Group	1 (5.88%)	16 (94.12%)	17	0.482
	Control Group	3 (12.50%)	21 (87.50%)	24	
No Disease	Treatment Group	26 (22.61%)	89 (77.39%)	115	0.430
	Control Group	20 (18.35%)	89 (81.65%)	109	
Diabetes Mellitus	Treatment Group	5 (20.83%)	19 (79.17%)	24	0.477
	Control Group	3 (13.04%)	20 (86.96%)	23	
Preeclampsia	Treatment Group	4 (23.53%)	13 (76.47%)	17	0.175
	Control Group	2 (8.33%)	22 (91.67%)	24	
No Disease	Treatment Group	3 (2.61%)	112 (97.39%)	115	0.061
	Control Group	9 (8.26%)	100 (91.74%)	109	
Diabetes Mellitus	Treatment Group	1 (4.17%)	23 (95.83%)	24	0.276
	Control Group	3 (13.04%)	20 (86.96%)	23	
Preeclampsia	Treatment Group	1 (5.88%)	16 (94.12%)	17	0.299
	Control Group	4 (16.67%)	20 (83.33%)	24	
No Disease	Treatment Group	5 (4.35%)	110 (95.65%)	115	0.000
	Control Group	29 (26.61%)	80 (73.39%)	109	
Diabetes Mellitus	Treatment Group	2 (8.33%)	22 (91.67%)	24	0.197
	Control Group	5 (21.74%)	18 (78.26%)	23	

Preeclampsia	Treatment Group	0 (0%)	17 (100%)	17	0.014
	Control Group	7 (29.17%)	17 (70.83%)	24	

DISCUSSION

This study investigated the neuroprotective role of antenatal magnesium sulfate (MgSO_4) in preterm infants and revealed significant improvements in several key neonatal outcomes. Notably, MgSO_4 administration was associated with a significant reduction in intraventricular hemorrhage (IVH) (6.4% vs. 16.0%, $p = 0.007$), neonatal mortality (3.2% vs. 10.3%, $p = 0.013$), and cerebral palsy (4.5% vs. 26.3%, $p < 0.001$). The strongest effect was observed in reducing cerebral palsy, with a 21.8% absolute risk reduction (95% CI: 14.2% to 29.4%). While the need for mechanical ventilation was slightly higher in the treatment group (22.4% vs. 16.0%), the difference was not statistically significant ($p = 0.151$). Gender-based stratification showed more pronounced benefits in male infants, while female infants exhibited a higher rate of mechanical ventilation following treatment. Subgroup analysis by maternal comorbidities confirmed the neuroprotective effect of MgSO_4 in reducing cerebral palsy among neonates of mothers with no disease and preeclampsia, and in lowering IVH in infants of diabetic mothers. Our findings are consistent with those of Bansal and Desai (2021), who reported a decrease in IVH incidence from 16% in untreated infants to 8% in those receiving MgSO_4 [14]. Cans C in (2000) presented data from European cerebral palsy (CP) registries, improving surveillance and understanding of CP prevalence and patterns across Europe [15]. Papile LA et al., identified the incidence and grading of subependymal and intraventricular hemorrhage in very low birth weight infants, forming the basis for the Papile classification [16]. Chollat C et al., reviewed bridges translational research and clinical practice, discussing the mechanisms and evidence supporting magnesium sulfate's neuroprotective role in preterm infants [17]. Monteagudo BF et al., evaluated the neuroprotective impact of antenatal magnesium sulfate in preterm infants after implementing a standardized administration protocol in a tertiary hospital [18]. The pronounced reduction in cerebral palsy observed in our study parallels the findings of Crowther et al., who confirmed MgSO_4 's effectiveness in lowering cerebral palsy risk through meta-analysis [19]. The robust neuroprotective effect we observed supports its inclusion in preterm labor protocols. Interestingly, our study identified gender-specific differences, particularly a higher incidence of mechanical ventilation in treated female neonates. This echoes the hypothesis presented by McLeod et al., who suggested that male and female fetuses may respond differently to MgSO_4 due to neurobiological and hormonal factors [20]. Such differential responses merit further investigation. Subgroup findings in our study also support those of Burhouse et al., who emphasized the feasibility and success of integrating MgSO_4 protocols in

diverse clinical settings, including those with maternal comorbidities [21]. The reduction in cerebral palsy among neonates of mothers with preeclampsia in our study further affirms MgSO_4 's protective role across risk profiles. Safety remains a crucial aspect of MgSO_4 use. Our study did not report any treatment-related complications, aligning with prior literature indicating minimal maternal or neonatal side effects when MgSO_4 is administered with proper monitoring [14]. Moreover, as noted by Ayed et al., timing is critical, with administration ideally occurring 4–6 hours prior to delivery for optimal neuroprotection [22]. While our study did not analyze timing in depth, we adhered to this recommended window in most cases. In summary, our findings reinforce the evidence supporting MgSO_4 as a safe and effective neuroprotective intervention in preterm infants. Its use significantly reduces IVH, neonatal mortality, and cerebral palsy, especially in specific subgroups. These results advocate for the broader implementation of MgSO_4 protocols, particularly in resource-limited settings, and emphasize the need for further studies to optimize dosage, timing, and subgroup-specific effects.

This study is limited by its single-center design and relatively small sample size, which may affect the generalizability of the findings. In addition, limited analysis of dosing timing and long-term neurodevelopmental follow-up restricts deeper evaluation of magnesium sulfate outcomes. Future multicenter, large-scale studies with long-term follow-up are recommended to further validate neurodevelopmental outcomes and optimize timing and dosing protocols of antenatal magnesium sulfate. Further research should also explore gender-based differences in response to treatment.

CONCLUSIONS

This study demonstrated that antenatal administration of magnesium sulfate significantly reduces the incidence of intraventricular hemorrhage, neonatal mortality, and cerebral palsy in preterm infants. The treatment was especially effective in male neonates and in those born to mothers without comorbidities or with preeclampsia. No significant impact was found on the need for mechanical ventilation. These findings support the inclusion of MgSO_4 in clinical protocols for neuroprotection in preterm deliveries.

Authors' Contribution

Conceptualization: SB

Methodology: VA, SM

Formal analysis: SU

Writing and Drafting: RS, SZC, VA, SM

Review and Editing: SB, SU, RS, SZC, VA, SM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Etiology of Short Stature in Children Presenting At a Tertiary Care Hospital

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ABSTRACT

Short stature is frequently a rationale for consultation with pediatric endocrinology departments. It may arise from a multitude of origins, encompassing both physiological variations and pathological conditions. **Objective:** To ascertain the prevalence of various etiologies of short stature in pediatric patients attending a tertiary care medical facility. **Methods:** This cross-sectional study was carried out within the Pediatric Department of Shalamar Hospital, Lahore from August 2024 to February 2025. Subjects comprised 180 children exhibiting short stature as per operational definition, height falling beneath the 3rd percentile or two standard deviations below the mean corresponding to age and gender, included via non-probability consecutive sampling. Comprehensive history taking, physical assessments, anthropometric evaluations, and pertinent diagnostic tests were conducted. Data were analyzed using SPSS version 25.0 and various etiologies of short stature were presented as percentages and frequencies. Data were stratified by age, gender, residence, and socioeconomic status. **Results:** Familial Short Stature (FSS) constituted the predominant diagnosis among the pediatric population, impacting 20.6% of the subjects, followed closely by Constitutional Delay of Growth and Maturation (CDGM) and Primary Malnutrition, each accounting for 16.1%. Growth Hormone Deficiency (GHD) was identified in 15.6% of cases, while Hypothyroidism was present in 11.1%. Less prevalent etiologies included Celiac Disease (8.3%), Type 1 Diabetes Mellitus (T1DM) (7.8%), and Turner Syndrome, which affected 4.4% of the cohort. **Conclusions:** The main causes of short stature in children are familial and constitutional growth delay, along with endocrine disorders like hypothyroidism and growth hormone deficiency. Timely intervention is essential for optimal growth potential.

INTRODUCTION

Short stature, characterized as a measurement falling beneath the 3rd percentile or exceeding 2 standard deviations below the normative mean for age and sex, is modulated by an array of genetic, environmental, nutritional, and endocrinological determinants that affect growth on a global scale [1, 2]. Short stature negatively affect the health related quality of life [3]. Globally, around 144.0 million children under five suffer from short stature [4]. In Pakistan, UNICEF reports that 38% of children under 5 are stunted [5]. Common causes include idiopathic short stature such as familial short stature and constitutional growth and maturation delay [6, 7]. A comprehensive review explored the causes, diagnostic approach, and clinical evaluation of short stature in children [8].

Constitutional growth and maturation delay: growth velocity is normal, bone age corresponds with height age but is less than chronological age, and there is a delayed onset of puberty with a family history. Familial short stature: no delay in bone age, normal growth velocity, and a final height that is short yet remains within the target height range [9]. Additional etiologies: chronic illnesses, endocrine abnormalities, skeletal dysplasias, and genetic or chromosomal anomalies [10-13]. In a study, the prevalent etiologies of reduced stature encompassed Familial Short Stature (FSS) at 21.3%, hypothyroidism at 17.2%, Growth Hormone Deficiency (GHD) at 10.7%, Type 1 Diabetes Mellitus (T1DM) at 9.5%, Constitutional Delay of Growth and Maturation (CDGM) at 6.5%, primary malnutrition at 4.7%,



celiac disease at 3.6%, and Turner syndrome at 3% [10]. In an alternative study, the distribution of different etiologies of short stature was elucidated: 11.8% exhibited a deficiency in growth hormone, 42% were classified as having familial short stature, 15.8% demonstrated constitutional growth delay, and 6.6% were diagnosed with celiac disease [14, 15].

Data on short stature etiology in Pakistan is scarce. Being a resource-limited developing country, over a third of children under 5 are stunted. Short stature commonly prompts emotional and social stress in children, motivating my study on identifying and preventing its causes by age group. The aim was to decrease disease burden and improve quality of life by addressing avoidable factors leading to short stature promptly.

METHODS

The study was conducted at the Department of Pediatrics, Shalamar Hospital Lahore, over a period of 6 months from August 2024 to February 2025. A cross-sectional study design was employed with non-probability consecutive sampling technique. A sample size of 180 children was calculated using 3% prevalence of Turner syndrome as reported in a study using formula for single proportion with 95% confidence interval and 2.5% margin of error [10]. The investigation encompassed children aged 3 to 12 years of both gender presenting with short stature, operationally defined as height or length falling below the 3rd percentile on the CDC growth charts or below 2 standard deviations on the WHO charts, adjusted for age and sex. Children exhibiting contractures, scoliosis, kyphosis, or abnormalities of the lower limbs were systematically excluded from participation in the study. The research protocol received ethical clearance from the Hospital Ethical Committee of Shalamar Medical and Dental College, Lahore (IRB no 0794) and written informed consent was procured from the parents or guardians of the pediatric subjects prior to enrollment. Comprehensive demographic and clinical data were gathered for each participant. Standing height was assessed without footwear or headgear utilizing a stadiometer and subsequently plotted on the relevant CDC or WHO growth charts. Target height was computed employing the mid-parental height formula: $[(\text{father's height in cm}) + (\text{mother's height in cm}) + 13] \div 2$ for male subjects, and $[(\text{father's height in cm}) - 13 + (\text{mother's height in cm})] \div 2$ for female subjects. The upper to lower segment ratio (US/LS) was calculated by deducting sitting height from standing height. Weight was measured accurately using an electronic scale. Parents were requested to provide historical medical records. Laboratory investigations encompassed a complete blood count, Erythrocyte Sedimentation Rate (ESR), urinalysis, hepatic and renal function tests, bone metabolism parameters, Anti-tTG IgA and IgG, free T4, and Thyroid-Stimulating Hormone (TSH).

Elevated levels of Anti-tTG prompted further evaluation via duodenal biopsy. Additionally, hand and wrist radiographs were analyzed for signs of rickets and to estimate bone age, utilizing the Greulich and Pyle Atlas as a reference tool. Short stature causes categorized as follows: Familial Short Stature (FSS) – bone age equals or exceeds chronological age, both above height age; Hypothyroidism – Free T4 < 0.93ng/dL, TSH > 6.4 uIU/ml; Growth Hormone Deficiency (GHD) – levels < 10ng/ml on insulin stress test; Type 1 diabetes mellitus (T1DM) – HbA1c ≥ 6.5%; Constitutional delay of growth and maturation (CDGM) – bone age equals or below height age, both under chronological age; Primary malnutrition – weight < 60% of expected per NCHS standards, history of reduced caloric intake; Celiac disease – duodenal mucosal changes in biopsy, transglutaminase antibodies raised (IgA > 7U/ml, IgG > 17U/ml); Turner syndrome – short neck, low set ears, shield-like chest, and 44A+OX genotype. Growth hormone deficiency was assessed with insulin tolerance test in those children with strong clinical suspicion and all baseline investigations were normal. The blood glucose level was checked at baseline via glucometer and rapid acting insulin given at a dose of 0.1IU/kg intravenously. Blood samples for blood glucose and serum growth hormone were drawn at 0, 30, 60, 90 and 120 minutes and values below 10ng/ml were considered growth hormone deficient. Data collected were analyzed using SPSS version 25.0 to present mean ± standard deviation for quantitative variables like age, height, and weight. Qualitative data such as gender, socio-economic status, residence, and causes of short stature were shown as frequencies and percentages. Stratification based on gender, age, residence, and socio-economic status was done to address effect modifiers. Chi-square tests were used to assess associations between categorical variables. Where expected cell counts were below 5, Fisher's Exact Test was applied instead. In cases where subgroup sizes were too small to meet test assumptions and could not be meaningfully grouped, results were interpreted with caution, a significance threshold of $p \leq 0.050$ was applied post-stratification.

RESULTS

The study comprised 94 males (52.2%) and 86 females (47.8%). Regarding age distribution, 112 children (62.2%) were between 7-12 years, while 68 children (37.8%) were between 3-6 years, with a mean age of 7.47 ± 2.54 years. Most participants (73.9%) resided in rural areas, with only 26.1% from urban settings. The socioeconomic status distribution showed that 43.3% belonged to low socioeconomic status, 38.9% to middle, and 17.8% to high socioeconomic status. Among the causes of short stature, Familial Short Stature (FSS) was the most prevalent, affecting 37 children (20.6%), followed by Constitutional Delay of Growth and Maturation (CDGM) and Primary Malnutrition, each accounting for 29 cases (16.1%). Growth Hormone Deficiency (GHD) was identified in 28 children

(15.6%), while Hypothyroidism was diagnosed in 20 children (11.1%). Less common causes included Celiac Disease (8.3%), Type 1 Diabetes Mellitus (T1DM) (7.8%), and Turner Syndrome, which was the least common cause, affecting only 8 children (4.4%).

Table 1: Frequency Distribution of Different Variables (n=180)

Variables	Categories	Frequency (%) / Mean $\pm$ SD
Gender	Male	94 (52.2)
	Female	86 (47.8)
Age Groups	3-6 Years	68 (37.8)
	7-12 Years	112 (62.2)
	Mean Age (Years)	7.47 $\pm$ 2.54
Residence	Rural	133 (73.9)
	Urban	47 (26.1)
Socio-Economic Status	Low	78 (43.3)
	Middle	70 (38.9)
	High	32 (17.8)
	Familial Short Stature (FSS)	37 (20.6)

Causes of Short Stature	Growth Hormone Deficiency (GHD)	28 (15.6)
	Constitutional delay of growth and maturation (CDGM)	29 (16.1)
	Primary Malnutrition	29 (16.1)
	Hypothyroidism	20 (11.1)
	Type 1 Diabetes Mellitus (T1DM)	14 (7.8)
	Celiac Disease (CD)	15 (8.3)
	Turner Syndrome	8 (4.4)

Tables 2-5 presented the stratification of various causes of short stature with respect to gender, age groups, residence, and socio-economic status among the 180 children included in the study. Table 2 compares short stature causes between males and females, noting no significant differences except for T1DM and Turner syndrome. Type 1 Diabetes Mellitus (T1DM) was more common in males (11.7% vs. 3.5%), while Turner syndrome only occurred in females.

Table 2: Stratification of causes of short stature with respect to gender

Causes of Short Stature	Categories	Gender		p-Value
		Male Frequency (%)	Female Frequency (%)	
Familial Short Stature (FSS)	Yes	19 (20.2)	18 (20.9)	0.905 ^a
	No	75 (79.8)	68 (79.1)	
Growth Hormone Deficiency (GHD)	Yes	15 (16.0)	13 (15.1)	0.876 ^a
	No	79 (84.0)	73 (84.9)	
Constitutional delay of growth and maturation (CDGM)	Yes	14 (14.9)	15 (17.4)	0.642 ^a
	No	80 (85.1)	71 (82.6)	
Primary Malnutrition	Yes	15 (16.0)	14 (16.3)	0.953 ^a
	No	79 (84.0)	72 (83.7)	
Hypothyroidism	Yes	12 (12.8)	8 (9.3)	0.460 ^a
	No	82 (87.2)	78 (90.7)	
Type 1 Diabetes Mellitus (T1DM)	Yes	11 (11.7)	3 (3.5)	0.051 ^b
	No	83 (88.3)	83 (96.5)	
Celiac Disease (CD)	Yes	8 (8.5)	7 (8.1)	0.928 ^b
	No	86 (91.5)	79 (91.9)	
Turner Syndrome	Yes	0 (0.0)	8 (9.3)	0.002 ^b
	No	94 (100.0)	78 (90.7)	

(^aChi-Square Test, ^bFisher Exact Test)

Table 3 showed that older kids had more growth hormone deficiency, while younger ones had more celiac disease.

Table 3: Stratification of Causes of Short Stature with Respect to Age Groups

Causes of Short Stature	Categories	Age Groups Frequency (%)		p-Value
		3-6 Years	7-12 Years	
Familial Short Stature (FSS)	Yes	13 (19.1)	24 (21.4)	0.710 ^a
	No	55 (80.9)	88 (78.6)	
Growth Hormone Deficiency (GHD)	Yes	4 (5.9)	24 (21.4)	0.005 ^b
	No	64 (94.1)	88 (78.6)	
Constitutional delay of growth and maturation (CDGM)	Yes	15 (22.1)	14 (12.5)	0.091 ^a
	No	53 (77.9)	98 (87.5)	
Primary Malnutrition	Yes	12 (17.6)	17 (15.2)	0.662 ^a
	No	56 (82.4)	95 (84.8)	

Hypothyroidism	Yes	8 (11.8)	12 (10.7)	0.828 ^a
	No	60 (88.2)	100 (89.3)	
Type 1 Diabetes Mellitus (T1DM)	Yes	3 (4.4)	11 (9.8)	0.256 ^b
	No	65 (95.6)	101 (90.2)	
Celiac Disease (CD)	Yes	12 (17.6)	3 (2.7)	0.001 ^b
	No	56 (82.4)	109 (97.3)	
Turner Syndrome	Yes	1 (1.5)	7 (6.3)	0.262 ^b
	No	67 (98.5)	105 (93.8)	

(^aChi-Square Test, ^bFisher Exact Test)

Table 4 indicated hypothyroidism was more prevalent in urban areas. Turner syndrome cases were in rural regions.

Table 4: Stratification of Causes of Short Stature with Respect to Residence

Causes of Short Stature	Categories	Residence		p-Value
		Rural Frequency (%)	Urban Frequency (%)	
Familial Short Stature (FSS)	Yes	28 (21.1)	9 (19.1)	0.781 ^a
	No	105 (78.9)	38 (80.9)	
Growth Hormone Deficiency (GHD)	Yes	20 (15.0)	8 (17.0)	0.747 ^a
	No	113 (85.0)	39 (83.0)	
Constitutional Delay of Growth and Maturation (CDGM)	Yes	25 (18.8)	4 (8.5)	0.112 ^b
	No	108 (81.2)	43 (91.5)	
Primary Malnutrition	Yes	20 (15.0)	9 (19.1)	0.510 ^a
	No	113 (85.0)	38 (80.9)	
Hypothyroidism	Yes	11 (8.3)	9 (19.1)	0.041 ^b
	No	122 (91.7)	38 (80.9)	
Type 1 Diabetes Mellitus (T1DM)	Yes	11 (8.3)	3 (6.4)	1.000 ^b
	No	122 (91.7)	44 (93.6)	
Celiac Disease (CD)	Yes	10 (7.5)	5 (10.6)	0.506 ^b
	No	123 (92.5)	42 (89.4)	
Turner Syndrome	Yes	8 (6.0)	0 (0.0)	0.114 ^b
	No	125 (94.0)	47 (100.0)	

(^aChi-Square Test, ^bFisher Exact Test)

Table 5 revealed a socio-economic link with hypothyroidism more common in high-status groups. The absence of celiac disease and Turner syndrome in high-status groups was noteworthy. These findings support previous research on short stature causes across demographics, such as the male predominance in type 1 diabetes and the higher hypothyroidism prevalence in urban and high-status children, possibly due to better healthcare access.

Table 5: Stratification of Causes of Short Stature with Respect to Socio-Economic Status

Causes of Short Stature	Categories	Socio-Economic Status			p-Value
		Low Frequency (%)	Middle Frequency (%)	High Frequency (%)	
Familial Short Stature (FSS)	Yes	14 (17.9)	16 (22.9)	7 (21.9)	0.746 ^a
	No	64 (82.1)	54 (77.1)	25 (78.1)	
Growth Hormone Deficiency (GHD)	Yes	10 (12.8)	12 (17.1)	6 (18.8)	0.661 ^a
	No	68 (87.2)	58 (82.9)	26 (81.3)	
Constitutional Delay of Growth and Maturation (CDGM)	Yes	15 (19.2)	8 (11.4)	6 (18.8)	0.394 ^a
	No	63 (80.8)	62 (88.6)	26 (81.3)	
Primary Malnutrition	Yes	15 (19.2)	11 (15.7)	3 (9.4)	0.440 ^a
	No	63 (80.8)	59 (84.3)	29 (90.6)	
Hypothyroidism	Yes	7 (9.0)	5 (7.1)	8 (25.0)	0.021 ^b
	No	71 (91.0)	65 (92.9)	24 (75.0)	
Type 1 Diabetes Mellitus (T1DM)	Yes	4 (5.1)	8 (11.4)	2 (6.3)	0.338 ^b
	No	74 (94.9)	62 (88.6)	30 (93.8)	
Celiac Disease (CD)	Yes	9 (11.5)	6 (8.6)	0 (0.0)	0.138 ^b
	No	69 (88.5)	64 (91.4)	32 (100.0)	
Turner Syndrome	Yes	4 (5.1)	4 (5.7)	0 (0.0)	0.399 ^b

	No	74 (94.9)	66 (94.3)	32 (100.0)	

(^aChi-Square Test, ^bFisher Exact Test)

DISCUSSION

The present study identified Familial Short Stature (FSS) as the most prevalent cause of short stature (20.6%), followed by Constitutional Delay of Growth and Maturation (CDGM) and primary malnutrition (16.1% each), Growth Hormone Deficiency (GHD) (15.6%), hypothyroidism (11.1%), celiac disease (8.3%), Type 1 Diabetes Mellitus (T1DM) (7.8%), and Turner syndrome (4.4%). These findings are consistent with several previous studies that have reported normal variants of growth as the predominant causes of short stature in children. Sultan *et al.*, conducted a study in 214 children with short stature and found that constitutional growth delay (17.3%), familial short stature (15%), malnutrition (9.8%), celiac disease (6.5%), and growth hormone deficiency (6.1%) were the five most common etiological factors [13]. Similarly, a study by Hussein *et al.*, reported that 63.6% of children with short stature had normal variants, with 42% having familial short stature, 15.8% having constitutional growth delay, and 5.5% having a combination of both [16]. A study analyzed the causes and clinical characteristics of short stature in children at a tertiary care reported most common causes were growth hormone deficiency and normal variant short stature [17]. In a recent study from Bangladesh, Karim MR *et al.*, identified familial short stature as the most common cause (51%), followed by constitutional growth delay (14%) and hypothyroidism (12%) and in another recent study conducted by Islam *et al.*, common causes were normal growth variant (59.26%) and endocrinal causes comprised (31%) [18, 19]. Another study from Bangladesh by Jasim S *et al.*, also reported familial short stature as the most common cause (20.57%), followed by hypothyroidism (13.14%) and familial short stature co-existing with nutritional problems (8.6%) [20]. However, some studies have reported different patterns. According to this study, three main etiological groups were identified normal variant of growth delay (55%), endocrinological diseases (28%) and non-endocrinological (17%) [21]. Similarly, Penugonda N *et al.*, reported that growth hormone deficiency (28%) and normal variant short stature (26%) were the predominant causes of short stature [17]. The prevalence of endocrine disorders in this study (34.5% combined for GHD, hypothyroidism, and IDDM) is higher than reported by some studies but lower than others [14, 15, 17, 21]. This variation might be attributed to differences in study settings, referral patterns, and diagnostic criteria. The findings of growth hormone deficiency in 15.6% of cases is higher than reported by Sultan *et al.*, (6.1%) but lower than reported by Penugonda N *et al.*, (28%) [13, 17]. The prevalence of hypothyroidism (11.1%) in this study reported by Islam MR and Mosharaf M (12%), and Jasim S *et al.*, (13.14%), but lower than reported by Lashari *et al.*, (15%)

[19-21]. The prevalence of celiac disease (8.3%) is higher than reported in most studies, which might reflect increased awareness and improved diagnostic facilities [18, 19, 21]. The study's limitations include its cross-sectional design hindering assessment of temporal relationships and long-term outcomes. It was conducted at a single tertiary care center, potentially causing referral bias and limiting generalizability. A small sample size of 180 children may have limited statistical power, especially for uncommon causes. Diagnostic criteria for certain conditions, like growth hormone deficiency, relied on single stimulation tests rather than multiple, affecting accuracy. Socioeconomic classification was based solely on monthly income.

The study did not consider seasonal growth variations or psychosocial factors. Despite these limitations, it offers valuable insights into short stature etiology in children at a regional tertiary care hospital. Future studies should explore natural history and treatment outcomes of short stature causes with larger samples and longer follow-up.

CONCLUSIONS

In conclusion common causes of short stature are familial and constitutional growth delay, along with endocrine disorders like hypothyroidism and growth hormone deficiency. It stresses the need for thorough evaluation, early diagnosis, and tailored interventions to enhance growth outcomes and quality of life.

Authors' Contribution

Conceptualization: AF

Methodology: AF, QUZ, HN, NM, HS

Formal analysis: AF, HN, HS

Writing and Drafting: AF, QUZ, HN, NM, HS

Review and Editing: AF, QUZ, HN, NM, HS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Prevalence of Vitamin D Deficiency in Newly Diagnosed Multiple Myeloma Patients

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ABSTRACT

Multiple Myeloma (MM) is a plasma cell disorder with skeletal complications. Vitamin D deficiency may contribute to these complications. **Objective:** To check vitamin D levels and determine the prevalence of Vitamin D deficiency in newly diagnosed MM patients. **Methods:** A prospective cross-sectional study was conducted from July 2024 till February 2025 at Liaquat National Hospital, Karachi, including 85 newly diagnosed MM patients. Serum 25-hydroxyvitamin D (25(OH)D) levels were measured. Demographic and laboratory data, including hemoglobin, calcium, creatinine, LDH, uric acid, and serum protein electrophoresis, were collected. Blood samples for vitamin D analysis were collected in red-top tubes. All the data analysis was done by IBM SPSS Version 22.0. **Results:** A total of 85 newly diagnosed MM patients (mean age: 55 ± 8.6 years) were evaluated for vitamin D deficiency. Males comprised 54 (63.5%) patients, while females accounted for 31 (36.5%). The mean vitamin D level was 21.79 ± 7.2 ng/mL. 56 (65.9%) of the patients had Vitamin D deficiency (<20 ng/mL), 22 (25.9%) had insufficiency (20-29 ng/mL), and only 7 (8.2%) had sufficient levels (≥ 30 ng/mL). Urban residents had significantly lower vitamin D levels than rural residents ($p = 0.030$). **Conclusions:** Vitamin D insufficiency was prevalent in newly diagnosed MM patients and may contribute to skeletal complications. Variations in vitamin D levels based on patient residence suggest further investigation into potential contributing factors.

INTRODUCTION

Vitamin D deficiency is a pressing international health challenge, affecting around 14% of the population worldwide. The prevalence varies across regions, with reported deficiency rates of 24%, 37%, and 40% in U.S, Canada and Europe [1]. A meta-analysis conducted by Siddiquee MH revealed that Pakistan has the highest prevalence among South Asian nations at 73%, with Bangladesh and India both at 67%, followed by Nepal at 57%, and Sri Lanka at 48% [2]. Serum Vitamin D3 levels are used to evaluate vitamin D status in clinical practice [3]. Beyond its well-established role in bone metabolism, vitamin D exhibits anti-proliferative effects on various cell types. Previous studies have shown an association between vitamin D deficiency and adverse clinical outcomes in hematological malignancies such as follicular lymphoma, Non-Hodgkin Lymphoma (NHL), and peripheral

T-cell lymphoma [4-7]. Similarly low levels of vitamin D have been linked to worse prognoses in Multiple Myeloma (MM) and solid tumors, including colorectal and breast cancers [8, 9]. MM is a malignant hematological disorder primarily affecting the elderly and is characterized by significant skeletal complications. It accounts for approximately 1-2% of all cancers and over 17% of hematological malignancies [10]. While genetic mutations have been implicated, MM is not classified as a hereditary disease. Clinically, it most often presents with bone involvement, including bone pain and pathological fractures. Given that vitamin D plays a critical role in calcium absorption and bone ossification, its deficiency could significantly contribute to the bony manifestations of MM [11, 12]. A study by Graklanov et al., involving 148 recently diagnosed MM patients, reported deficiency of vitamin D in 24% of cases [13].



Although vitamin D deficiency has been associated with adverse outcomes in multiple malignancies, its prevalence and impact in multiple myeloma patients remain underexplored in Pakistan. Moreover, no local data are available to determine vitamin D status in newly diagnosed MM patients within this population. Thus, current study aimed to measure vitamin D3 levels and determine the prevalence of vitamin D deficiency in newly diagnosed MM patients in Pakistan.

METHODS

It was a prospective descriptive cross-sectional study and carried out from July 2024 to February 2025 at the Haematology Department of Liaquat National Hospital in Karachi, Pakistan. The study was conducted after obtaining Ethical Review Committee approval from Liaquat National Hospital (Ref App No: 1027-2024-LNH-ERC). All procedures adhered to the ethical guidelines of the 1964 Helsinki Declaration and its amendments. Written informed consents were obtained from the patients before enrollment. 85 patients were included in total and calculated the sample size by using WHO sample size calculator, based on a confidence level of 95% and desired precision of 0.1% and an expected prevalence rate of vitamin D deficiency of 32.5%, as reported in similar studies of hematological malignancies. The following formula was used for the calculation [14].

$$n = \frac{Z^2 \times p(1-p)}{E^2}$$

All newly diagnosed were included MM patients presenting to the Hematology OPD at Liaquat National Hospital aged more than 18 years with no history of vitamin D3 replacement in the last one year. All patient were omitted with bone pain due to malignancies other than MM, autoimmune disorders, amyloid-related systemic diseases and patients with age-related bone changes. All newly diagnosed patients of MM presenting in hematology OPD qualify the inclusion criteria were screened for vitamin D deficiency. The samples of blood for vitamin D3 analysis were collected in red-top tubes, centrifuged at 6000 rpm and measured using the Electrochemiluminescence Immunoassay (ECLIA) on the Roche Elecsys E-411 analyzer, following the manufacturer's standardized protocol. Internal and external quality controls were run with each batch to ensure accuracy and reproducibility. Vitamin D levels were categorized based on their concentration; levels below 20ng/mL were considered deficient, those ranging from 21 to 29ng/mL were classified as insufficient, and levels of 30ng/mL or higher were regarded as normal. A structured proforma was used to collect patient information, including demographics and laboratory parameters which were Hemoglobin, vitamin D levels, serum calcium, serum creatinine, LDH, uric acid, serum protein electrophoresis, serum immunofixation, serum immunoquantification, free light chain assay, bone marrow

biopsy findings and radiographic findings (X-ray, CT, or MRI reports). All the data analysis was done by SPSS Version 22. Frequency and percentage were computed for qualitative variables like gender, residence, Vitamin D status, immunofixation, bone marrow findings and radiographic findings. Continuous variables (e.g., age, weight, height, hemoglobin, immunoquantification, free light chain assay, vitamin D levels, LDH, uric acid) were expressed in mean. Data's normality were evaluated by Shapiro-Wilk test. Stratification was performed for age, weight, gender, hemoglobin, creatinine, and calcium to evaluate their effects on the outcome. Fisher's exact test or the Chi-square test (as appropriate) were used for statistical comparisons with a $p \leq 0.050$ was considered significant.

RESULTS

85 patients were included in the study. Male patients comprised 63.5%, while females accounted for 36.5%. The overall mean age was 58.58 ± 9.24 years and the mean weight was 60.14 ± 9.02 kg. 80% of patients were from urban areas, while 20% were from rural areas. The patient's demographics and the key laboratory parameters observed in the study population are shown in Table 1.

Table 1: Frequency Distribution of Different Variables (n=180)

Demographic and Laboratory Variables	Frequency (%)
Age	
Less than 50	16 (18.8)
More than 50	69 (81.2)
Weight	
Less than 60Kg	41 (48.2)
More than 60Kg	44 (51.7)
Sex	
Male	54 (63.5)
Female	31 (36.5)
Hemoglobin	
Less than 10gm/dl	63 (74.1)
More than 10gm/dl	22 (25.8)
Residence	
Urban	68 (80)
Rural	17 (20)
Creatinine	
Less than 2gm/dl	50 (58.8)
More than 2gm/dl	35 (41.2)
Calcium	
Less than 11gm/dl	81 (95.3)
More than 11 gm/dl	4 (4.7)
Free Light Chain	
Kappa	48 (56.5)
Lambda	37 (43.5)
Immunoquantification	
IgA	17 (20)
IgM	12 (14.1)
IgG	56 (65.9)

Among the 85 patients, the distribution of immunoglobulin subtypes was as follows: IgG (65.9%), IgA (20.0%), and IgM (14.1%). Additionally, the light chain distribution showed a predominance of kappa chains (56.5%) over lambda chains (43.5%). Imaging findings were documented in 28.2% (n=24), while 71.8% had no radiographic abnormalities. Among those with imaging findings, 66.7% showed osteoclastic activity while 33.3% exhibited bone marrow infiltration. The overall mean of vitamin D3 level was 21.79 ng/mL. Based on predefined criteria 65.9% (n=56) of patients were vitamin D deficient, 25.9% (n=22) of patients had insufficient levels of vitamin D3 and 8.2% had normal vitamin D levels (n=7) (Figure 1).

Figure 1: Vitamin D3

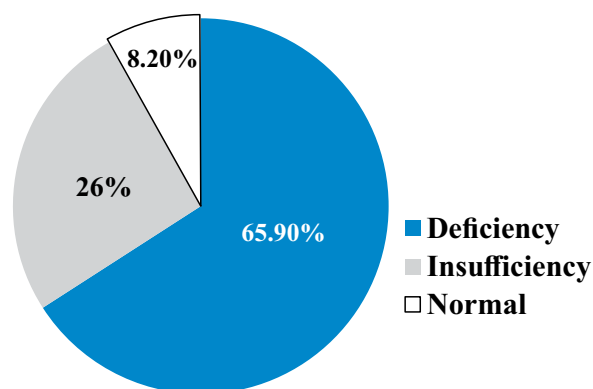


Figure 1: Status of Vitamin D3 in Multiple Myeloma Patients

A notable association of vitamin D levels was seen with place of residence ($p = 0.004$). However, no meaningful statistical relationship was identified among vitamin D levels and other demographic or laboratory variables. Findings were summarized in table 2.

Table 2: Correlation of Vitamin D Deficiency with Demographic and Laboratory Profile of Multiple Myeloma Patients

Demographic and Laboratory Parameters	Total	Vitamin D Level			p-Value
		Normal Frequency (%)	Insufficient Frequency (%)	Deficient Frequency (%)	
Number	22	6	9	7	
Age					0.820
Less than 50	16	12 (75)	3 (18.8)	1 (6.3)	
More than 50	69	44 (63.8)	19 (27.5)	6 (8.7)	
Weight					0.066
Less than 60kg	41	31 (75.6)	6 (14.6)	4 (9.8)	
More than 60kg	44	25 (56.8)	16 (36.4)	3 (6.8)	
Sex					0.719
Male	54	37 (68.5)	13 (24.1)	4 (7.4)	
Female	31	19 (61.3)	9 (29)	3 (9.7)	
Hemoglobin					0.928
Less than 10gm/dl	63	41 (65.1)	17 (27)	5 (7.9)	
More than 10gm/dl	22	15 (68.2)	5 (22.7)	2 (9.1)	
Residence					≤0.050
Urban	68	46 (67.6)	20 (29.4)	2 (2.9)	
Rural	17	10 (58.8)	2 (11.8)	5 (29.4)	
Creatinine					0.608
Less Than 2gm/dl	50	31 (62)	15 (30)	4 (8)	
More Than 2gm/dl	35	25 (71.4)	7 (20)	3 (8.6)	
Calcium					0.699
Less Than 11gm/dl	81	52 (64.2)	22 (27.2)	7 (8.6)	
More Than 11gm/dl	4	4 (100)	0 (0)	0 (0)	
Bony Lytic Lesions	16	14 (87.5)	1 (6.3)	1 (6.3)	1.000
Free Light Chain					0.443
Kappa	48	29 (60.4)	15 (31.3)	4 (8.3)	
Lambda	37	27 (73)	7 (18.9)	3 (8.1)	
Immunoquantification					0.364
IgA	17	9 (52.9)	6 (35.3)	2 (11.8)	
IgM	12	7 (58.3)	3 (25.0)	2 (16.7)	
IgG	56	40 (71.4)	13 (23.3)	3 (5.4)	
BM Plasma Cells %	85	56	27	7	0.118

DISCUSSION

Patients with Multiple Myeloma (MM) are often found to be vitamin D deficient and the incidence of this condition is impacted by both treatment-related and disease-related variables. Ismail *et al.*, 2023 meta-analysis evaluated the frequency of vitamin D inadequacy and insufficiency in MM patients worldwide. 61% of 430 patients in Europe had the greatest frequency, according to the survey. A comprehensive research conducted in North America revealed that 41% of MM patients had inadequate vitamin D and 20% had deficiency [9]. However, data from Asia and Africa remain scarce despite the vast populations of these regions. This study contributed to this dataset, revealing that 69.5% of MM patients were vitamin D deficient and 25.9% had insufficient levels. Notably, there is no association of vitamin D status with age, weight or gender, though the area of residence played a role. This could be attributed to inadequate dietary intake, limited sun exposure, and decreased vitamin D synthesis in older individuals. The findings were consistent with previous study investigating the association between vitamin D insufficiency and hemoglobin and creatinine levels [15]. Additionally, studies have identified a positive interaction between increased C-reactive protein (CRP), low albumin levels and low vitamin D levels [9]. However, this study did not explore these parameters. Similarly, another study showed an association between vitamin D deficiency and increased plasma cell counts in the bone marrow, but this was not observed in the cohort [16]. There is ongoing debate regarding the association between low vitamin D levels and International Staging System (ISS) classification in MM. While studies by Graklanov *et al.*, found no significant correlation, other reports suggest that vitamin D deficiency prevalence increases with higher ISS stages [13]. However, the research did not assess this correlation. Vitamin D insufficiency has also been implicated in musculoskeletal pain and carry an increased risk of bony fractures, which are often overlooked in MM patients due to the nature of the disease [17]. This study failed to find a significant correlation between bone lytic lesions and vitamin D levels, a finding consistent with a study conducted in Japan [18]. Nevertheless, this differs from the findings of Sfeir *et al.*, who documented a notable correlation [14]. Furthermore, inadequate levels of vitamin D has been linked to a higher prevalence of peripheral neuropathy (PN) in MM patients. Prior research suggests that adequate vitamin D supplementation may decrease both the severity and occurrence of PN [19, 20]. Vitamin D has been studied for its potential effects on the immune system, cancer progression, and treatment-related side effects [21, 22]. Some studies also propose that patients with MM require significantly higher doses of vitamin D than those currently recommended in clinical guidelines to achieve sufficient levels [20]. Emerging evidence also indicates a potential role of Vitamin D Receptor (VDR)

polymorphism in MM pathogenesis and prognosis [4, 23, 24]. Myeloma cells express VDR, and activation of this receptor by vitamin D has demonstrated anti-proliferative effects on malignant cells. However, the precise molecular mechanisms underlying this process remain unclear, highlighting the need for larger-scale studies to further elucidate this association.

This study had few limitations. First, the sample size was relatively small due to the limited number of newly diagnosed MM patients presenting at this center during the study period. Secondly, the predominance of urban patients further limited the generalizability of these findings. Additionally, the key risk factors such as sun exposure, sunscreen use, fracture history, and dietary intake of vitamin D were not accounted for, which may have influenced the results. Future research focusing on levels of vitamin D in MM patients across different Asian populations would provide valuable insights into regional variations in deficiency prevalence and its clinical impact.

CONCLUSIONS

This study showed that patients with multiple myeloma have a high prevalence of vitamin D insufficiency, with significant variations observed based on geographic location. Given the substantial influence of vitamin D on bone health, immune function, and overall patient outcomes, it is crucial to monitor vitamin D levels closely in these patients. Supplementation should be considered as part of the systematic management of MM, and further studies is needed to understand its potential role in disease progression and skeletal complications.

Authors' Contribution

Conceptualization: RSR

Methodology: SD, SP

Formal analysis: SMA, SP

Writing and Drafting: SMA, NR, SD

Review and Editing: RSR, SMA, NR, SD, SP

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Cut-Off Value of Neutrophil to Lymphocyte Ratio in the Diagnosis of Non-Perforated Versus Perforated Appendix

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ABSTRACT

Neutrophil-To-Lymphocyte Ratio (NLR) gives diagnostic clue about non-perforated and perforated appendixes. However, there are many variations in its cut-off values in diagnosis of non-perforated and perforated appendixes, and there is no single value to differentiate severity of appendicitis. **Objective:** To determine the optimal NLR cutoff value for diagnosing perforated vs. non-perforated appendicitis in patients presenting with acute appendicitis. **Methods:** This cross-sectional analysis was carried out at Surgical Department of Mayo Hospital, Lahore from July 2022 to January 2023. Total 105 patients with acute appendicitis undergoing open appendectomy were enrolled after written informed consent. The patients were grouped according to perforated and non-perforated appendicitis, and NLR value was compared in both groups. Continuous and categorical variables were presented as mean $\pm$ SD and frequency (%). **Results:** Non-perforated appendix group comprised 84 (80%) patients, whereas perforated appendix group comprised 21 (20%) patients. Mean NLR in perforated appendicitis group was higher as compared to non-perforated group (14.7 ± 12.6 vs. 7.36 ± 8.93 , $p = 0.01$). Cut-off point for NLR was obtained at 5.71, with sensitivity and specificity noted was 66.7 % and 62%, respectively. **Conclusions:** The study highlighted the potential of NLR as predictive marker for distinguishing between perforated and non-perforated appendicitis. Its clinical utility is supported by identified cut-off value of 5.71, suggesting its role in aiding timely intervention and reducing complications. The findings reinforce the importance of NLR, particularly in identifying patients at higher risk of appendiceal perforation.

INTRODUCTION

Appendicitis, an acute inflammation of the appendix, most commonly occurs between ages 10 and 20 but can affect all age groups [1]. It has higher prevalence in males, with a male-to-female ratio of 1.4:1 [2]. It presents with periumbilical colicky pain that intensifies over 24 hours. As inflammation progresses, visceral pain transitions to somatic pain, leading to localized tenderness and peritoneal signs [3]. Classic symptoms occur in only 50% of cases, with vomiting (61–92%) and anorexia (74–78%) being common [4]. Acute appendicitis is linked to multiple factors, including obstruction, infection, diet, and

socioeconomic status, with varying epidemiology between Western and Eastern societies [5]. Diagnosis is primarily clinical, with pain migration being a key indicator [3]. Surgery remains the standard treatment. In most cases of acute appendicitis, WBC count is elevated; however, its diagnostic specificity is limited, as many other conditions causing right lower quadrant pain can also lead to increased WBC levels [6]. Repeated WBC assessments over time may improve specificity, except in cases of perforation, where an initial drop may occur [7]. Neutrophilia is commonly observed and has predictive

value, particularly in severe cases [8]. However, due to their limited specificity, WBC and differential leukocyte counts alone are not highly reliable for confirming appendicitis. NLR has emerged as a useful biomarker in distinguishing perforated from non-perforated appendicitis, aiding in early diagnosis and management decisions [9].

Recent studies have shown promising results for NLR in diagnosing and predicting complicated appendicitis in both pediatric and adult patients, but no consensus exists on its optimal cut-off value [10]. Thus, this study aims to determine the optimal NLR cut-off for predicting perforated versus non-perforated appendicitis. This study will be valuable to surgeons by aiding in early diagnosis and timely intervention, thereby improving patient outcomes and minimizing the risks of complications, morbidity, and mortality associated with appendicitis.

METHODS

This comparative cross-sectional study was conducted after taking ethical approval from IRB (No.18/RC/KEMU) at Department of General Surgery, Mayo Hospital, Lahore for duration of 6 months July 2022 to January 2023. Sample size of 105 patients was estimated using 95% confidence level and 30% absolute precision with expected sensitivity of Neutrophil to Lymphocyte ratio of 97.1%, expected specificity of 25.2%, expected sensitivity=97.1% and expected prevalence of acute appendicitis of 30% [11]. Patients were enrolled using non-probability convenient sampling. Before enrolment written consent was obtained from all patients or guardians. Patients of either gender aged between 13 to 60 years diagnosed having acute appendicitis (Alvarado score >7) were included. All patients having diagnosis of appendicitis with some other conditions like pregnancy, chronic liver or kidney disease, history of abdominal TB, or typhoid fever were excluded. Biodata and duration of symptoms was noted. The study incorporated detailed assessment of clinical presentation, laboratory parameters, and imaging findings. Clinical evaluation included symptoms such as abdominal pain, nausea, vomiting, fever, and localized tenderness. Laboratory parameters analyzed included complete blood count, and NLR was calculated from CBC report before undergoing appendectomy. All patients had open appendectomy under general anaesthesia using 5cm skin incision given at McBurney's point. The appendix was surgically removed and sent to the histopathology laboratory, where it was classified as perforated (showing perforation or gangrene at the tip, body, or base) or non-perforated (exhibiting hyperemic, edematous, or swollen wall without signs of perforation or gangrene). Data were analyzed using SPSS version 26.0. Quantitative variables were expressed as mean $\pm$ standard deviation, while qualitative variables were reported as frequencies and percentages. Diagnostic value of NLR was assessed through ROC analysis, and optimal cut-off value for

predicting disease was determined based on highest accuracy of classification. Categorical variables were compared using chi-square test, whereas continuous variables using independent t-test, p-value of 0.050 was considered statistically significant. Prior to applying the independent t-test, normality of the data was assessed using the Shapiro-Wilk test and expected cell counts for all categories were greater than 5, satisfying the assumptions for the chi-square test.

RESULTS

As per findings of histopathology, division of the patients was done in two groups: where the group, having non-perforated appendix comprised of 84 patients (80%) whereas group having perforated appendix comprised of 21 patients (20%). Table 1 illustrates the comparison of sex and age between perforated and non-perforated appendicitis groups. Age was found to be comparable between perforated and non-perforated groups, 24.6 ± 10.7 years and 22.1 ± 7.8 years, respectively. Males comprised 57.1% of perforated appendicitis group, compared to 48.8% in non-perforated group. Females accounted for 49.2% in perforated group and 57.2% in non-perforated group ($p = 0.490$). Mean duration of symptoms was prolonged in perforated appendicitis patients 3.05 ± 2.08 days' vs 1.98 ± 2.25 days in non-perforated appendicitis patients, ($p = 0.050$). Abdominal pain was reported in 67% of patients with non-perforated appendicitis ($n = 56$), compared to 81% in perforated appendicitis group ($n = 17$) ($p = 0.203$). Nausea/vomiting occurred in 83% of on-perforated appendicitis group ($n = 70$), and 86% in perforated appendicitis group ($n = 18$) ($p = 0.791$).

Table 1: Comparison of Patients Related Characteristics between the Perforated and Non-Perforated Group ($n = 105$)

Variables	(Non-Perforated Appendix) Mean $\pm$ SD/ Frequency (%)	(Perforated Appendix) Mean $\pm$ SD/ Frequency (%)	p-Value
Age (Years)	22.1 ± 7.8	24.6 ± 10.7	0.310
Male	41 (48.8)	12 (57.1)	0.490
Female	43 (51.2)	9 (42.9)	
Duration of symptoms (Days)	1.98 ± 2.25	3.05 ± 2.08	0.050
Abdominal Pain	56 (67)	17 (81)	0.203
Nausea/Vomiting	70 (83)	18 (86)	0.791

As shown in table 2, mean NLR value was significantly higher in perforated appendicitis group (14.7 ± 12.6) compared to non-perforated group (7.36 ± 8.93) ($p = 0.010$). Significantly greater proportion of patients with perforated appendicitis (66.7%) had NLR values above predicted cut-off (5.71), whereas significantly larger number of patients with non-perforated appendicitis (61.9%) had NLR values below cut-off ($p = 0.010$).

Table 2: Comparison of Neutrophil-to-Lymphocyte Ratio(NLR)in Patients with Non-Perforated and Perforated Appendicitis (n = 105)

NLR	Non-Perforated Appendix Frequency (%) /Mean $\pm$ SD	Perforated Appendix Frequency (%) /Mean $\pm$ SD	p-Value
>5.71	32 (38.1)	14 (66.7)	0.010
$\leq$ 5.71	52 (61.9)	7 (33.3)	
Mean $\pm$ SD	7.36 $\pm$ 8.93	14.7 $\pm$ 12.6	0.010

Table 3: ROC Analysis of Neutrophil-to-Lymphocyte Ratio(NLR)in Differentiating Perforated and Non-Perforated Appendicitis

Area	Standard Error ^a	Asymptotic Significant ^b	Asymptotic 95% Confidence Interval		Sensitivity	Specificity
			Lower Bound	Upper Bound		
0.731	0.056	0.001	0.622	0.840	66.7% (95% CI: 46.5% - 86.9%)	62% (95% CI: 51.6% - 72.4%)

^a Under the nonparametric assumption;

^b Null hypothesis: true area = 0.5

In figure 1 ROC curve showed the diagnostic performance of NLR in distinguishing perforated from non-perforated appendicitis.

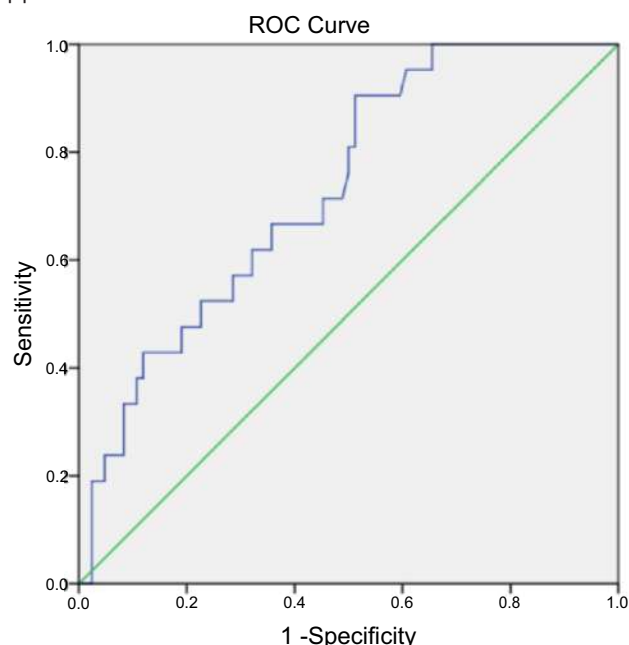


Figure 1: ROC Curve for NLR differentiating perforated and non-perforated appendicitis(N=105)

DISCUSSION

In the current study, the incidence of perforated appendicitis was found to be only 20%, while the remaining 80% had non-perforated appendicitis, in line with study conducted by Zeb *et al.*, in which 19.5% incidence of perforated appendix was observed [12]. However, Al Amri *et al.*, found higher proportion (31%) of patients to have perforated appendicitis [13]. In contrast, Ali *et al.*, found only 9% of patients with perforated appendicitis [14]. Abdominal pain is universally reported symptom, with delayed presentation associated with higher risk of perforation. This aligns with the findings, where patients with perforated appendix had longer duration of symptoms compared to those with non-perforated appendicitis [15].

Based on ROC curve (Figure 1), cut-off point for NLR was obtained at 5.71 with sensitivity of 66.7 % and specificity of 62 %. The area under the curve(AUC) for NLR was 73.1% ($p = 0.001$)(Table 3).

NLR has emerged as valuable biomarker in predicting perforated appendicitis, providing cost-effective alternative to imaging techniques, especially where resources are limited [16, 17]. In this study, mean NLR value was significantly higher in perforated appendicitis group (14.7 ± 12.6) compared to non-perforated group (7.36 ± 8.93) ($p = 0.010$), and greater proportion of patients with perforated appendicitis (66.7%) had NLR values above predicted cut-off (5.71), whereas larger number of patients with non-perforated appendicitis (61.9%) had NLR values below the cut-off ($p = 0.010$), yielding sensitivity of 66.7% and specificity of 62%. These findings align with existing literature, where studies have reported an association between high NLR and appendiceal perforation. Gunasekaran *et al.*, found that patients with perforated appendicitis had a mean NLR of 8.8 compared to 3.2 in non-perforated cases (p -value < 0.001) and also determined that NLR at a cut-off of 3.78 yielded a sensitivity of 65.9% and specificity of 93.1% for differentiating between perforated and non-perforated appendicitis [18]. However, in a study by Chen *et al.*, NLR at a cut-off > 10.83 demonstrated higher predictive values (sensitivity 96.3% and specificity 85.0%) for early perforation [19]. NLR has been identified as an independent predictor for complicated appendicitis, with cut-off values of > 1.7 and > 10.1 predicting complicated appendicitis with sensitivities of 74% and 68.57% and specificities of 69% and 56.98% [20]. These findings further support the role of NLR as predictive marker for appendiceal perforation. Given that NLR can be derived from routine blood tests, its use as a diagnostic adjunct in suspected appendicitis cases may enhance early detection and improve clinical decision-making, particularly in settings where advanced imaging modalities are not readily available.

This study is limited by its relatively small sample size and single-center design, which may restrict the generalizability of the findings. Additionally, the absence of serial NLR measurements and reliance on a single preoperative value may affect the accuracy of predictive

assessment. Future studies should include larger, multicenter cohorts and evaluate serial NLR trends to improve predictive accuracy for appendiceal perforation. Combining NLR with other inflammatory markers and clinical scoring systems may further enhance diagnostic precision.

CONCLUSIONS

The study highlighted the potential of NLR as predictive marker for distinguishing between perforated and non-perforated appendicitis. Its clinical utility is supported by identified cut-off value of 5.71, suggesting its role in aiding timely intervention and reducing complications. The findings reinforce the importance of NLR, particularly in identifying patients at higher risk of appendiceal perforation.

Authors' Contribution

Conceptualization: LG, MA

Methodology: MA, LG, QD, MN, KSA, MS

Formal analysis: MA

Writing and editing: MA, QD, MN, KSA

Review and Editing: MA, LG, QD, MN, KSA, MS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



The Knowledge, Experiences, and Barriers Associated with Male Involvement in Family Planning at Tehsil Lal Qila, District Dir (Lower), KPK, Pakistan

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ABSTRACT

Pakistan is one of the world's most populous countries, with a high growth rate affecting the country's socioeconomic progress negatively. Family Planning (FP) can reduce fertility rates, enhance maternal and child health. With the use of FP, mothers will have a low risk of pregnancy-related complications, and the best care can be provided to a child. Moreover, FP has a significant role in accelerating the Sustainable Development Goals (SDGs). Investing in FP will lower poverty and improve economic stability. **Objectives:** To explore the knowledge, experiences, and barriers associated with male involvement in family planning in Tehsil Lal Qila, Dir Lower, KPK. Also, to propose strategies to promote male participation in FP through improved awareness, accessibility, and inclusion in reproductive health programs. **Methods:** A qualitative exploratory design was used with a total of 12 in-depth interviews with male clients using a purposive sampling technique. The data were analysed using content analysis. **Results:** Myths and misbeliefs about FP, the unavailability and unaffordability of contraceptives, pressure from intimate partners and relatives, lack of proper FP services, and gender discrimination were significant barriers to the use of FP. **Conclusions:** Collaborative efforts among various stakeholders, for instance, community-level awareness campaigns, accessible and affordable FP services, male involvement in healthcare initiatives (alongside females), and improved communication skills among healthcare providers working in FP programs can promote the use of FP.

INTRODUCTION

Pakistan is one of the developing states where the population is increasing rapidly. In 1950, the population of Pakistan was 39,448,232, which became 172,800,05 in 2008 [1]. FP is the greatest way to reduce the fertility rate and control population overgrowth through contraception, which will positively affect the country's socioeconomic development in significant aspects like education and the economy [2]. According to the WHO, FP is a process that permits individuals to attain the desired number of children and to identify the gap between pregnancies. FP can be attained by the utilization of contraceptive methods [3]. There are different types of contraceptives for males and females. Male contraceptive options are condoms,

vasectomy, and withdrawal methods. For females, there are many contraceptive options, i.e., injections, Intrauterine contraceptive devices (IUCD), Norplant, breastfeeding, contraceptive pills, etc. [4]. FP benefits maternal and child health, households, communities, and the state [3]. According to the WHO, FP positively impacts the mother's health and the productive results of every pregnancy. With the appropriate gap between two pregnancies, mothers will have a low risk of pregnancy-related complications, and the best care can be provided to a child [4]. FP has a significant role in accelerating the Sustainable Development Goals (SDGs). Investing in FP will lower poverty and improve economic stability. The Country



Office (CO) of UNFPA in Pakistan showed a concentrated analysis in 2019, which reported that for every dollar invested in FP programs in Pakistan, approximately \$5 in net healthcare costs could be saved [5]. A research study performed in Kenya concluded that the main reason for FP failure is the disagreement of males regarding birth spacing. Men do not participate in contraceptive activities for various reasons. Firstly, they believe that health care workers might force them to undergo a vasectomy procedure. Secondly, they did not want to follow the instructions and guidelines of reproductive health teams due to misconceptions of being diagnosed with HIV, and their extramarital relationships might be disclosed to their female partners. The study suggested that different projects should be arranged regarding the clearance of stigma and misbeliefs about FP and providing education related to the advantages of contraceptive practices in which both male and female partners can be focused together, and male reproductive health workers should raise awareness amongst men in the community [6]. Developed states like the United States of America (USA) have had a significantly better approach to FP for the previous 50 years, while in low-income and middle-income states, there are many hurdles to the use of contraceptive practices [6]. In Pakistan, the use of advanced contraceptives is only 26%, while in underprivileged areas, the use is much lower (less than 20%) [7, 8]. There are many social challenges to contraceptives in Pakistan, including resistance from husbands, lack of motivation, lack of education, cultural and religious perspectives, accessibility issues, and communication gaps [9]. A study in Karachi aimed to discover the root causes and challenges of long-term low use of contraceptives among female clients and important service providers of Pakistan's community-based FP initiative. They concluded that females feared having side effects with the uptake of contraceptives. Moreover, the lack of a husband's approval and willingness was another challenge. In addition, the mother-in-law's influence and the wish to have more sons were also reducing FP use. The above three challenges were the cause which led to the low uptake of FP in Pakistan [6]. In the Pakistani Context, where the society is patriarchal, the male involvement can enhance the uptake of contraceptives [10]. However, husbands' disapproval is a key challenge to the practice of contraceptives [11]. According to the researcher's knowledge, no study has been conducted about the knowledge, experiences, and barriers in the current setting of Tehsil Lal Qila District Dir Lower, KPK, Pakistan. The use of condoms is 9.0 %, and male sterilization is 9.0%; however, among females, sterilization, IUDs, and birth control pills are preferred methods. Contraceptives among communities in KPK (Khyber Pakhtunkhwa) even differ more dramatically. In

KPK, where the rate of practice is 31%, the most commonly used methods are condoms (9.6%), the withdrawal method (7.2%), and injectable contraceptives (5.3%) [12]. Research suggests many innovative approaches to increase the contraceptive prevalence rate (CPR). Many countries are now focusing on male involvement in FP. The support of husbands for their partners will highly influence the use and uptake of modern FP methods, and the husband's disagreement is a barrier to the use of FP among women. Sociodemographic variables, the communication between a couple regarding the use of FP, and fertility preferences play an essential role in the use of contraceptives. Research shows a great need for male involvement in FP around the globe. Therefore, increasing male involvement in FP will improve the prevalence of contraceptives [6].

Despite the importance of family planning in improving maternal health and socioeconomic outcomes, contraceptive use remains low in rural areas of KPK, particularly due to male-related barriers. However, limited evidence exists from Tehsil Lal Qila, District Dir Lower regarding men's knowledge, experiences, and barriers toward family planning practices. This study aims to assess the knowledge, experiences, and barriers related to family planning among men in Tehsil Lal Qila, District Dir Lower, KPK, Pakistan.

METHODS

The qualitative descriptive exploratory study was carried out from June to October 2023 in rural settings of Tehsil Lal Qila, District Dir lower KPK. Before the conduct of the study, an IRB approval letter was obtained (Ref: 2023-8274-23911) from the Ethical Review Committee of Aga Khan University. Approval for the study was provided by the Ethical Review Committee of the Aga Khan University, Karachi, and written permission was taken from the head of the community (The mayor of the Tehsil). The study participants were selected through purposive sampling. Purposive sampling was preferred to ensure the inclusion of those participants who had relevant knowledge and experiences to deliver rich insights into the focus of the study within the specific rural area of Tehsil Lal Qila. The study participants were selected based on eligibility criteria, which were above 18 years, and married male. The in-depth interviews (IDI) of 12 interviews from participants, the saturation point was achieved. For initiating interviews and recruiting participants, formal consent was taken in written form, and the goals of the study were explained to every participant. The researcher performed word-for-word transcription for the recorded audio interviews. The researcher organized the data for analysis. In this respect, the researcher compiled all the collected data rigorously. In the research coding process, the researcher read and reviewed all Pashto, Urdu, and English transcripts to familiarized themselves with the data and understand the meaning of the transcripts. The similar meaning in the transcripts was given the same or

common code. For the said purpose, the researcher repetitively listened to the audio recordings when required. Moreover, in the qualitative study, coding is a key step. This is because coding is a logical technique that splits the data into more manageable pieces that can reflect participants' responses to the research question [13]. Categories are broad units of information made up of multiple codes combined to form a common idea [14]. To develop categories, the researcher, along with other team members, looked for similarities and differences in the data and merged all similar codes in a separate column. Similar categories were merged into separate themes to categorize the data and gain a clear understanding of the findings. The researcher represented the data in hierarchical and table form, mentioning themes, categories, and enriched quotations from the participants for accurate reporting and understanding of the study results.

RESULTS

In qualitative content analysis, three main themes emerged.

Theme 1: Understanding FP from the community men's lens.

Category 1: Definition of FP: The participants defined FP as having few children with appropriate intervals. For instance, they mentioned that FP is a gap of 2 to 3 years after each pregnancy. My concept about FP is that the children should be fewer children and there should be a gap after each child. The next child should be planned after a specific interval, this is called FP. FP is making a plan and having a pregnancy with a two- or three-year gap. (IDI 01) Similarly, another participant stated, "When a mother gives birth to her first baby and then she takes a break for two to three years, then this is called FP" (IDI 09).

Category 2: Significance of using FP: This category further has two subcategories. The Subcategory One - The Benefits of using FP: The participants perceived FP as beneficial for the family, children, mother, father, and the overall society. They believed that practicing FP reduces the childbearing and rearing load on mothers and reduces the financial burden on fathers. Women have a higher workload and lower stress if she has more children while caring for them. A mother having more children will have more mental stress and more workload. Having an FP will also affect the health of the mother. Delivering a baby is not an easy task, so with FP, the mother will have proper time to heal and recover. (IDI 01). Subcategory Two - The Disadvantages of Using FP: The participants believed that FP has many disadvantages, harms, and side effects that will negatively impact the mother's health. The common side effects reported by the participants included: irregular bleeding, depression, hair loss, headache, skin problems and overall body weakness and fatigue, and changes in sexual desire. FP is against the natural process, as you are disturbing the natural process, so definitely, the

person who uses the contraceptive will experience negative effects on her body. You know that every medication has side effects, so contraceptive medications also have adverse effects. (IDO 02).

Category 3: Sources of Knowledge regarding Contraceptives: The participants shared different sources from which they got knowledge and information regarding FP from discussions with friends in gatherings, social media, TV channels, and various internet platforms. Additionally, religious scholars and visiting to a hospital as a source of information. "First of all, the concept of FP I learned from my community, like from my friends. I have also got a lot of information from the media, but most of the information I got from my society and community" (IDI 01). Likewise, another participant verbalizes, "Religious scholars also say this, they also say and recommend having an interval of two to three years between two children" (IDI 07).

Category 4: The Common Modalities of FP Available to Community Men: Condom was the most commonly used method because of its easy usage and having no side effects, followed by tablets and injections. Contraceptive tablets were considered safe, and almost all of them were unaware of the concept of female condoms. In addition, the withdrawal method and exclusive breastfeeding were being practiced in the community for birth control. Furthermore, very few commented on emergency contraceptives as a way of FP. One of the participants explained his favoured FP method as follows: "My personal preference is a condom because medicines don't have good results" (IDI 09). Moreover, a few participants shared the use of medicines and injections as the preferred modality for the practice of FP. "For practicing FP, females' medicines, injections, and tablets are used mostly" (IDI 07). Furthermore, in comparison to contraceptive injections, contraceptive tablets were considered safe, as shared by a few of the participants, "One method I know is injections, I know about injections, but I think it is not a good method of contraception because it has a bad effect on health. Another method is the use of medicines like tablets" (IDI 12). Likewise, regarding the awareness about female condoms, one of the participants commented, "No, I don't know about condoms that are used for females. Condoms are usually used for males" (IDI 12). Moreover, while describing the withdrawal method as a way of FP, a participant stated, "People use different methods, some people use medicines, and some people use injections, which delay pregnancy for some time. In our area, people also use home treatment like people ejaculating outside (withdrawal method)" (IDI 02).

Theme 2: Challenges Encountered by Community Men in Practicing FP

Five categories emerged from this theme, which are given below.

Category 1: The Unavailability of Accessible FP Services for Male: The unavailability of contraceptives was the main

challenge to men while practicing FP. Generally, they verbalized that they didn't have the availability of contraceptive medications and condoms in the markets in the community. Furthermore, free contraceptives and doctors were available in some hospitals like BHUs, but they were far away from the community. I told you that condoms and contraceptive medications are not available in the markets in this community, so people used to go to the city to purchase them. Thus, lack of accessibility is also one of the reasons for the discontinuation of family planning among some couples. (IDI 02) Similarly, another participant vocalized the issue of unavailability of condoms as follows, "There are many challenges to men in the use of FP, like contraceptives, condoms, etc., are not available in the shops of this village" (IDI 11).

Category 2: Myths and Misbeliefs regarding the Use of Contraceptives: The participants discussed that people in the community had various myths and misbeliefs regarding the use of contraceptives. They believed that contraceptives cause permanent infertility. Moreover, they state that the projects/initiatives in progress for FP are being run by foreign agents, and they intend to lower the country's population by the use of contraceptives. Some participants stated, "Yes, people think that FP might affect their power of reproduction and they may become sterile due to contraceptives" (IDI 10). Likewise, other participants expressed the same concerns when they said, "People in this community say that contraceptives affect the fertility of women" (IDI 09). Furthermore, FB projects working on a foreign agenda in the said area was also a notion prevalent among the participants, as evident from the following view, "They say that FP projects are working on a foreign agenda to kill the kids of our country and lower the population" (IDI 07). Meanwhile, some others perceived FP as the killing of children, thus being a sinful act.

Category 3: Unaffordability to Buy Contraceptives: The participants discussed various financial barriers to the use of FP. They were unable to purchase contraceptives due to low income, high inflation, and high prices of medicines. A participant iterated the limitations of his means as follows: "I have many other things on which I have to spend money, so it is difficult for me to spend money on purchasing contraceptives" (IDI 05). Similarly, another participant stated that, You know that nationally and internationally, there is inflation and the prices are very high, and most people work on a daily wage basis, so for them, it is difficult to fulfil their needs daily. Hence, they can't purchase medicines because of the high prices. (IDI 07).

Category 4: The Pressure from Relatives and Intimate Partners: The participants described that men experience pressure from relatives and intimate partners in various forms, due to which their practice of FP is low. Moreover, mothers-in-law and elders in the family expect a greater number of kids from a couple. Furthermore, the wives oppose the use of F because of the fear that, due to this probable infertility, their husbands will get another excuse

to get remarried in the future. Yes, of course, when a person marries, the relatives expect a child in the first year of marriage. The relatives and friends will ask them why they don't have a son or daughter yet. And the wife will be asked to have a consultation. (IDI 02). Similarly, a participant describing the pressure from the mother-in-law stated, "Yes, most of the mothers-in-law and elders want more children, so due to their wish, the use of contraception among couples is affected" (IDI 08). Similarly, in terms of experiencing pressure from an intimate partner, a participant explained that, In this community, most people might have the issue that if a man wants to use contraceptives, his wife will oppose its use because she thinks that this might permanently cause infertility and in case of infertility, they fear husbands for doing second marriage female partners to show resistance towards the use of FP. (IDI 02).

Category 5: Gender Discrimination: This category has two further subcategories, which are given below in detail. Subcategory One - The Desire to Have More Sons as Next of Kin. Exploring the challenges to the use of FP, the majority of the participants discussed that couples in this locality had a general tendency to desire to have more male children. Due to the preference for male boys, their practice of using contraceptives is low. "Yes. People want to have more kids as sons so that they can have strong financial support in the future" (IDI 11). Another participant stated the same, "Yes, of course, people wish to have more male babies to have more support in the future." (IDI 03). Similarly, another participant stated, "First of all, if I were to talk about tribal areas like mountainous areas! People in those areas desire more children because they want to have strong back support and authority in the form of sons. It is ignored because they have fights between tribes, so they want to have more manpower and more children. (IDI 03). Subcategory Two - More Expectations from Females for Using Contraceptives. While conducting interviews with the participants, it was observed that there were only two options of contraceptives available for males, condoms and vasectomy. However, for females, there were many options like contraceptive tablets, injections, IUDs, emergency contraceptives, etc. Few participants highlighted that males prefer to ask females to use contraceptives, and they don't use condoms because they felt uncomfortable practicing FP with condoms. A participant verbalized this inhibition as follows, "One of the issues is that there is a difference between sexual pleasure while using a condom, that's why males don't prefer to use, and most males prefer to convince females to use contraceptive medicines and injections" (IDI 08).

Theme 3: The Proposed Strategies to Enhance the Uptake of Contraceptives among Men
This theme includes two categories.

Category 1: Community-Level Strategies: This category has two further subcategories, and the details of each category are given below: Subcategory One - Frequent

Awareness Sessions at the Community Level to Enhance the Use of Contraceptives. The participants shared that there was a lack of awareness regarding the use of FP. For example, some participants discussed that due to the beliefs in various myths and misperceptions, couples don't continue their use. They also shared that people do not know the methods of continuing the practice of FP, as a participant said, "I was using contraceptive medications, but I stopped because someone told me that they cause harmful effects" (IDI 11). To overcome these barriers, the participant gave different kinds of recommendations, as a participant verbalized, The government should create awareness and education at the school level. The education will benefit a lot in promoting FP in the future. So, both girls and boys should be educated at the school level about the need, importance, and methods of FP, and this will ultimately promote FP. (IDI 02) Subcategory Two-The Availability of Affordable and Free-of-Cost Contraceptives and FP Services to Men. The majority of the participants shared that they were unable to purchase contraceptives because of their low income. They suggested that FP can be promoted by the government through providing free-of-cost contraceptives and FP services at the community level. A participant stated that Hospitals are very necessary in this area so that doctors are there and provide guidance regarding healthy FP methods. The hospital and doctors' facilities should be free of cost so that people can avail themselves of these facilities. Medicines and condoms should be provided to people in this community free of cost (IDI 10). In terms of governmental role in the promotion of FP, a participant shared that, "Government can arrange seminars to create awareness regarding FP and to provide accessible services to the public. The availability of contraceptives should be made available at low cost or free of cost" (IDI 05).

Category 2: Strategies at the Service Provider's Level: This category includes two further subcategories: Subcategory One-The Inclusion of Men as Healthcare Workers in Initiatives Related to Maternal and Child Health. Due to cultural traditions, female workers in NGOs working for FP cannot educate women in their homes in front of elders in the families. Hence, the recommendations were to include males as healthcare members in initiatives related to maternal and child health. A participant stated, "In most of them, the workers are females. It would be better if they had male workers, then it would be more productive" (IDI 04). Another participant shared that, as I told you about the important information, I want to tell you that a program is needed. Male workers are needed in the community to create awareness in public and visit homes to make people understand the use and advantages of FP. (IDI 07). Subcategory Two - Enhanced Communication and Counselling Skills of the Existing Services Provided through Job Training. The participants discussed that in this community, female health workers who were representing FP programs face difficulties in their line of

work, due to cultural restrictions, traditions, limitations, and gender discrimination. This means that female workers don't feel comfortable when they visit home to promote FP. Therefore, they need to be trained in communication and counseling skills to work in the environment. The FP projects working in this Tehsil are providing free contraceptive medicines, but Lady health workers [LHWs] do not perform their duties to give them to the public, because sometimes they don't feel comfortable when they enter someone's home and males are there. So, they avoid visiting homes. (IDI 06). Likewise, another participant highlighted the challenges faced by LHW as follows: LHWs are actively working for FP in this community, but they have challenges, like when they go to a house, people see them with ill intentions and malice. As in the village, when LHWs go home, they cannot give teachings and awareness regarding FP because of some cultural restrictions (IDI 07).

DISCUSSION

Although many initiatives were taken regarding the enhancement of FP in the country, the current study has brought attention to the important issues regarding the lack of appropriate and persistent knowledge, which leads to the low uptake of contraceptives in the community. Most of the participants in the current study defined FP as maintaining a gap between two children. A study conducted in Karachi, Pakistan, also reported that the participants viewed FP as the gap between children [15]. Moreover, while discussing the FP modalities, condoms were reportedly the most commonly practised contraceptive after tablets and injections because of their safety and ease of use. Furthermore, the findings of this study were parallel to the study conducted in Karachi, Pakistan [16]. Moreover, most of the men knew the ways of using FP. However, they had limited knowledge regarding vasectomy and IUDs. In addition, very few of them commented on breastfeeding as a way of contraception. The results were concurrent with the study conducted in three provinces of Pakistan [17]. It was found that the majority of the men were aware that FP can postpone unintended pregnancies, but they did not have enough information about some available contraceptive methods, as a study conducted in eastern Nepal as they concluded the same results [6]. The study found that males were aware that practising FP has benefits for maternal and child health and is beneficial for a household. Moreover, literature also supports the same findings [17]. In addition, the participants perceived that FP has financial benefits, for instance, a small family will have lower expenses. Also, the finding is similar to a study conducted in South Africa [18]. The participants in the current study reported different harms and disadvantages of practicing contraceptives, such as bleeding and disturbance of the menstrual cycle. These findings were parallel with a study conducted in Kinshasa, DRC (Capital of

the Democratic Republic of Congo)[6]. Likewise, a study in Sweden concluded that the majority of the men reported the fear of potential side effects of change in fertility and sexuality due to the use of contraceptives. The current study also found the same results [6]. In addition, a study in Karachi, Pakistan, reported that the participants believed that the use of contraceptives causes side effects, such as weakness, infection, and mental illness. The current study also reported similar [15]. In terms of sources of knowledge about FP and particularly contraceptives, a study in urban areas of Karachi, Pakistan, found that the majority of the men got information about FP from the internet, private hospitals, and from their respective spouses. Moreover, similar results were reported in the current study [19]. Moreover, the current study reported that men also seek knowledge from electronic media like TV channels, and while interacting with workers and healthcare workers. Similarly, a study conducted in Karachi reported parallel findings [15]. The study also found various barriers towards the use of contraceptives, for instance, the participants believed in different myths that FP can lead to sterility and contraceptives can even cause cancer. These findings are consistent with the qualitative study conducted in Kinshasa, DRC [6]. Further, a study in Karachi, Pakistan, supports the findings of the current study that a mother-in-law is considered the authority for deciding the family size and the use of contraceptives [16]. Moreover, the current study found that there was intimate partner pressure, for instance, pressure from a wife on her husband to not use FP due to the fear of permanent sterility. However, the result of the current study was different from a study conducted in South Africa, where males have more influence and exert pressure on their intimate partner to stop using contraceptives [6]. Also, the study found that the use of FP was low in the community due to the lack of accessible services and gender discrimination to have more sons. The results are similar to a study conducted in Nepal [20]. The current study found that due to the wish to have more children. A study in Bangladesh supports the findings [21]. The findings of the current study are concurrent with a study conducted in eastern Nepal that the lack of accessibility and affordability is due to ancestral, traditional, and religious beliefs, misconceptions, and myths [6]. The findings of the current study are parallel with the results of a study conducted in South Africa that male feel ashamed to buy condoms as well as a lack of affordability [22]. The study's participants recommended that creating awareness and educating students at the school level can promote the use of FP, and the results were supported by research in the USA [23]. Furthermore, it was found that community leaders and religious scholars should be involved to make the FP programmes more successful. A study in Kenya suggested similar recommendations [6]. Literature supports similar findings of another study conducted in Punjab, Pakistan, which

states that affordable contraceptives can enhance the practice of contraceptives [6]. Similarly, another study conducted in Karachi, Pakistan, also supports the finding of including males in FP programmes. However, the current study's setting that is, District Dir, is a developing rural area, whereas, Karachi is an urban area and a bigger city of Pakistan [16]. Moreover, another study conducted in Tanzania also supported the findings of the current study [6]. Similar to another study in Pakistan, the current study also recommended that the practice of FP can be promoted by providing free-of-cost services at the community level [6]. Furthermore, the current study's findings suggest that for enhancing the practice of FP in the community, gender equality. A study in Karachi, Pakistan, found parallel results [15]. Moreover, the current study found that initiatives were needed at the community level and at the service provider level. The findings of the current study are parallel to a study conducted in Tanzania [6]. The discussion underscores that while men in the research study had basic knowledge of FP, gaps remained in understanding methods like vasectomy and IUDs, along with misconceptions about side effects and adverse effects. It focuses on barriers like social stigmatization, affordability problems, and religious beliefs, contrasting these findings with studies from various contexts such as South Africa and Nepal. The study underscores the need for culturally suitable interventions, engaging religious scholars, and making FP services more affordable and easily accessible to promote acceptance and their use in rural areas.

This study is limited by its qualitative design and focus on a single rural district, which may limit the transferability of findings to other settings. In addition, reliance on self-reported perceptions may introduce recall and social desirability bias. Future research should include larger, mixed-method or quantitative studies across diverse rural and urban populations to better understand FP knowledge and practices. Community-based interventions involving men, religious leaders, and healthcare providers should also be evaluated for their effectiveness in improving contraceptive uptake.

CONCLUSIONS

It was concluded that this study draws attention to enduring disparities in community acceptance, accessibility, and awareness of family planning (FP). Participants' primary understanding of FP was child spacing, but they had little knowledge of long-term procedures like vasectomy and IUDs. FP uptake was further hampered by sociocultural influences, religious beliefs, economic limitations, and misconceptions regarding the adverse effects of contraceptives. These difficulties were exacerbated by structural obstacles such as social stigma and service inaccessibility. Furthermore, Targeted interventions should include education,

debunking myths, and boosting male involvement to improve FP utilization.

Authors' Contribution

Conceptualization: JK

Methodology: TS

Formal analysis: SZS

Writing and Drafting: IK

Review and Editing: JK, TSA, NZS, IK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article


Assessing Medical Students' Interest in Community Medicine/Public Health as a Career Path: A Cross-Sectional Study at Sahiwal Medical College, Sahiwal, Pakistan

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ABSTRACT

Public health should be the priority of underdeveloped countries like Pakistan to have better management plans for combating diseases. But it was observed that medical students are less interested in a career as a public health specialist, and they are less inclined towards community medicine. **Objectives:** To determine the preferences of the undergraduate medical students towards the choice of subject for specialization and to determine their attitude towards community medicine as a future career. **Methods:** A cross-sectional questionnaire-based study was conducted at a public sector medical college of Punjab using a convenient sampling technique. After receiving approval and having informed consent from the 315 study participants, we shared the questionnaire via WhatsApp in the form of Google Forms. The data were then analyzed using SPSS version 26.0. **Results:** Out of the total 315 participants, 170 (54%) were females and 145 (46%) were males. The majority (96%) of the students were inclined towards opting for clinical sciences after graduation. Surgery 139 (44.1%) and Medicine 84 (26.6%) were the most preferred fields for specialization, only 9 (2.8%) students preferred community medicine (p -value=0.001). When asked for the reason for not choosing community medicine, the majority, 189 (60%), said that they are not impressed by this subject. Career dissatisfaction was identified as the second main reason (14.6%) for not opting for this subject as a future career path. **Conclusions:** It was concluded that appropriate teaching methodology should be adopted and the curriculum should be designed in such a way that it may increase students' interest in community medicine.

INTRODUCTION

The decision-making process behind medical students' specialization choices is crucial for both the students and the healthcare system. Specialization determines the future career pathways for medical students and significantly impacts the distribution of physicians across the various medical fields. This distribution is essential for ensuring that all areas of healthcare are adequately staffed, thereby promoting balanced and comprehensive healthcare delivery [1]. There are striking differences in the popularity of specialty fields in many countries. Fields

such as surgery, internal medicine, pediatrics, obstetrics and gynecology tend to attract a large proportion of medical students, while specialties such as community medicine, anesthesia and clinical medicine are not generally preferred. This unequal division can result in shortages in essential services, particularly in the underrated fields like community medicine, which is crucial in the provision of public health and preventive care [2]. Medical students usually enter their medical colleges /universities with a career plan that often evolves

throughout their studies. Recent studies have shown that medical students are more often interested in becoming a hospital-based clinical specialist and are less interested towards community medicine as a career option [3]. Factors that can influence specialization choices by the medical students may include their interests, perceived competence, and personal values and beliefs about the medical profession. External factors, including job opportunities, financial incentives, work-life balance, and public perceptions of medical diversity, can also influence the speciality selection process [4]. Gender also plays an important role in this, with studies showing that male and female students tend to lean towards different majors/specialities due to social and cultural influences [5]. Females usually prefer pediatrics and obstetrics and gynecology, and men usually go for surgical specialities [6]. In the United Kingdom, social factors, such as working hours and social considerations, significantly influence student decision-making. In contrast, economic incentives and prestige are more important in Turkey, while personal interests and psychological issues are the main motivators in Saudi Arabia, Taiwan, Pakistan and India [7]. In Pakistan, due to the lack of career guidance services, many students are opting for medicine and surgery but are less inclined towards community medicine or public health. The majority of the medical students are leaving the country and going abroad for professional excellence [8]. There is also a shortage of doctors working in the rural areas of the country. Despite the importance of community medicine in preventive care in public health, it has generally received little attention from medical students. This is of great concern because community medicine plays an important role in addressing public health issues, promoting health education and preventing disease [9]. The perception of the students that community medicine is a profession with little prestige or economic value has contributed to its decline in popularity. Student perceptions of community medicine and an understanding of factors that may prevent them from choosing it as a profession will help policymakers and stakeholders to design interventions to promote this important profession [10]. The findings of this study will provide valuable insights into the primary preferences of medical students and the main factors that influence their decisions regarding the selection of their future speciality field.

Understanding these aspects can help medical schools and policymakers to develop strategies to encourage a more balanced distribution of future physicians across all specialities, including community medicine. This will improve the overall health system's effectiveness and responsiveness to meet medical needs. This study aims to assess the preference of future undergraduate medical students towards speciality and particularly their attitudes

towards community medicine and public health as a career option, and also to identify barriers to choosing this speciality.

METHODS

After taking approval from the institutional review board (IRB) letter (S. No 104/IRB/SLMC/SWL), a cross-sectional study was conducted during the year 2024 (May-September) at Sahiwal Medical College, a public sector medical college of Punjab, Pakistan. For data collection, a convenient sampling technique was used, and a questionnaire that was taken from a recently published research paper [11] was validated through peer review and pilot testing. Cronbach's alpha was applied to check the reliability (value=0.807). As this study mainly focused on students' preference regarding the community medicine subject, so excluded the 3rd year as they have not studied this subject yet. 1st year and 2nd year classes in the respective institutes are being taught this subject in a modular system. 3rd year, 4th year and final year are being taught via traditional systems. In the traditional system, community medicine is a subject in the 4th year. So, the 4th year and final year were also familiar with this subject. The above-mentioned reason made 1st, 2nd, 4th and final year students fit the inclusion criteria. The following sample size was calculated. $\text{Sample size} = Z_{1-\alpha/2} \sqrt{p(1-p)} / d$. $Z_{1-\alpha/2} = 1.96$, $p = 0.32$, $d = 0.05$. The p-value was calculated from the reference paper [11]. Sample size = 315. Confidentiality index = 95%. After taking informed consent from all the study participants, the questionnaire [11] was shared with them via WhatsApp in the form of Google Forms, and the data were collected. The response rate was 100%, 315 forms were shared, and all were filled out by the students and were included in the analysis. The data were analyzed via IBM SPSS version 26.0, results were derived in terms of frequencies and percentages. The qualitative variables were compared using the Chi-square test and Fisher's test where cell counts < 5. A p-value less than 0.050 was considered significant.

RESULTS

Out of the total 315 participants, 170 (54%) were female and 145 (46%) were male. 258 (81.9%) were hostilities and 57 (18.1%) were day scholars. 94 (29.8%) students were from the 1st year, 85 (27%) students were from the 2nd year, 103 (32.7%) students were from the 4th year, and 33 (10.5%) students were from the final year. After graduation majority, 303 (96.2%), said to proceed in clinical sciences rather than basic sciences (Table 1).

Table 1: Inclination of undergraduate medical students towards opting for basic and clinical sciences after graduation and the likely determinants contributing to this choice

Determinants		After Graduation, Where Do You Like to Proceed?		p-value
		Basic Sciences (n=12)	Clinical Sciences (n=303)	
Gender	Female	06 (1.9%)	164 (52%)	0.503*
	Male	06 (1.9%)	139 (44.1%)	
Residence	Day Scholar	05 (1.5%)	52 (16.5%)	0.047*
	Hostel-lite	07 (2.2%)	251 (79.6%)	
Parents' Profession	Doctor	02 (0.6%)	24 (7.6%)	0.260**
	Other	10 (3.1%)	279 (88.5%)	
House Locality	Urban	11 (3.4%)	243 (77.1%)	0.288**
	Rural	01 (0.3%)	60 (19%)	
Year of Study	1 st Year	02 (0.6%)	92 (29.2%)	0.349**
	2 nd Year	03 (0.9%)	82 (26%)	
	4 th Year	04 (1.2%)	99 (31.4%)	
	Final Year	03 (0.9%)	30 (9.5%)	

(*p-value was calculated by Pearson chi-squared test. **p-value was calculated by Fischer-Freeman-Halton Exact test as the cell count was <5)

Gender-wise choice of specialities for pursuing the specialization was calculated (Table 2).

Table 2: Gender-wise choice of specialities for pursuing the specialization

Variables	Gender		Total (n= 315)	p-value
	Female (n= 170)	Male (n= 145)		
Surgery	69 (21.9%)	70 (22.2%)	139 (44.1%)	0.001
Medicine	40 (12.7%)	44 (13.9%)	84 (26.6%)	
Gynecology and Obs.	24 (7.6%)	01 (0.3%)	25 (7.9%)	
Radiology	06 (1.9%)	04 (1.3%)	10 (3.1%)	
Community Medicine	04 (1.3%)	05 (1.6%)	09 (2.8%)	
Orthopedics	04 (1.3%)	03 (0.9%)	07 (2.2%)	
Others	23 (7.3%)	18 (5.7%)	41 (13.0%)	

(*p-value calculated by Fischer-Freeman-Halton Exact test as the cell count <5)

class/medical year-wise choice of specialities for pursuing the specialization was analyzed in 1st, 2nd, 4th and 5th year students (Table 3).

Table 3: Class/Medical Year-Wise Choice of Specialties for Pursuing the Specialization

Variables	Class				Total (n= 315)	p-value*
	1 st Year (n=94)	2 nd Year (n=85)	4 th Year (n=103)	5 th Year (n=33)		
Surgery	56 (17.8%)	39 (12.3%)	36 (11.4%)	08 (2.5%)	139 (44.1%)	0.004
Medicine	15 (4.7%)	23 (7.3%)	34 (10.8%)	12 (3.8%)	84 (26.7%)	
Gynae & Obs.	05 (1.6%)	07 (2.2%)	07 (2.2%)	06 (1.9%)	25 (7.9%)	
Radiology	05 (1.6%)	01 (0.3%)	04 (1.3%)	00 (0%)	10 (3.2%)	
Community Medicine	01 (0.3%)	02 (0.6%)	04 (1.3%)	02 (0.6%)	09 (2.9%)	
Orthopedics	03 (0.9%)	03 (0.9%)	01 (0.3%)	00 (0%)	07 (2.2%)	
Others	09 (2.9%)	10 (3.2%)	17 (5.4%)	05 (1.6%)	41 (13.0%)	

(*p-value calculated by Fischer-Freeman-Halton Exact test as the cell count was <5)

Determinants for choosing community medicine as a career option were analyzed (Table 4).

Table 4: Determinants for Choosing Community Medicine as A Career Option

Determinants		Choose (n=9)	Don't Choose (n=306)	p-value*
Gender	Female	4 (1.3%)	166 (52.7%)	0.402
	Male	5 (1.6%)	140 (44.4%)	
Residence	Day scholar	3 (0.9%)	54 (17.1%)	0.211
	Hostellite	6 (1.9%)	252 (80%)	
Parents' Profession	Doctor	2 (0.6%)	24 (7.6%)	0.165
	Other	7 (2.2%)	282 (89.5%)	

House Locality	Urban	9 (2.8%)	245 (77.8%)	0.140
	Rural	0 (0%)	61 (19.3%)	

(*p-value calculated by Fischer-Freeman-Halton Exact test as the cell count <5).

Assessing the reason why our study participants did not choose the community medicine subject/ public health as a future career option (Table 5).

Table 5: Reason for Not Choosing Public Health as A Future Career Option

Reasons	Frequency (%)
I am not impressed by the subject	189 (60%)
career dis-satisfaction	46 (14.6%)
Lack of growth opportunities	36 (11.4%)
Lack of acceptance of public health workers in society	12 (3.8%)
This subject is not projected well by the faculty/PG	08 (2.5%)
Unable to earn well by choosing this field	06 (1.9%)
I can't earn name and fame by choosing this field	03 (01%)
Nobody has performed satisfactorily in this field	03 (01%)
PG/faculty of this field feels dissatisfied	02 (0.6%)
Public health specialists are not acknowledged by others	01 (0.3%)
I will choose Community Medicine in future.	09 (2.8%)

Scopes of community medicine/ public health specialists as per the perception of students were analyzed. 315 responses were measured (Figure 1).

Chart Title

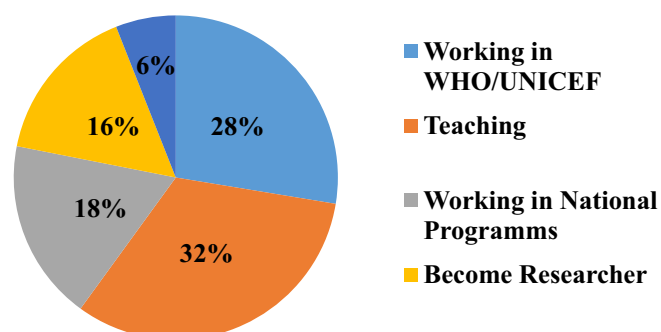


Figure 1: Community Medicine/ Public Health Specialists as Per the Perception of Students

DISCUSSION

Majority (96.2%) of the students were inclined towards choosing clinical sciences after graduation. The most preferred subject for specialization is surgery, with 44.1% of the respondents indicating it as their choice. This high percentage might be because students are fascinated by hands-on practice [12]. Following Surgery, Medicine is the second most popular choice, with 26.7% of respondents expressing a preference for this field. The reason for preferring medicine is the diversity and broad scope of internal medicine. Also, doctors in medicine come across a variety of diseases that make it an interesting field [13]. Gynecology and obstetrics and Radiotherapy follow 7.9% and 3.2% of preferences by students, respectively. Most of the female undergraduate students prefer gynecology as

it's a highly rewarding field and focuses mainly on women's health issues, while Radiology's relatively lower percentage might indicate a niche yet crucial field that appeals to those interested in cancer treatment and imaging technologies [14]. The 'Others' category, comprising 13% of the responses, Community Medicine and Orthopedics, with preferences of 2.9% and 2.2% respectively, are the least chosen fields. The same results were there in a recent study [15]. Our collected data highlights the barriers in choosing community medicine as a speciality by the students and also their perception regarding community medicine. A majority (60%) of the respondents were not impressed by the subject, and that was the reason for their lack of interest in community medicine. This could be because of the non-procedural and perceived less dynamic nature of the field in comparison to compared to Surgery and Medicine, both of which have a bunch of high-impact specialities [16]. The second and third major reasons for not choosing community medicine (public health), as cited by a substantial portion (26%) of respondents, were poor career satisfaction (14.6%) and lack of growth opportunities in this field (11.4%), respectively. This is more likely because of concerns of respondents about job opportunities, career growth, and the long-term viability of this field [17]. This perception regarding this particular field may be because of limited exposure to the diverse career paths available within public health and community medicine. Other major reasons associated with less percentage of students inclined towards community medicine were their perceived inability to earn significant money (1.9%) or recognition (3.8%). These factors indicate that financial incentives and good societal status in promising fields are more often preferred by the students [18]. The comparatively lower financial rewards and lower societal recognition in community medicine could deter graduates from pursuing this path. Another notable reason is the perception that community medicine is not projected by faculty or postgraduate programs (2.5%). This reflects a potential issue with how the field is presented and supported during medical training. Insufficient encouragement and visibility from faculty may contribute to a lack of enthusiasm and support for Community Medicine [19]. Our study reveals that 1.0% of respondents believe nobody has done well in this field, which depicts that there is a lack of successful role models in this subject speciality. This belief could be based on lack of information about the achievements and impacts of professionals in Community Medicine. The small percentages of respondents citing factors like "not acknowledged by others" (0.3%) or "PG/faculty feels dissatisfied" (0.6%)

suggest that peer and faculty opinions might have minimal impact compared to other, more significant factors. However, these responses still highlight the importance of a supportive educational environment and positive role modelling [20]. Overall, this data indicates a strong need for increased efforts to enhance the appeal of Community Medicine. Addressing the lack of interest and perceived career prospects could involve improving educational exposure, showcasing successful professionals in the field, and highlighting the importance and impact of community health initiatives. Efforts to increase recognition and financial incentives could also play a role in making Community Medicine a more attractive career choice. The most favoured career scope for Community Medicine specialists, as per students' perception, is teaching, as indicated by 32.4% of respondents. Community Medicine specialists can use their expertise to educate medical students, the community, and junior public health professionals regarding preventive care and health promotion [21]. The second most popular career path, as per the perception of 15.9% of respondents, is becoming a researcher. As the methodology of doing research is being taught in community medicine and students are also asked to do research as a part of the curriculum of community medicine; that's why the students are perceiving that community medicine specialists have a scope in research [22]. Working in national programs is another significant career path, selected by 18.1% of respondents chose working in a national program as a perceived scope of community medicine specialists. They can play a vital role in managing and organizing public health programs and awareness campaigns, and seminars at the national level [23]. The option of working with international organizations such as the WHO or UNICEF is preferred by 27.6% of respondents. Community medicine specialists can work with international organizations to influence public health at a global level [24]. Becoming an administrator is considered a viable option by 6.0% of respondents. Administrative roles in community medicine are crucial for managing public health programs at a mass scale.

This study is limited by its single-institution setting and reliance on self-reported perceptions, which may introduce response bias and limit generalizability. Additionally, the cross-sectional design does not capture how career preferences may evolve over time with increased clinical exposure. Future multicenter longitudinal studies are recommended to explore changes in specialty preferences over time and to evaluate the impact of targeted interventions on improving interest in community medicine.

CONCLUSIONS

It was concluded that in our study, a few students, 9(2.8%), were interested in community medicine/ public health in specific reference to choosing it as a future speciality.

Amendments should be made in the curriculum, and lectures should be integrated with clinical ward rotations so that students can have a clear understanding of the prevalent community diseases. This will surely encourage students to adopt it willingly as a future speciality because we, being developing countries, are in dire need of enthusiastic public health professionals so that we can fight the communicable and non-communicable diseases.

Authors' Contribution

Conceptualization: M

Methodology: M, MH², HI, MIUH

Formal analysis: M, MH¹

Writing and Drafting: MH¹, MHR, MIUH

Review and Editing: M, MH¹, MH², HI, MHR, MIUH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparative Effectiveness of Duloxetine and Pelvic Floor Exercises for Stress Urinary Incontinence in Postmenopausal Women: A Quasi-Experimental Study in a Secondary Care Setting, Islamabad

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ABSTRACT

Stress urinary incontinence has great impact on female daily activities, emotional well-being, and overall quality of life; hence the need of most effective treatment is mandatory. **Objective:** To evaluate the effectiveness of Duloxetine and Pelvic Floor Muscle Training (PFMT) in the management of Stress Urinary Incontinence (SUI) in postmenopausal women. This study also aims to estimate symptom reduction, adherence rates, quality of life, and associated factors. **Methods:** Sample consist of 100 participants who were randomly assigned to two groups: Duloxetine (n=50) and PFMT (n=50). Reduction in weekly incontinence episodes over the period of 12 weeks was considered as the primary outcome. Improvement in quality of life, adherence rates, strengthening pelvic floor muscle and reduction in adverse effects was considered as the secondary outcome. **Results:** A considerable reduction in the weekly incontinence episodes was seen in both groups and no statistically significant difference ($p = 0.08$) was found among two groups. Similarly, quality of life scores was also improved significantly ($p < 0.001$), post intervention with PFMT group exhibiting a marginal advantage. Only the PFMT group exhibited significant pelvic floor muscle strengthening ($p < 0.001$). Mild adverse effects, including nausea and fatigue, were reported in 12% of participants in the Duloxetine group, while PFMT had no reported side effects. **Conclusions:** Both Duloxetine and PFMT effectively reduced SUI symptoms and improved quality of life. However, PFMT had advantages in adherence, safety, and pelvic floor muscle strengthening, making it the preferred first-line treatment.

INTRODUCTION

Urinary Incontinence (UI), a stern concern that often fallouts in frustration, community avoidance, and distress, affects lots of postmenopausal women. It has a big influence on daily life, making relationships and chores thought-provoking [1]. Stress Urinary Incontinence (SUI) and Mixed Urinary Incontinence (MUI) are the furthestmost common forms between postmenopausal women. In addition to involuntary urine outflows caused by SUI, laughing and sneezing put additional pressure on the bladder. Urgency Urinary Incontinence (UUI) and SUI

combined to form MUI, which is characterized by a solid need to urinate that roots leakage [2]. Because of hormonal and physiological changes that are essential to onset of UI, women are more susceptible to UI during postmenopausal phase [3]. Lack of estrogen in postmenopausal women results in structural changes in urethra, including decreased collagen, synthesis, thinning of the epithelium and impaired closure mechanisms. Given these factors targeted therapy for SUI and MUI is clinically required [4]. The importance of specific treatment



strategies is also highlighted by the rising incidence of UI in aging persons [5]. Pelvic floor muscle dysfunction, which is often exacerbated by age-related muscle weakness and past birth trauma, exacerbates the symptoms of urinary incontinence [6]. The management of SUI within MUI in postmenopausal women primarily includes pharmacological and non-pharmacological interventions [7]. Duloxetine, a Serotonin-Norepinephrine Reuptake Inhibitor (SNRI), has emerged as a promising pharmacological treatment for SUI and MUI [8]. Duloxetine acts by enhancing neurotransmitter activation's nucleus of the sacral spinal cord, leading to bigger contraction of the urethral sphincter and higher urinary control [9]. Clinical investigations have established that duloxetine boosts value of life, lessens the frequency of incontinence occurrences, and reduces the intensity of signs as informed by patients [10]. However, side effects such as tiredness, dry mouth, nausea, and light-headedness often limit its use and can influence patient compliance [11]. The effectiveness of duloxetine in relation to non-pharmacological methods, including Pelvic Floor Muscle Training (PFMT), is currently being investigated, despite the fact that it is regarded as a second-line pharmaceutical treatment for UI [12]. Additionally, more research is required to ascertain whether duloxetine medication is long-term tolerable and adhered to by postmenopausal women. Numerous RCTs have confirmed PFMTs effectiveness in lowering incontinence episodes, enhancing muscle performance, and increasing patient satisfaction. PFMT being the first-line conservative treatment for SUI and MUI, provides a long-term, safe alternative to pharmacological treatments because it carries fewer risks [13]. However, the efficacy of PFMT depends on patient adherence, proper technique, and the availability of supervised training [13]. Regardless of its frequency and effect, UI is still underdiagnosed and poorly treated in Low-Middle-Income Countries (LMICs), where patients find it hard to pursue treatment due to societal standards and a lack of medicinal resources. Numerous females suffer in quiet as a consequence, which intensifies their emotional and psychological health problems.

Despite extensive research on duloxetine and PFMT as separate interventions, direct comparative studies remain limited, particularly in LMICs where healthcare disparities pose challenges to UI diagnosis and treatment. In Pakistan, cultural stigmas, inadequate access to specialized continence care, and inconsistent healthcare-seeking behaviors contribute to these challenges. To fill this gap, this study will conduct a quasi-experimental trial in a secondary care hospital in Islamabad, Pakistan. By comparing the effectiveness of duloxetine and PFMT, evaluating patient adherence and satisfaction, and analyzing treatment sustainability, this research aimed to

generate valuable insights into the barriers and facilitators influencing UI management in a resource-limited setting.

METHODS

This quasi-experimental study was conducted at Federal General Hospital, Chak Shahzad, Islamabad, a secondary care hospital. Ethical approval No. F.3-144/ADMN-EC-FGH was obtained from the Ethics Review Committee (ERC) of the said institute. Before study initiation and written informed consent was secured from all participants, ensuring confidentiality and compliance with ethical guidelines. Sample size was calculated using the Cohen's power analysis formula based on the assumption that have two independent groups with statistical power (80%), moderate effect size ($d=0.3$) and 5% significance level.

$$n = (((Z_{\alpha/2} + ZB)^2 \cdot 2\sigma^2 / (d^2)))$$

Where, $Z_{\alpha/2}$ the critical value for the chosen significance level (1.96 for 5%) and ZB is the critical value for the desired power (0.84 for 80%). According to this calculation the sample size calculated is 50 for both groups. This formula helps to decrease the risk of Type I and Type II errors while maintaining feasible sampling and reliable study outcomes [14]. The study was conducted over three months/12 weeks (July 2024 – September 2024). This time period was selected based on prior research studies and time required to produce expected treatment outcomes, ensuring optimum time for Duloxetine's neurochemical effects and PFMT-induced muscle adaptation. The study included postmenopausal women (≥ 45 years) with confirmed menopausal status, experiencing at least two episodes of Stress Urinary Incontinence (SUI) per week within Mixed Urinary Incontinence (MUI), and with no prior UI treatment in the past six months. The optimal age limit for menopause in Asian women fall in this range as reported by a recent study in India [13, 14]. This ensures the inclusion of hormonally stable patients, having sufficient clinical symptoms and susceptibility to treatment with removal of all confounding factors. Exclusion criteria included urgency-predominant UI, severe overactive bladder symptoms, history of pelvic surgeries, neurological disorders, severe pelvic organ prolapse, uncontrolled diabetes, recurrent UTIs, chronic kidney disease, medications affecting urinary function (e.g., alpha-blockers, diuretics, estrogen therapy, anticholinergics), and severe psychiatric or cognitive conditions affecting adherence. Participants were assigned to one of two intervention groups. The Duloxetine Group received duloxetine 40 mg twice daily for 12 weeks, with regular monitoring for adherence, side effects, and symptom improvement. The PFMT Group underwent a structured Pelvic Floor Muscle Training (PFMT) program for 12 weeks, which included weekly supervised sessions with a physiotherapist and daily home-based exercises. Data were collected at baseline, 6 weeks, and 12 weeks through structured bladder diaries, questionnaires, clinical

assessments, and follow-up interviews. The primary outcome was a reduction in weekly incontinence episodes, measured using a bladder diary. Secondary outcomes included quality of life improvement, assessed using the I-QOL and UDI-6 questionnaires which are widely used validated open assess questionnaires used for the said purpose. These questionnaires were utilized in different setting and it demonstrated internal consistency and reliability in various settings with a Cronbach's alpha value ranging from 0.77-0.99 [15-18]. It is used in this study without any modification as it exhibited universal acceptance and participants also reported no difficulty in its understanding. The I-QOL score range from 0 to 100 and a higher score indicates better quality of life whereas UDI-6 scores also range from 0 to 100 and a higher score here indicates more a higher tendency of symptom distress. Adherence rates were recorded via self-reported logs and follow-up interviews. Adherence rates were recorded via self-reported logs and follow-up interviews. Pelvic floor muscle strength was measured using a simple handheld air filled perineometer in the PFMT group by an experienced physiotherapist. Training was provided to the patients by the physiotherapist for home-based exercises and their understanding was evaluated and improved on each weekly visit. Adverse effects were documented through self-reports and clinical monitoring in the duloxetine group. Descriptive and inferential statistics was used to evaluate the results. Shapiro wilk test was used to assess the normality of the data. Continuous variables e.g., age, BMI, weekly incontinence episodes were reported as Mean $\pm$ Standard Deviation (SD) whereas categorical variables e.g., education level, adherence rates were represented as frequencies and percentages. Based on normality of data paired t-test was used to find differences in the same group outcomes, pre and post intervention whereas independent t-test was used to find differences in outcomes between groups. All collected data were recorded on standardized Case Report Forms (CRFs), manually reviewed for completeness, and entered into SPSS (version 23.0) for statistical analysis. Data entry was double-checked for accuracy, and any discrepancies were resolved through cross-verification with original records.

RESULTS

The baseline demographic and clinical characteristics were comparable, with no statistically significant differences in age, duration of menopause, BMI, parity, baseline incontinence episodes, or comorbid conditions ($p > 0.05$).

Table 1: Baseline Demographic and Clinical Characteristics (n=100)

Characteristics	Group A (Duloxetine) Mean $\pm$ SD/ Frequency (%)	Group B (PFMT) Mean $\pm$ SD/ Frequency (%)	p-Value
Age (Years)	58.4 $\pm$ 5.2	57.9 $\pm$ 5.5	0.650
Duration of Menopause (Years)	8.1 $\pm$ 3.7	8.4 $\pm$ 3.5	0.720
BMI (Kg/m ²)	27.8 $\pm$ 3.1	27.4 $\pm$ 3.0	0.540
Education Level			
Primary	12 (24%)	10 (20%)	0.780
Secondary	18 (36%)	20 (40%)	
Higher	20 (40%)	20 (40%)	
Parity (Number Of Children)	3.2 $\pm$ 1.1	3.4 $\pm$ 1.0	0.430
Baseline Weekly SUI Episodes	9.8 $\pm$ 2.3	10.1 $\pm$ 2.1	0.580
Hypertension	15 (30%)	14 (28%)	0.820
Diabetes Mellitus	10 (20%)	12 (24%)	0.630
History of UTI	8 (16%)	9 (18%)	0.790

Note: Continuous variables are presented as Mean $\pm$ SD (for normal data) or Median (IQR) (for non-normal data)

A marked decrease ($p < 0.001$, paired t-test) in weekly incontinence episodes was seen in both intervention groups and at 12 weeks. But the results dictate absence of any significant results between two groups ($p = 0.08$, independent t-test). The duloxetine group demonstrated a mean reduction of 5.6 episodes per week (95% CI: 5.0-6.2, $p < 0.001$), while the PFMT group showed a slightly greater reduction of 6.2 episodes per week (95% CI: 5.7-6.7, $p < 0.001$). But it should be noted that this is only the numerical advantage, and does not yield any statistically significant difference, demonstrating that treatments in both intervention groups was effective in alleviating symptoms with PFMT exhibiting a slightly greater but comparable benefit. Quality of life scores assessed using the Incontinence Quality of Life (I-QOL) and Urogenital Distress Inventory (UDI-6) scores, showed significant improvements in both groups as study participants in the duloxetine group experienced an average increase of 18 points in the I-QOL score, while those in the PFMT group showed a slightly higher improvement of 20 points ($p < 0.001$, paired t-test). Meanwhile, the reduction in UDI-6 scores was 8 points in the duloxetine group and 9 points in the PFMT group ($p < 0.001$, independent t-test), which indicates a significant decrease in urinary distress symptoms. Although PFMT showed a slightly greater improvement in quality of life, both interventions were effective in reducing the impact of incontinence. The results of the study showed that the PFMT group had significantly higher treatment adherence, with 88% of participants finishing the entire training program, compared to 74% in the duloxetine group. The duloxetine group's reduced adherence rate could be the result of worries about drug side effects, which could have affected

the effectiveness of treatment as a whole. This implies that for postmenopausal women with stress urine incontinence, a non-pharmacological therapy option such as PFMT may be a more viable and enduring option. According to perineometer readings, the PFMT group showed a significant increase in pelvic floor muscle strength, while the duloxetine group showed no such changes. Perineometer readings increased by an average of 10 cmH₂O in participants undergoing PFMT ($p < 0.001$), indicating increased muscular strength and function. On the contrary, the duloxetine group showed no measurable improvement in pelvic floor strength, indicating the mechanical benefits of structured muscle training in managing stress urinary incontinence. Mild adverse effects were reported exclusively in the duloxetine group, with 12% of participants experiencing nausea and fatigue, while no adverse effects were observed in the PFMT group. This highlights the well-tolerated nature of pelvic floor muscle training as a non-invasive intervention, whereas duloxetine, despite its efficacy, may present mild side effects that could impact patient adherence and overall satisfaction with treatment. Chi-square analysis of demographic factors and treatment outcomes showed that higher education was significantly associated with better adherence ($p = 0.015$). Women with higher education levels were more likely to adhere to treatment, with adherence rates of 67.5% in the higher education group compared to 57.9% in the secondary education group and 23.8% in the primary education group. A significant correlation was also observed between parity and quality-of-life improvement, with women having fewer children (≤ 2) experiencing greater benefits ($p = 0.048$). This suggests that lower parity may be associated with better treatment response and improved quality of life.

Table 2: Chi Square score of education and adherence level

Education Level	High Adherence ($\geq 80\%$) Frequency (%)	Low Adherence ($< 80\%$) Frequency (%)	p-Value
Primary	5 (23.8%)	16 (76.2%)	0.015*
Secondary	22 (57.9%)	16 (42.1%)	
Higher	27 (67.5%)	13 (32.5%)	

Note: $p \leq 0.050$ is considered statistically significant and is marked with an asterisk(*)

Both duloxetine and PFMT effectively reduce stress urinary incontinence episodes and improve quality of life in postmenopausal women. However, PFMT had some advantages over duloxetine that includes higher adherence rates (88% vs. 74%), no adverse effects, and significant increase in pelvic floor strength. Also, demographic variables played a key role, with women who had higher education levels exhibiting better adherence and those with fewer children experiencing greater quality-of-life improvements. These findings suggest that PFMT may be the favourite first-line intervention, while duloxetine remains a workable alternative for those unable

to commit to exercise-based therapy.

Table 3: Association of parity and quality of life

Parity	I-QOL Improvement ≥ 15 Frequency (%)	I-QOL Improvement < 15 Frequency (%)	p-Value
≤ 2 children	25 (73.5%)	9 (26.5%)	0.048*
> 2 children	22 (53.7%)	19 (46.3%)	

Note: $p \leq 0.050$ is considered statistically significant and is marked with an asterisk(*)

DISCUSSION

Both duloxetine and PFMT considerably reduced weekly incontinence episodes over the period of 12 weeks but this was statistically non-significant within the same group but upon comparison of two groups, significant reduction in the PFMT group (6.2 vs. 5.6 episodes, $p = 0.08$) was observed. This suggests that both treatments are effective, with the choice depending on patient preference, tolerability, and long-term sustainability. These findings align with previous studies which demonstrated that structured PFMT led to greater long-term symptom benefits than pharmacological interventions alone [13]. Also, another study reported that patients with these conditions should undergo PFMT and can consider duloxetine as a second line treatment [19]. Furthermore, another study found that while Duloxetine provided rapid symptom relief, adherence rates were significantly lower due to side effects, making it less favourable for long-term management [20]. Both interventions significantly improved quality-of-life measures, including I-QOL and UDI-6 scores, with PFMT showing slightly greater benefits (+20 vs. +18 in I-QOL, $p < 0.001$). This highlights the added advantage of pelvic muscle strengthening in providing long-term relief and enhancing daily functioning. Adherence rates were higher in the PFMT group (88%) compared to the duloxetine group (74%), likely due to adverse effects such as nausea and fatigue, reported by 12% of participants. Although mild, these side effects affected medication compliance, a challenge noted in previous pharmacotherapy trials [21]. Additionally, the chi-square analysis revealed that education level significantly influenced adherence rates ($p = 0.015$), with higher-educated women more likely to adhere to both interventions [22]. This suggests that patient education and awareness play crucial roles in treatment success. Another important finding was the correlation between parity and treatment effectiveness. Women with ≤ 2 children experienced greater quality-of-life improvements ($p = 0.048$), possibly due to less pelvic floor damage from childbirth. Repeated pregnancies and vaginal deliveries are well-established risk factors for pelvic floor dysfunction, leading to weakened urethral support and higher SUI severity. This finding aligns with studies which suggest that women with multiple vaginal deliveries often require more intensive rehabilitation or surgical

interventions to achieve comparable symptom relief due to decreased muscle tone [23]. Given the study findings, PFMT should be prioritized as the first-line intervention for SUI in postmenopausal women due to its higher adherence, superior pelvic floor strengthening effects, and absence of adverse effects. These results align with a study which reported PFMT to be the first line treatment option for SUI [24, 25]. Duloxetine remains a viable alternative for patients who cannot engage in structured PFMT or require rapid symptom relief, but clinicians should be mindful of potential side effects that may impact compliance. Moreover, patient education should be integrated into treatment plans, particularly for women with lower education levels, to enhance adherence and optimize outcomes. Parity should also be considered as multiparous women require longer rehabilitation programs or adjunct therapies to achieve similar improvements. The short duration of 12 weeks prevents conclusions about long-term effectiveness and adherence.

The short duration of follow-up (12 weeks) limits assessment of long-term effectiveness and sustainability of both PFMT and duloxetine. Additionally, the relatively small sample size and reliance on self-reported adherence may affect the generalizability and accuracy of outcomes. Future research should assess outcomes over 6 to 12 months to evaluate sustained benefits and relapse rates. Additionally, we did not include a combination therapy group (duloxetine plus PFMT), which could have provided insights into potential synergistic effects. Future studies should explore the long-term sustainability of PFMT, the potential benefits of combination therapies, and the role of patient education in improving adherence and treatment success.

CONCLUSIONS

This study concluded that both duloxetine and PFMT successfully improve stress urinary incontinence in postmenopausal women. However, PFMT established higher adherence, greater pelvic floor muscle strengthening, better quality-of-life improvements, and no side effects, making it the preferable first-line treatment. Duloxetine remains a possible alternative but had lower adherence and mild adverse effects. Additionally, higher education was concurrent to better adherence, and lower parity was related with greater quality-of-life improvements. Based on these findings, PFMT should be prioritized for managing stress urinary incontinence, while future research should explore long-term outcomes and combination therapies.

Authors' Contribution

Conceptualization: AR¹, AR²

Methodology: AR¹, AI, AR²

Formal analysis: AR²

Writing and Drafting: AR¹, AI, AA

Review and Editing: AR¹, AI, AR², AA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Single Dose Intravenous Tranexamic Acid Efficacy in Reducing Blood Loss in Total Hip Replacement

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ABSTRACT

Total Hip Replacement is a commonly performed procedure for Hip joint degeneration. Despite its hazards, blood transfusion has to be performed due to significant perioperative blood loss. The effects of pre-operative intravenous single-dose tranexamic acid in our population have been presented in this study. **Objectives:** To compare the mean blood loss during and after total hip replacement for hip osteoarthritis with or without a single dose of tranexamic acid.

Methods: This quasi-experimental study was performed in the Orthopedic Surgery Department Unit II, Nishtar Medical University Hospital, Multan, from October 2022 to March 2024. In the experimental group, tranexamic acid (20mg/kg) was administered intravenously ten minutes before skin incision, while in the control group, no such drug was given. Preoperative and postoperative Hematocrit data were collected. THA was done as per standard protocol. The operative blood loss and blood transfusions were recorded and compared with the controls.

Results: Among 60 patients, the mean age was 54.85 ± 12.23 years. Male were 19 (31.7%) and female were 41 (68.3%). BMI was 26.04 ± 3.48 Kg/m². Mean age ($p=0.746$), mean BMI ($p=0.633$), age ($p=0.417$), gender ($p=0.781$) and BMI ($p=0.749$) were comparable in both groups. The estimated total loss of blood was significantly less in patients receiving intravenous tranexamic acid (1169.10 ± 191.92 ml vs. 1730.07 ± 203.62 ml; $p<0.001$) as compared to the control group.

Conclusions: It was concluded that a pre-operative intravenous single dose of tranexamic acid decreased blood loss during surgery significantly in patients having total hip arthroplasty regardless of gender, age and BMI.

INTRODUCTION

Osteoarthritis affects life quality and is the major cause of morbidity in patients with advancing age [1]. Surgery is a choice for patients who have failure of conservative management [2]. Heavy intraoperative bleeding is a critical issue during total hip arthroplasty that usually has high mortality and morbidity [3]. Such bleeding may need transfusion of blood that is usually allogenic. Blood transfusion has risks and bears costs as well, along with issues in arranging sufficient blood products. So interest has been generated in blood-sparing protocols. These include red cell salvage (intraoperative), hypotensive anesthesia, local anesthesia, re-transfusion of autologous

blood and the antifibrinolytic drugs [4]. Antifibrinolytic medicines are easily accessible and promote hemostasis and decrease bleeding, resulting in a decrease in the need for blood transfusion [5]. The efficacy of such medicines has been assessed in hepatic, cardiovascular, orthopedics and other surgeries. Two such drugs are tranexamic acid and aprotinin, whose efficacy is proven in many surgeries [6]. When primary fibrinolysis is the main cause of bleeding, tranexamic acid effectively inhibits fibrinolysis and so promotes hemostasis without the risk of complications like thrombosis or embolism. The possible prothrombotic effects of tranexamic acid are also a matter



of concern among many orthopedic surgeons, which has yet to be investigated in further studies providing evidence of a high level [7]. Even with these good results, valid data is lacking regarding its safety. Thus, the use of tranexamic acid in routine remains a concern. Data on perioperative outcomes are rare. Further, population-based data is not available, with limited randomized trials including selected patients. It can be seen that there is wide variation not only in the conduct of studies with some retrospective, dose, as well as mode of administration, but also in the results. It was thus necessary to conduct another study to increase the evidence of effectiveness and safety of tranexamic acid from a developing country to reduce the costs associated with the procedure and complications in the peri-operative period with this promising intervention, which is still not being used frequently locally. There is no local study according to our knowledge.

Although tranexamic acid has demonstrated effectiveness in reducing blood loss during various surgical procedures, its routine use in total hip arthroplasty remains limited due to concerns regarding safety and inconsistent evidence related to dosage, administration routes, and perioperative outcomes. Moreover, there is a lack of local, population-based data from developing countries like Pakistan to support its widespread adoption. This study aims to compare mean blood loss with or without tranexamic acid, during and after total hip arthroplasty for hip osteoarthritis.

METHODS

This quasi-experimental study was done at the Orthopedic Surgery Department, Unit II, Nishtar Medical University (NMU) Hospital, Multan, from October 2022 to March 2024 after approval from the institutional ethical review board of NMU vide NO. 13321/NMU. The sample size was 60 patients, calculated with 80% test power and 95% CI., predicted mean blood loss for the tranexamic group was 1107 ± 508 ml, while the non-tranexamic acid group was 1729 ± 552 ml [8]. Non-probability consecutive sampling was used for the inclusion of the patients. Patients of both genders, having an age between 40-80 years, having pain in the hip joint for the last 3 months with evidence of grossly decreased space of the joint with osteophytes and deformity of the head of the femur and acetabulum on Antero Posterior as well as Lateral view were included. The patients were selected for Total Hip Arthroplasty and were included in the study after proper consent. Patients with medical contraindication to tranexamic acid, which include previous attacks of seizures, severe kidney failure with creatinine clearance less than 30 mL/min or having bleeding disorders, thromboembolic disorders like thrombosis in deep veins, pulmonary emboli, ischemic heart disease, acute lower-limb ischemia and stroke, were excluded from the study. Detailed assessment comprising history (age, gender, etc.), examination and relevant laboratory investigations (hematocrit) was carried out.

Patients were randomly divided into the two groups by the lottery method: the tranexamic group and the control group. In the tranexamic group, ten minutes before incision, an intravenous tranexamic acid (20 mg per kg) was administered as a single dose. Patient's detailed assessment was done again, and a daily hematocrit level postoperatively was collected. All blood transfusions were recorded. The standard blood management protocol was adhered to, which calls for a stringent transfusion Hb trigger of 8.0 and the infusion of 500 mL of plasma expander volume expansion before considering a transfusion in the event of postoperative hypotension, lightheadedness, or dizziness. Total hip arthroplasty was done as per standard protocol. All the patients were monitored regularly for cardiac or brain ischemia signs, along with deep vein thrombosis. Using the Gross formula, total blood loss (TBL) was computed from hematocrit levels: $TBL = \text{Predicted Blood Volume} \times (\text{Preoperative Hematocrit} - \text{Postoperative Hematocrit}) / \text{Average Hematocrit}$ [9]. The difference between hematocrit values before surgery and hematocrit values on the 8th day after surgery was considered the hematocrit reduction. Blood volume (BV)(ml) = $70 \times \text{weight (kg)}$. SPSS (version 24.0) was used to enter all of the data for statistical analysis. Numerical variables, i.e. age, BMI and total blood loss, are presented by mean $\pm$ SD. The frequency and proportion of categorical variables, such as gender, have been displayed. To compare the mean blood loss between two study groups (i.e. tranexamic acid and controls) independent sample t-test was applied at 95 % CI with p-value equal to or less than 0.05. Data were also stratified by gender, age and BMI, and post-stratification independent sample t-test was reapplied, with a p-value ≤ 0.05 being considered significant, while the Mann-Whitney U test was applied for data that was not normally distributed. To calculate the effect size, Cohen's d was used.

RESULTS

The mean age of the patients was 54.85 ± 12.23 years, with a range of 40 to 80 years. The patients' BMIs ranged from 20.3 to 33.2 kg/m^2 , with a mean of $26.04 \pm 3.48 \text{ kg/m}^2$ (Table 1).

Table 1: Baseline Features (n=60)

Characteristics	Participants (n=60)
Age	
Overall Years	54.85 ± 12.23
40-59 Years	39 (65.0%)
60-80 Years	21 (35.0%)
Gender	
Male	19 (31.7%)
Female	41 (68.3%)
BMI	
Overall	26.04 ± 3.48
20-25 Kg/m^2	25 (41.7%)
25-30 Kg/m^2	27 (45.0%)
$\geq 30 \text{ Kg/m}^2$	8 (13.3%)

The distribution of the two groups in this study was similar in terms of mean age ($p=0.746$), mean BMI ($p=0.633$), age ($p=0.417$), gender ($p=0.781$), and BMI ($p=0.749$) (Table 2).

Table 2: Baseline Characteristics of Study Groups ($n=60$)

Characteristics	Tranexamic Acid (n=30)	Controls (n=30)	p-Value
Age			
Overall Years	55.37 ± 13.49	54.33 ± 11.02	0.746
40-59 Years	18 (60.0%)	21 (70.0%)	0.417
60-80 Years	12 (40.0%)	9 (30.0%)	
Gender			
Male	10 (33.3%)	9 (30.0%)	0.781
Female	20 (66.7%)	21 (70.0%)	
BMI			
Overall	25.82 ± 3.21	26.26 ± 3.77	0.633

20-25 Kg/m ²	13 (43.3%)	12 (40.0%)	0.749
25-30 Kg/m ²	14 (46.7%)	13 (43.3%)	
≥ 30 Kg/m ²	3 (10.0%)	5 (16.7%)	

According to the independent sample t-test and chi-square test, the observed difference was statistically insignificant

Compared to the controls, patients who received intravenous tranexamic acid experienced a considerably lower estimated total blood loss (1169.10 $\pm$ 191.92ml vs. 1730.07 $\pm$ 203.62ml; $p<0.001$). There were also highly significant differences across different age, gender, and BMI categories, and it is evident from the findings that these changes in blood loss are consistent across various subgroups (Table 3).

Table 3: Comparison of Total Blood Loss (ml) Between the Study Groups ($n=60$)

Characteristics	Tranexamic Acid (Mean $\pm$ SD)	Controls (Mean $\pm$ SD)	p-Value	Cohen's d
Age				
Overall	1169.10 $\pm$ 191.92	1730.07 $\pm$ 203.62	<0.001*	2.84
40-59 Years	1171.28 $\pm$ 199.88	1734.29 $\pm$ 212.17	<0.001*	2.78
60-80 Years	1165.83 $\pm$ 188.00	1720.22 $\pm$ 193.90	<0.001*	2.90
Gender				
Male	1152.70 $\pm$ 204.46	1742.89 $\pm$ 209.70	<0.001*	2.86
Female	1177.30 $\pm$ 190.28	1724.57 $\pm$ 205.97	<0.001*	2.76
BMI				
20-25	1162.00 $\pm$ 218.12	1751.67 $\pm$ 221.17	<0.001*	2.69
25-30	1172.29 $\pm$ 190.60	1709.15 $\pm$ 196.26	<0.001*	2.78
≥ 30	1185.00 $\pm$ 108.30	1732.60 $\pm$ 218.39	0.007*	2.98

*The observed difference was statistically significant. Independent sample t-test

DISCUSSION

Total hip replacement is the best treatment for patients with failure of conservative management for osteoarthritis hip [10]. The antifibrinolytic medication tranexamic acid, which increases haemostasis, has a well-established track record in general surgery to decrease the bleeding volume and ultimately decrease the requirement of the allogenic transfusion [11]. Nonetheless, there was debate surrounding the available data about tranexamic acid's ability to lower surgical blood loss during and following total hip replacement. The male-to-female ratio in the current study group was 1:2.2, where 19 (31.7%) were males and 41 (68.3%) were female. The patients in our study had a mean BMI of 26.04 $\pm$ 3.48 kg/m². Regardless of the patient's age, gender, or BMI, we discovered that the estimated total blood loss was considerably lower in patients receiving intravenous tranexamic acid (1169.10 $\pm$ 191.92ml vs. 1730.07 $\pm$ 203.62ml; $p<0.001$) than in controls. Haratian et al., also observed a reduction in blood transfusion volume in patients receiving tranexamic acid and thus minimizing perioperative loss of blood [12]. Many studies have revealed that tranexamic acid in total hip arthroplasty is a successful way of decreasing blood loss; therefore, it is an effective

way to achieve hemostasis in clinical situations. Likewise, researcher found similar findings in trauma and significant hemorrhage, showing broader applicability of tranexamic acid [13]. In a retrospective study, Akti et al., evaluated the role of tranexamic acid (TXA) on the blood losses in patients of total hip arthroplasty. They studied 120 patients, among whom 45 were male and 75 were female, having 57.2 $\pm$ 4.9 years of age with a range of 45 to 67 years. Their patients had primary osteoarthritis. Sixty-seven patients underwent THA without the use of TXA, and 53 patients received TXA. They found a significant difference ($p<0.05$) between their groups regarding intraoperative blood loss, blood in the drain, total blood loss and the blood transfusion. They recommended routine use of tranexamic acid if not contraindicated [14]. Magill et al., examined 534 patients in a randomized control trial, having 233 in group 1 (1g IV TXA intraoperative + 24 hrs. postoperatively), 235 in group 2 (1g IV TXA intraoperative only) and 66 in group 3 (no TXA at all). There was no significant difference in the mean intraoperative Blood Loss between the two experimental groups, 848.4 ml $\pm$ SD 463.8 in group 1 and 843.7 ml $\pm$ 478.7 in group 2; the mean difference was -4.7 ml (95% confidence

interval was -82.9 to 92.3); $p=0.916$) [15]. Their study results also support the intraoperative use of TXA, as per our study results. Vles et al., reported the results of their randomized controlled trial, in which 60 patients received intravenous administration of 1.5 g of tranexamic acid was administered just before wound closure, and in other 60 patients' topical application of 3.0 g of tranexamic acid was given by a subfascial drain at the end of the procedure. Post-operative blood loss was calculated. They found no significant difference statistically as far as the post-operative blood loss is concerned. This study also provides evidence that tranexamic acid is an effective tool for blood loss prevention in hip arthroplasty [16]. Zheng et al., reported similar results. They assessed 56 RCTs having different regimens. They found that all high doses of tranexamic acid were effective for decreasing total blood loss, without the risk of pulmonary embolism or deep vein thrombosis when compared with placebo. They recommended a medium dose of 20-40 mg/kg or 1.5-3.0 g of combined Intravenous/Intra-Articular tranexamic acid to control the bleeding in total hip arthroplasty patients [17]. Zha and his colleagues retrospectively analyzed prospectively collected data of seventy patients who underwent total hip arthroplasty. They studied two groups: the tranexamic acid group of 39 patients who received 1.5 g intravenous tranexamic acid and the control group of 31 patients who did not receive tranexamic acid. Total blood loss as well as postoperative hemoglobin drop in the tranexamic acid group was significantly lower as compared to the control group, with a p value of <0.050 [18]. Avci et al., retrospectively studied the effect of two doses of TXA intravenously before and after surgery in THA patients on total blood loss and blood transfusion need. In this study, total mean blood loss, decrease in hemoglobin levels and amount of blood transfusion were lower in the TXA group compared to the control group ($p=0.001$; $p=0.001$; $p=0.001$, respectively). They concluded that TXA is an effective and reliable way in THA for significantly reducing blood loss and the need for blood transfusion without causing an increase in thromboembolic complications [19]. Khanna et al., investigated 60 patients who were undergoing Total hip arthroplasty. The TXA group received IV tranexamic acid at a dose of 15mg/kg, and the other group received no drug. They noted less direct blood loss (p value= <0.001) in the tranexamic group as compared to a control group, which is 988 vs 1295 ml. They found tranexamic acid, given before incision, to be efficient in reducing Direct and Indirect blood loss in the Total hip arthroplasty procedure [20]. Khorram et al., searched PubMed, Web of Science, Scopus, Embase, and the Cochrane Library and selected 14 studies having 1358 patients for inclusion in their meta-analysis. They reported the TXA role in decreasing total blood loss in all approaches. They further noticed that the lateral approach (LA) maintains the postoperative Hb level more effectively (WMD=1.081, 95 % CI: 0.620-1.541), while the

posterolateral approach has significantly less Intraoperative blood loss (PLA; WMD = -70.578, 95 % CI: [-130.389] - [-10.766]) and the posterior approach (PA) was associated with a reduction in total blood loss (WMD = -392, 95 % CI: [-474.439] - [-310.231], p -value <0.001) [21]. Current study is the first of its kind in our population and has found that pre-operative Intravenous tranexamic acid bolus reduced blood loss during surgery significantly in contrast to controls in patients who are having a complete hip replacement or arthroplasty for grade IV osteoarthritis without regard to patients' age, gender and BMI. Based on this evidence, it can be recommended that in future practice, patients undergoing total hip arthroplasty for osteoarthritis hip should receive an intravenous bolus of TXA to reduce loss of blood and subsequent requirement for post-operative transfusion with its associated complications.

The relatively small sample size and single-center design may limit the generalizability of the findings to broader populations. Additionally, variations in surgical technique and perioperative management were not fully controlled, which could influence blood loss outcomes. Future large-scale, multicenter randomized trials are recommended to further validate the optimal dosing and administration protocols of tranexamic acid in total hip arthroplasty.

CONCLUSIONS

It was concluded that a pre-operative intravenous tranexamic acid as a single dose reduced operative blood loss significantly as compared to controls in patients having total hip arthroplasty for grade IV osteoarthritis, regardless of patient's gender, age and BMI.

Authors' Contribution

Conceptualization: RSWR

Methodology: MBUDZ, RSWR, MA

Formal analysis: MAT, IS

Writing and Drafting: MBUDZ

Review and Editing: MBUDZ, RSWR, MA, MAT, IA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Physical Activity among Middle-aged Adults after Total Hip Arthroplasty Following One Year

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ABSTRACT

Total hip arthroplasty is one of the common surgical procedures that is used to treat the diseases of the hip joint and improve mobility and physical activity. Evaluating the physical after total hip arthroplasty is critical to understanding recovery and outcomes for long-term effectiveness. **Objective:** To evaluate physical Activity after total hip arthroplasty following one Year. **Methods:** The questionnaire-based descriptive case series included 50 subjects (27 Male and 23 Female) after total hip arthroplasty. The sample size was collected using the WHO calculator. Physical Activity and pain were evaluated using the Harris Hip Score. The data were analyzed using SPSS version 20. **Results:** Middle-aged patients aged 55-65 years were evaluated using the Harris Hip Score. Physical Activity was gradually fair to good in patients with total hip arthroplasty following one Year. In 50 patients of THA, the grades of total Harris hip score were with 14 patients (28%) in Poor grade (<70), 17 patients (34%) in Fair grade (70-79), 18 patients (36%) in Good grade (80-89) and one patient (2%) in Excellent grade (90-100). **Conclusions:** It was concluded that the majority of middle-aged adults, after total hip arthroplasty, presented with fair to good (34 % & 36 %) physical activity following one Year.

INTRODUCTION

Total hip arthroplasty is one of the most significant and successful surgical procedures. It is considered one of the most successful surgeries to treat degenerative hip conditions in the last thirty years [1]. Total hip arthroplasty is the landmark of modern surgical history and clinical results. It improves Physical Activity, pain, and quality of life [2]. Total hip arthroplasty is a successful and cost-effective procedure in orthopedic surgeries. There is a significant increase in total hip arthroplasty procedures globally among young patients, which is to improve physical activity, physical demands, and quality [3]. Physical Activity, as described by the World Health Organization, is any movement of skeletal muscles that results in the use of

energy [4]. Adequate PA brings along benefits such as enhanced mobility, highlighted resistance to falls, highlighted resistance to death, and enhanced mental health. Individuals suffering from hip and knee OA are generally less likely to engage in activities that promote Physical Activity [5]. Maintaining sufficient PA reduces OA pain and tackles other activity-related comorbidities like obesity, cardiovascular diseases, and diabetes [6]. The general knowledge about the improvement of physical Activity as one of the significant measures to lessen pain and improve the range of movement among patients with OA of the hip or knee is undoubtedly true. According to the International Surgical Outcomes, the patient who



underwent orthopedic surgery had complications [7]. This is particularly taking into consideration the complications that occur in total hip arthroplasty (THA). There is evidence supporting the fact that complications following THA contribute to higher hospital length of stay, reduced mobility, and other adverse effects [7]. The HHS (Harris Hip Score) was designed to make quantitative measurements of hip surgery results, and it is aimed at gauging several kinds of hip disabilities. These include the area of pain, functional status, no deformity present, and flexibility of the affected part [8]. The pain domain describes the degree of pain and how it impacts severity levels, while the function domain embraces daily functioning. Sixteen of the items, in total, each have a maximum of one hundred points [9]. The degree of pain is the primary consideration when considering the recommendation for THA [10]. Self-reported pain is commonly evaluated by disease-specific measures when evaluating the effectiveness of care. The objective of pain relief is also established at 3, 6, 9, and 12 months following THA [11]. The patients may get long-term pain even after being treated with total hip arthroplasty. THA is the ultimate answer to many prolonged-standing hip joint disorders, and based on the above findings, most of the patients achieve notable improvements in functional performance and pain levels [12]. Acute post-surgical pain is a severe reason behind the bothersomeness of particular individuals [13].

Although total hip arthroplasty (THA) is highly effective in reducing pain and improving function, there is limited evidence on long-term physical activity outcomes, particularly beyond the immediate postoperative period and within local populations. This gap restricts a comprehensive understanding of recovery patterns and the development of targeted rehabilitation strategies to optimize patient outcomes. This study aims to contribute to the knowledge of post-total hip arthroplasty physical activity by examining it after one year. It may help the physical therapist plan the rehabilitation process and identify vital components, namely stability, mobility, and balance.

METHODS

The descriptive case series study was conducted after ethical approval. The approval of the study was followed by the IRB letter from the ethical review committee of Lahore College of Physical Therapy with reference number 22199. We used non-probability convenience sampling to collect data from the Ghurki Trust Teaching Hospital. 50 patients were included in the study. The study was conducted in 6 months between 02/05/2022 and 02/11/2022 after IRB approval. The inclusion criteria included patients between 55 and 65 years of age, both male and female, unilateral total hip arthroplasty due to OA, a posterior surgical approach with cemented fixation, and an inserted metal

prosthetic implant. Exclusion criteria included the Prior total joint arthroplasty of any joint (hip, ankle, knee), Revision of total hip arthroplasty (THA), Severe musculoskeletal impairments, and Psychiatric illness. Information and data were collected via the Harris Hip Score in domains of pain, physical limitation, fixed deformities, and degree of movement. The data were analyzed via SPSS version 20.0. A non-probability convenience sampling technique was used for the statistical analysis. Consent was obtained from patients orally and in writing. The sample size was calculated by using World Health Organization (WHO) software under the following formula: $0.07 \text{ prevalence (P)} [14]$, 95% confidence interval $(1-\alpha)$, and 0.08 precision (d) . To evaluate the differences in the Harris Hip Score across the age group and gender, the Mann-Whitney U test was followed because of the ordinal and non-parametric nature of the data. Statistical significance was followed by using the two-tailed test, with the $p\text{-value} < 0.05$, which was considered statistically significant.

RESULTS

Out of 50 patients, 70 % ($n=35$) fall into the Age of 55-60 years, and 15 (30%) fall into the Age of 61-65 years. 27 (54%) were male and 46% ($n=23$) were female (Table 1).

Table 1: Descriptive Statistics of Demographics

Characteristics	Frequency (%)
Age	
55-60 Years	35 (70.0%)
61-65 Years	15 (30.0%)
Gender	
Male	27 (54.0%)
Female	23 (46.0%)
Total	50 (100.0%)

Out of 50 patients, 4 (8%) had no pain, 19 (38%) with slight pain, 24 (48%) with mild pain and 3 (6%) were with moderate pain. Out of 50 patients, 2 (4%) were using no supporting device, 32 (64%) were using a cane for prolonged walking, 15 (30%) were using the cane for most of the time in most activities, and 1 (2%) were using one crutch. Out of 50 patients, 3 (6%) were able to walk unlimited distances, 33 (66%) were able to walk six blocks (30 minutes), 13 (26%) were able to walk three blocks (10-15 minutes) and 1 (2%) able to walk indoors only. Out of 50 patients, 28 (56%) had no limp, 20 (40%) had a slight limp, and 2 (4%) had a moderate limp. Out of 50 patients, 6 (12%) were able to do activities with ease, 32 (64%) had difficulty doing those activity, and 12 (24%) were unable to do those activities. Out of patients, 3 (6%) were climbing stairs without a railing, 45 (90%) were using a railing to climb stairs, 1 (2%) were unable to do stairs, and 1 (2%) were in any manner. Out of 50 patients, 36 (72%) were able to sit in an ordinary chair for one hour, 13 (26%) were able to sit on a high chair for 30 minutes, and 1 (2%) were unable to sit on a chair with comfort. Out of 50 patients, 50 (100%) had less than 3.2 cm LLD. Out of 50

patients, 1(2%) were in the range of flexion 45>55 degrees, 1 (2%) with 55>65 degrees, 10 (20%) with 65>75 degrees, 13 (26%) with 70>75 degrees, 20 (40%) with 75>80 degrees and 5 (10%) with 80>90 degrees. Out of 50 patients, 2 (4%) were with a range of total external rotation of 0>5 degrees, and 48 (96%) with a range of 5-10 degrees. Out of 50 patients, 4 (8%) fall in the range of 0>5 degrees of total Adduction, and 46 (92%) with a range of 5>10 degrees (Table 2).

Table 2: Descriptive Statistics of Domains of Harris Hip Score

Domain	Frequency (%)
Pain	
No pain	4 (8.0%)
Slight	19 (38.0%)
Mild	24 (48.0%)
Moderate	3 (6.0%)
Supportive Device	
None	2 (4.0%)
Cane for Long Walks	32 (64.0%)
Cane Most Times	15 (30.05)
One Crutch	1 (2.0%)
Distance Walked	
Unlimited	3 (6.0%)
Six Blocks	33 (66.0%)
Three Blocks	13 (26.0%)
Indoors Only	1 (2.0%)
Limp	
None	28 (56.0%)
Slight	20 (40.0%)
Moderate	2 (4.0%)
Activities - Shoes, Socks	
With Ease	16 (32.0%)
With Difficulty	22 (44.0%)
Unable	12 (24.0%)
Climbing Stairs	
Without Railing	13 (26.0%)
With Railing	35 (70.0%)
Unable	1 (2.0%)
In Any Manner	1 (2.0%)
Using Public Transport	
Able	23 (46.0%)
Unable	27 (54.0%)
Sitting	
Comfortable	36 (72.0%)
High Chair	13 (26.0%)
Unable	1 (2.0%)
Less Than 30 Degrees Fixed Flexion	
Yes	50 (100%)
Fixed Adduction Less Than 10 Degrees	
Yes	50 (100%)
Total Flexion	
45>55	1 (2.0%)
55>65	1 (2.0%)
65>70	10 (20.0%)

70>75	13 (26.0%)
75>80	20 (40.0%)
80>90	5 (10.0%)
Total Abduction	
0>5	2 (4.0%)
5>10	2 (4.0%)
10>15	46 (92.0%)
Total External Rotation	
0>5	2 (4.0%)
5>10	48 (96.0%)
Total Adduction	
0>5	4 (8.0%)
5>10	46 (92.0%)

The median Score was about 78 (IQR: 72–82) in the male and 74 (IQR: 70–78) in the female. That difference was significant statistically (Mann-Whitney U=220.5, p=0.032), indicating that the male patients showed better post-operative physical functions and outcomes. Patients aged 55–60 years have a median Harris Hip Score of about 76 (IQR: 70–80), those aged 61–65 had a median of 72 (IQR: 68–76). The difference was statistically significant (Mann-Whitney U=210.0, p=0.045), suggesting that the younger patients in the middle-aged cohort achieved better functional outcomes one year after the total hip arthroplasty (Table 3).

Table 3: Comparison of Harris Hip Score by Gender and Age Group

Variables	Group	Median HHS (IQR)	Mann-Whitney U	p-value
Gender	Male	78 (72–82)	220.5	0.032
	Female	74 (70–78)		
Age Group	55–60 Years	76 (70–80)	210.0	0.045
	61–65 Years	72 (68–76)		

In the sample size of 50 patients of THA, the grades of total Harris hip score were as follows: 14 patients (28%) in Poor grade, 17 patients (34%) in Fair grade, 18 patients (36%) in Good grade, and one patient (2%) in Excellent grade (Table 4).

Table 4: Descriptive Statistics of Total Scoring of Physical Activity according to Harris Hip Score

Harris Hip Score	Frequency (%)
Poor <70	14 (28.0%)
Fair 70–79	17 (34.0%)
Good 80–89	18 (26.0%)
Excellent	1 (2.0%)
Total	50 (100.0%)

Physical activity was much improved in the patients as the mobility, in terms of the use of supportive devices and walking between blocks. About 98% of the patients can walk up to 3 blocks. 96% of patients were able to climb stairs, 26% of the patients could climb without railings, and 70% of the patients were able to climb with the support of railings. 46% of patients were also able to use public transport. So, with all other domains of pain, such as sitting

comfortably and flexion, adduction, abduction, and rotation, the overall physical activity was improved. The Harris hip score is one of the convenient tools to measure physical activity after total hip arthroplasty, so the tool was used to measure all those activities to assess the physical activity after total hip arthroplasty, following one year.

DISCUSSION

The purpose behind the current study was to assess and evaluate the physical activity after total hip arthroplasty following one Year in middle-aged adults (Aged 55-65). A prospective observational study used the University of California Angeles (UCLA) score and the Oxford Hip Score (OHS) to measure physical activity at three months after THA and one Year. The physical activity increased with the number of steps taken by the patient after postoperative rehabilitation. The study included 42 patients with unilateral THA. However, no significant improvements were found in the patient scores from three months of improvement and one year of results [15]. A qualitative retrospective study in Denmark was conducted to evaluate the physical activity after THA. The interviews in a Semi-structured manner were conducted for the 22 patients who were involved in a home program of rehab with physiotherapists after the THA. The pain was a significant barrier in the results because the intense pain limited the activity, and the absence of pain caused low motivation to exercise. The patients were found to be relatively physically active during the study [16]. A study was conducted to evaluate physical activity after three years of THA in 153 patients with a mean age of 61.4 years, and 86% of the population was female. Patients were evaluated for physical activity in terms of steps/day and performance of moderate to vigorous physical activity per week. The study used the Oxford Hip Score for the evaluation. The study concluded that physical activity continuously increased after three years post-THA. The study suggested that physical activity should be evaluated after a medium to long term time after THA to get high results [13]. A study conducted on 30 patients after THA measured the physical activity and pain after the procedure. The study measured the outcomes via the Harris Hip score, the 6-minute walk test, and the Oxford Hip Score. The study showed no significant improvement in physical activity three months and 12 months post-THA. The pain was significantly improved. The HHS and OHS score was improved after 12 months of surgery. The study concluded that the overall outcomes were not significant after 12 months of follow-up of the physical activity post THA [17]. A prospective cohort study with 571 THA patients evaluated the physical activity, followed up for three years. Interviews were conducted, and the participants were involved in physical activity for one year pre-THA. They followed up on the physical activity three years post-THA. Overall physical activity in these patients was improved, and their quality of life was also

increased if they followed the criteria of >1 per week after THA [11]. A narrative view after the total joint arthroplasty, pre- and post-physical activities, was conducted to assess the outcomes. The study concluded that the pain improved after the total hip arthroplasty. Still, the physical activity remains contradictory, and there are no significant improvements in physical activity after three months of the procedure. The study also concluded that there is weak evidence of improving physical activity after 12 months of THA [18]. A cohort study on 24 post-THA patients was conducted to evaluate Physical Activity during six of the procedures. Physical activity was assessed with the Sense Wear Pro Armband (SWA), and the patient was involved in the community rehabilitation program, which was designed to improve activity with structured exercises. Fourteen patients were in the intervention group, and ten patients were in the control group. The THA satisfaction questionnaire and the Osteoarthritis Outcome Score (HOOS) were followed by the Poulsen control group [19]. A retrospective cohort study was conducted, and 1053 active patients were compared with 1053 inactive patients two years after Total hip arthroplasty. The patients were evaluated via the Surgery Hip Replacement Expectations Survey and Hip Osteoarthritis Outcome Score. For the physical activity patients, 74% expected to be back to normal, as well as the ability to perform exercises and play sports, compared to the inactive patients, who had only 64%. Patients with higher expectation levels regarding exercise and sports had better HOOS scores specific to the sports and recreation subdomain. So, Physical activity was improved in the active patients as compared with the inactive patients [20].

The small sample size and short follow-up period (up to one year) may limit the ability to detect long-term changes in physical activity after THA. Additionally, reliance on subjective assessment tools (UCLA, OHS) without objective activity measurements may affect the accuracy of findings. Future studies should incorporate larger cohorts with longer follow-up and objective activity tracking methods to better evaluate long-term physical activity outcomes after THA.

CONCLUSIONS

It was concluded that physical activity varies in middle-aged adults after total hip arthroplasty after one year. The majority of middle-aged adults presented with fair to good physical activity following one year.

Authors' Contribution

Conceptualization: MWW

Methodology: MWW, SS, KH, AM, ZM

Formal analysis: MWW

Writing and Drafting: MWW

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All authors approved the final manuscript and take responsibility for the integrity of the work

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Original Article



Efficacy of 0.25% Bupivacaine Alone vs. with Dexmedetomidine for Ultrasound-Guided Supraclavicular Block in Upper Limb Surgery

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ABSTRACT

The pain after upper limb surgeries can be intense. The brachial plexus block is an effective and commonly used method to manage this pain, reduce opioid use, and facilitate smoother recovery. **Objective:** To see the effect of combining bupivacaine with dexmedetomidine in upper limb surgeries. **Methods:** Quasi-experimental research was carried out at Islam Medical College, Sialkot. 100 patients undergoing upper limb surgeries who were aged between 25 to 65 years. All the patients who were comprised allergies to study drugs, severe organ impairment, coagulopathy, neurological disorders affecting pain perception, and pregnancy were excluded and divided to receive either 0.25% bupivacaine alone or with dexmedetomidine. The outcome variables included pain, analgesia duration, sensory/motor block onset, and 24-hour analgesic consumption. Data were analyzed by SPSS version 23.0. The comparison of quantitative data was done by an independent sample t-test and chi-square test for insightful comparisons between qualitative variables, with the significance level at p -value < 0.05. **Results:** The average age of patients was 40.1 ± 11.5 and 39.8 ± 10.5 years in Group I and Group II, respectively. Male were more in both groups. Group II showed significantly longer analgesia duration (12.7 vs. 5.3 hours), faster sensory/motor block onset, and lower analgesic consumption ($p < 0.001$). There were no significant differences in adverse effects. **Conclusions:** It was concluded that combining dexmedetomidine with bupivacaine significantly extended analgesia, quickened sensory and motor block onset with a reduction in overall consumption of analgesia. Although sedation was more frequent, no major adverse events were observed.

INTRODUCTION

The pain after upper limb surgeries, particularly total shoulder arthroplasty, can be intense. The inter-scalene brachial plexus block is an effective and commonly used method to manage this pain, reduce opioid use, and facilitate smoother recovery [1]. However, the pain relief from a single injection of the anesthetic is usually short-term, even when additional medications are added. Continuous brachial plexus blocks can offer longer-lasting pain relief, but they need specialized expertise and more resources to perform [2]. Supraclavicular block has the

potential to provide the optimal analgesia under regional anesthetic for upper limb treatment when this is the shoulder, arm, elbow, or hand region. This block provides clavicular brachial plexus obstruction and is a reliable and efficient upper extremity anesthesia [3]. Local anesthetics are drugs that are used in regional anesthesia; an example is the common local anesthetic bupivacaine and the supraclavicular block. Bupivacaine is a long-acting amide-type local anaesthetic and the most of the time is specifically used for upper limb regional anesthesia



because of its potent and prolonged blockade of sensory and motor pathways [4]. Bupivacaine offers extended postoperative pain relief by obstructing voltage-gated sodium channels, effectively interrupting nerve signal transmission. Its considerable lipid solubility and strong protein affinity contribute to its long-lasting effects [5]. In the regional anesthesia procedures, like supraclavicular brachial plexus blocks, bupivacaine can uniquely target at lower doses while preserving motor function and the pain fibers. Its gradual dissociation offers prolonged pain relief, reduces the need for opioids, and enhances patient comfort, thus ideal during long surgeries and continuous nerve blocks [6]. To enhance postoperative and regional analgesic potential related to anesthesia there has been research done on various potential adjuvants such as opioids, clonidine and dexmedetomidine [7]. Dexmedetomidine is an α_2 -adrenoceptor agonist and has potential for use as an adjuvant in regional analgesia. The mechanism is that it prevents norepinephrine from being released, thus reducing sympathetic nervous system activity and increasing analgesia [8]. It is also associated with additional benefits as sedation and anxiolysis without significant respiratory depression, which comes very handy in the immediate postoperative era. Dexmedetomidine with bupivacaine has been applied in several techniques of regional anesthesia, and studies have shown mixed results in terms of better block quality, post-operative analgesia and decreased opioid consumption [9, 10]. Unprecedented revolution in the practice of delivering regional blocks with better precision and safety in locating the nerve by Ultrasound-guided (USG) technique [11]. Since it remains in front of the intended target tissue and the anatomical structures, the chances of complications such as nerve damage or accidental vascular puncture are reduced when positioning a needle under ultrasound guidance. Rather, postoperative analgesia is based on an element of reliability and reproducibility that may be improved with the precision of the USG technique [12, 13].

Although supraclavicular brachial plexus block with bupivacaine provides effective postoperative analgesia for upper limb surgeries, its duration remains limited, prompting the use of adjuvants like dexmedetomidine; however, existing evidence on their combined efficacy shows inconsistent results. This uncertainty limits optimal analgesic strategies for enhancing block duration and reducing opioid requirements. This study aims to compare the effect of combining bupivacaine with dexmedetomidine on the analgesia effect after post-operative recovery time in upper limb surgeries.

METHODS

A quasi-experimental research was conducted at Islam Medical College, Sialkot, from July to November 2024, after

ethical approval (Ref: 900/IMCS/ERC/000103. Participants were recruited using a convenience sampling method. Eligibility criteria of participants include patients undergoing upper limb surgeries who were aged between 25 to 65 years and who fall in ASA criteria I and II. All the patients who were comprised allergies to study drugs, severe organ impairment, coagulopathy, neurological disorders affecting pain perception, and pregnancy were excluded. The Open Epi software is used for sample size calculation by using duration of analgesia in the bupivacaine with dexmedetomidine Group was 722 ± 88.45 min and 210 ± 35.88 in Bupivacaine Alone Group, by taking 80% power of test, 5% margin of Error and 10% drop out rate is 100 (50 in each group) [14]. A written informed consent was taken. A total of 100 participants were enrolled to effectively assess the duration of analgesia and were equally divided into two groups of 50 each. Group I received 20 ml of 0.25% bupivacaine, while Group II received 20 ml of 0.25% bupivacaine combined with 50 μ g of dexmedetomidine for enhanced analgesic effect. Upon arrival in the preoperative area, baseline vital signs and pain scores were assessed by the Visual Analogue Scale (VAS). The total score of VAS was 10, where 0 indicates no pain and 10 shows the worst pain. An 18-gauge intravenous line was secured in each participant, ensuring proper preparation for the procedure. This structured approach reflects our commitment to delivering effective and high-quality pain management. VAS is a widely used tool for pain assessment, demonstrating a reliability of 0.95 [15]. Patients were monitored and pre-medicated with IV midazolam (1 mg). Using a high-frequency linear ultrasound probe, the brachial plexus was visualized, and a 22-gauge needle was used to administer the anesthetic solution according to the randomized group, ensuring safety with incremental injections. The study measured the duration of postoperative analgesia. It also examined the onset of sensory and motor blocks, along with total analgesic consumption within the first 24 hours. In response to pain complaints, rescue analgesia was administered as nalbuphine (0.1 mg/kg). Adverse events, including hypotension, bradycardia, nausea, vomiting, and sedation, were monitored closely. Data analysis was conducted using SPSS version 23.0. Normality of the data using the Shapiro-Wilk test before executing the t-tests. The quantitative variables, including age, VAS score, post op analgesia effect (duration in minutes), and the onset times for sensory and motor blockade through independent sample t-tests. For categorical variables, we utilized the chi-square test for insightful comparisons with the significance level at p -value < 0.050 .

RESULTS

The patients' mean age was 40.1 ± 11.5 and 39.8 ± 10.5 years in Group I and Group II, respectively, with no significant difference ($p=0.820$). Gender distribution was similar, with males comprising 62% in Group I and 52% in Group II, while

females made up 38% and 48%, respectively ($p=0.680$). ASA physical status classification was also comparable, with 44% of patients in Group I and 48% in Group II categorized as ASA I, and 56% and 52% as ASA II ($p=0.650$). The mean VAS score at baseline was 6.5 ± 1.2 and 6.7 ± 1.1 in Group I and Group II ($p=0.580$) (Table 1).

Table 1: Clinical Parameters of Patients ($n=100$)

Characteristics	Group I	Group II	p-value
Age	40.1 ± 11.5	39.8 ± 10.5	0.890
Gender	Male	31 (62%)	0.680
	Female	19 (38%)	
ASA Physical Status	I	22 (44%)	0.540
	II	28 (56%)	
Baseline Pain Score (VAS)	6.5 ± 1.2	6.7 ± 1.1	0.380

As compared to bupivacaine alone (5.3 ± 1.4 hours), there was a statistically significant prolonged duration of analgesia with (12.7 ± 2.1 hours) addition of dexmedetomidine to bupivacaine ($p<0.001$). Times of sensory and motor blockade onset were faster in Group II (Bupivacaine + Dexmedetomidine) than in Group I (Bupivacaine alone) at 8.3 ± 1.8 minutes and 12.3 ± 2.6 minutes ($p=0.002$ and 0.003 , respectively) and total analgesic (40.7 ± 15.8 mg vs 75.4 ± 20.2 mg, $p<0.001$) requirement was significantly lower among them (Table 2).

Table 2: Comparison of Analgesia Duration and Onset Time, and Total Analgesic Consumption among Study Groups

Characteristics	Group I	Group II	p-value	Test Used
Analgesia Duration				
Analgesia Duration in Hours,	5.3 ± 1.4	12.7 ± 2.1	<0.001	Independent t-test
Onset Time and Total Analgesic Consumption				
Onset of Sensory Block (min)	10.4 ± 2.3	8.3 ± 1.8	$<0.001^*$	Independent t-test
Onset of Motor Block (min)	15.2 ± 3.0	12.3 ± 2.6	$<0.001^*$	Independent t-test
Total Analgesic Consumption (mg)	75.4 ± 20.2	40.7 ± 15.8	$<0.001^*$	Independent t-test

The dextromethorphan and bupivacaine combination produced a significantly greater degree of sedation (16% vs. 0%, $p=0.010$) without increasing the rate of any other adverse effects, including bradycardia (8% vs. 2%, $p=0.36$), hypotension (10% vs. 4%, $p=0.240$), and nausea (4% vs. 6%, $p=0.650$). While Group II experienced significantly more sedation, the other adverse events were similar (Figure 1).

Adverse event

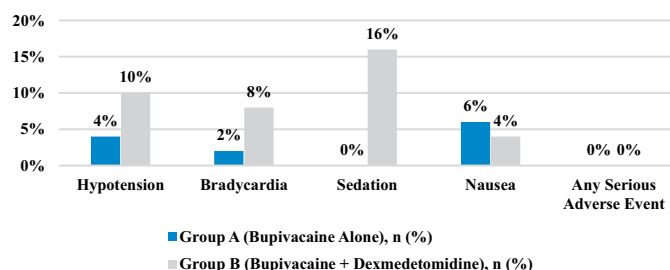


Figure 1: Comparison of Adverse Events in Both Drugs

DISCUSSION

This study evaluates the efficacy of dexmedetomidine as an adjuvant to 0.5% bupivacaine versus bupivacaine alone in spinal anesthesia, aiming to enhance analgesic onset, duration, and quality across upper limb surgery. Literature found that adding dexmedetomidine to bupivacaine enhances postoperative analgesia, reduces rescue analgesic use, and improves patient satisfaction without increasing severe side effects. It prolongs the duration of sensory evaluation, remains hemodynamically safe, and lowers the postoperative shivering incidence [16]. These findings align with results reported in similar studies, which show that additional trials have further enhanced the benefits of dexmedetomidine supplementation to local anesthetics, thereby improving regional anesthesia, as discussed in the current study. The block provided by bupivacaine combined with dexmedetomidine lasted appreciably longer than bupivacaine alone, reducing postoperative pain and the need for additional analgesics. Furthermore, patients receiving the combined technique reported superior fulfilment with their postoperative pain management [17]. Moreover, another study indicated that incorporating dexmedetomidine with bupivacaine in spinal anesthesia enhances pain relief without raising the risk of adverse effects. The findings indicated that combining dexmedetomidine with bupivacaine enhances postoperative analgesia and accelerates the onset of both motor and sensory nerve block, as observed in the current study [18]. It is suggested that Dexmedetomidine's contribution to the prolonged instances of analgesia is towards blocking nerve conduction, thus reducing pain signals. Previously conducted studies of brachial plexus blockade revealed that incorporation of Dexmedetomidine with Bupivacaine significantly extended analgesic effects. That our results support these previous findings has been attested, as the combination of Dexmedetomidine and Bupivacaine exhibits significantly longer duration and stronger analgesic effect than Bupivacaine on its own [19]. Dexmedetomidine significantly increased the effects of bupivacaine. There was an earlier onset of time to sensory and time to motor nerve block for Bupivacaine + Dexmedetomidine than Bupivacaine alone. In a like manner, another trial documented a much faster appearance of the sensory and motor blockade and longer analgesia duration when Bupivacaine was combined with Dexmedetomidine [14]. The current study revealed no adverse effects in both study groups, corroborating the safety of both treatments. Although differences in individual side effects were observed, hypotension and bradycardia were more common in bupivacaine plus dexmedetomidine, but were not significant. These findings correspond with previous reports showing that administering dexamethasone shortens the onset time and duration of sensory and motor blockade. There was a faster onset of sensory and motor

blocks significantly compared to the control group, with minimal side effects, which confirms the role of dexmedetomidine as a safe and useful adjunct for bupivacaine in regional anesthesia.[20]. Current results showed that bupivacaine when used with dexmedetomidine provided effective analgesia without the need to increase the rate of adverse effects such as bradycardia (8% vs. 2%, $p=0.36$), hypotension (10% vs. 4%, $p=0.24$) and nausea (There were no major events of high-grade toxicity in neither group, and safety profiles were similar, but not different ($p>0.05$), without significant adverse events being reported. These findings were confirmed by Sane et al., Intriguingly, no serious complications were reported in either group, which implies that adding dexamethasone did not increase the risk of complications[21].

The relatively small sample size and single-center design may limit the generalizability of the findings. Additionally, short-term follow-up restricts assessment of long-term analgesic outcomes and potential delayed adverse effects. Future large-scale, multicenter studies with extended follow-up are recommended to further evaluate the long-term safety and efficacy of dexmedetomidine as an adjuvant in spinal anesthesia.

CONCLUSIONS

The combination of dexmedetomidine to bupivacaine significantly enhanced its efficacy. Bupivacaine combined with Dexmedetomidine exhibited a faster onset of both sensory and motor block as compared to Bupivacaine alone. Furthermore, our findings demonstrated that the combination provided effective analgesia with no reported side effects.

Authors' Contribution

Conceptualization: SS

Methodology: SS, RHKN, SI, HFA

Formal analysis: RHKN, AM

Writing and Drafting: SI, SA

Review and Editing: SS, RHKN, SI, HFA, SA, AM

All authors approved the final manuscript and take responsibility for the integrity of the work

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Original Article



Assessing the Effects of Metformin on Lipid Metabolism in Women with PCOS

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a prevalent hormonal imbalance condition that is linked with insulin resistance and abnormal lipid metabolism. Metformin is a common drug given in the management of PCOS; the impact on the lipid profile and the role of adherence to therapy are not established. **Objectives:** To assess the therapeutic effects of Metformin on lipid profile, hormonal status, and insulin resistance in PCOS while exploring the influence of patient adherence on overall treatment response. **Methods:** One hundred and ten women with a diagnosis of PCOS in Health Net Hospital, Peshawar, were given Metformin (1500 mg/day) for six months. The assessments for the study included lipid profile, glucose, insulin level, HOMA-IR, and hormonal profiling both at baseline and after the treatment. Treatment adherence was evaluated with pill count and attendance to follow-up visits. Pre- and post-comparisons were done using paired t-tests, while group differences were examined using independent t-tests and chi-square tests. **Results:** Metformin significantly reduced total cholesterol (199.43 to 167.60 mg/dL, $p<0.001$), LDL-C (131.71 to 111.20 mg/dL, $p<0.001$), triglycerides (178.15 to 149.66 mg/dL, $p<0.001$), and VLDL-C (35.72 to 30.03 mg/dL, $p<0.001$), while HDL-C increased (39.70 to 45.24, $p<0.001$). Insulin resistance and androgen levels also improved, with greater benefits observed in adherent participants. **Conclusions:** It was concluded that metformin positively impacts lipid metabolism, hormonal levels, and insulin responsiveness in patients with PCOS. Adherence significantly enhances therapeutic outcomes, emphasizing the need for strategies that promote consistent medication use.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women, with a global prevalence of 4% to 21% [1]. It disrupts hormonal balance, ovulation, and metabolism, leading to infertility, menstrual irregularities, and androgen excess, and is often associated with insulin resistance, dyslipidemia, and increased cardio-metabolic risk [2, 3]. PCOS is a common endocrine disorder in reproductive-aged women, affecting 4% to 21% globally. It disrupts hormonal balance, ovulation, and metabolism, leading to infertility, menstrual issues, androgen excess, and increased risk of insulin resistance, dyslipidemia, and type 2 diabetes. Dyslipidemia is of

particular concern in PCOS because of the increased values of total cholesterol, LDL-C, triglycerides, and decreased HDL-C. These anomalies significantly increase the cardiovascular risk over a prolonged period [3]. The lipid abnormalities mentioned are strongly supported by insulin resistance, necessitating PCOS management to effectively address the metabolic control [4]. Metformin, originally used for type 2 diabetes, is now widely prescribed for PCOS. Though off-label, it is recommended by the 2013 Endocrine Society and 2023 global PCOS guidelines to improve ovulation and insulin sensitivity [2, 5]. Beyond glucose control, it also enhances lipid profiles by lowering



LDL-C and triglycerides and raising HDL-C, reducing cardiovascular risk [6]. Even so, results regarding Metformin's impact on lipid metabolism differ across populations, probably because of genetics, lifestyle, and dietary habits. Additionally, adherence is vital to the success of treatment, but very few studies have explored how adherence affects the metabolic results of Metformin therapy [7]. These gaps concerning the lack of adherence analysis create obstacles in assessing the practical utility of Metformin in managing PCOS.

This study aims to investigate Metformin's impact on lipid parameters, hormonal regulation, and insulin sensitivity in women diagnosed with PCOS. It also compares adherent and non-adherent participants and investigates how treatment adherence influences these metabolic outcomes. By addressing both metabolic responses and the role of adherence in a South Asian population, this study contributes novel insights that may improve therapeutic strategies and long-term outcomes in women with PCOS.

METHODS

This was a prospective quasi-experimental study conducted at Health Net Hospital, Peshawar, from May 15, 2023, to June 15, 2024. The study aimed to investigate the impact of Metformin on lipid parameters, hormonal balance, and insulin sensitivity in women with a confirmed diagnosis of PCOS. Ethical approval was obtained from the hospital's Ethics Review Committee (Ref No: 3057/HNH/HR). Consent to participate was secured from each subject after explaining the study protocol. The sample size for this study was determined using the formula appropriate for continuous outcome variables, as the primary endpoints included measures like lipid levels and insulin resistance. The calculation was based on the following parameters: Confidence level: 95% ($Z=1.96$), Power: 80% ($Z=0.84$), Assumed standard deviation (σ): 25 mg/dL for LDL-C, derived from prior studies evaluating lipid profiles in women with PCOS [8]. Minimum detectable difference (Δ): 10 mg/dL, considered clinically meaningful. Using the standard formula for comparing two means: $n=2 \times (Z_{\alpha/2} + Z_{\beta})^2 \times \sigma^2 / \Delta^2$. Plugging in the values: $n=2 \times (1.96 + 0.84)^2 \times 25^2 / 10^2 = 2 \times (2.8)^2 \times 625 / 100 = 2 \times 7.84 \times 625 / 100 = 9800 / 100 = 98$. Thus, the estimated sample size was approximately 98 participants. To enhance the study's statistical power and compensate for potential dropout or missing data, a 10% increase was applied: Adjusted sample size = $98 / 1 - 0.10 = 109$. This adjustment led to a final sample size of 110 participants. This sample size was consistent with that used in previous studies. Trolle et al., conducted a randomized, double-blinded, placebo-controlled cross-over trial involving 56 women with PCOS who completed both treatment phases, effectively utilizing 112 participant-periods. Their study assessed similar outcomes, including lipid profiles and insulin resistance, thereby supporting the adequacy of our sample size [9]. And Calculations in

Clinical Research by Chow et al., [10] and aligns with guidelines provided by the World Health Organization in Sample Size Determination in Health Studies by Lwanga and Lemeshow [11]. Inclusion criteria: Women aged 18–35 years with a diagnosis of PCOS utilizing Rotterdam criteria, as specified in 2003 [12] when either 2 of the following three indicators are provoke: (1) Disrupted or absent menstrual periods (2) higher-than-normal androgen values detected either clinically or through laboratory evaluation, and (3) the presence of multiple cysts on the ovaries observed via ultrasound imaging. Exclusion criteria: Prior Metformin use within 6 months, current use of lipid-lowering drugs, pregnancy or lactation, thyroid disorders, diabetes, Cushing's syndrome, and significant liver or kidney dysfunction. All participants received Metformin 1500 mg/day in divided doses of 500 mg three times daily, following published PCOS management guidelines [13]. Participants were also counselled about lifestyle modifications, including diet and physical activity. No other pharmacological treatments were allowed during the study period. This study involved a standard therapeutic intervention, not a clinical trial, so it did not require DRAP registration, as per Bio-Study Rules 2017 and DRAP Act 2012 guidelines. Data were collected in three phases: baseline (pre-treatment), treatment phase (with monthly follow-up), and post-treatment (at six months). The clinical data gathered consisted of the following: age, body mass index (BMI), duration of PCOS, menstrual irregularities, a family history of PCOS or diabetes, and lifestyle factors, including the level of physical activity and smoking habits. Venous blood samples were taken and analyzed for the lipid profile (total cholesterol (TC), LDL-C, HDL-C, triglycerides (TG), VLDL-C), fasting glucose, insulin, glycated hemoglobin (HbA1c), and insulin resistance calculated via HOMA-IR after an 8–10 hour overnight fast. Additionally, the reproductive and androgenic hormones assessed included 'luteinizing hormone (LH), follicle-stimulating hormone (FSH), the LH/FSH ratio, total testosterone, sex hormone-binding globulin (SHBG), and dehydroepiandrosterone sulfate (DHEA-S)' were assessed. Lipid parameters were measured using enzymatic colourimetric methods; fasting glucose was evaluated by the hexokinase method, insulin by electro-chem-luminescence immunoassay (ECLIA), and HbA1c via high-performance liquid chromatography (HPLC). Hormonal assays were performed using automated chemiluminescence immunoassay (CLIA) on platforms such as the Abbott Architect i2000. Manufacturer-provided reference ranges were used: Reference ranges used in this study were based on manufacturer specifications. For lipid parameters, total cholesterol was considered normal at values below 200 mg/dL, LDL-C under 100 mg/dL, HDL-C above 40 mg/dL, triglycerides under 150 mg/dL, and VLDL-C ranging between 5 and 40 mg/dL. Regarding reproductive and androgenic hormones, the expected ranges included luteinizing hormone (LH) from 1.9 to 12.5 mIU/mL, 'Follicle-stimulating hormone was within the range of 2.5–10.2 mIU/mL', testosterone between 15 and 70 ng/dL, sex

hormone-binding globulin (SHBG) from 18 to 114 nmol/L, and dehydroepiandrosterone sulfate (DHEA-S) between 65 and 380 µg/dL. Insulin resistance was evaluated using the HOMA-IR index, derived by taking the product of fasting insulin and glucose levels, then dividing that value by 405. A value exceeding 2.5 was considered reflective of insulin resistance. All laboratory testing was carried out in a centralized, ISO 15189-certified diagnostic facility adhering to international standards for medical laboratory quality and competence. Quality control was maintained by processing internal control samples at low, normal, and high levels with every batch, while external validation was ensured through participation in recognized quality assurance schemes. To ensure reproducibility, 10% of randomly selected samples were re-tested. The same equipment, protocols, and calibrators were used throughout the study to maintain consistency and reliability. Adherence was assessed through pill counts, follow-up attendance, and a structured adherence questionnaire adapted from previously validated tools [14].

Adherent group: Took ≥80% of prescribed doses and missed no more than 1 follow-up. **Non-adherent group:** Took <80% of doses or missed ≥2 consecutive follow-ups. To monitor adverse drug reactions (ADRs), a checklist-based ADR tool was used to record common side effects (nausea, diarrhea, abdominal discomfort) at each follow-up. ADRs were documented but not formally categorized using scales like Naranjo, as the study focused on treatment efficacy rather than pharmacovigilance. Safety was assessed based on the absence of severe ADRs and overall tolerability. The distribution of continuous variables was examined using the Shapiro-Wilk test. The analysis of the information was carried out using the SPSS program, version 26.0. Continuous data were summarized using mean values along with standard deviations, whereas categorical data were presented as counts and corresponding percentages. The assessment of the normality of continuous variables was performed by the Shapiro-Wilk's test revealed that the variables with normal distribution included. The Paired sample t-test was used to compare baseline and post-treatment values within the same group. The comparison of these variables for adherent and non-adherent groups was conducted through an independent sample t-test. Non-parametric methods were employed for data that did not exhibit normal distribution patterns, the Mann-Whitney U test was employed as an alternative to parametric analysis, including triglycerides, VLDL-C, HOMA-IR, DHEA-S, and the LH/FSH ratio. Categorical data, such as physical activity, family history, and reported side effects, were assessed using the 'Chi-square test'. Results were deemed significant when the p-value was equal to or below 0.050 (Figure 1).

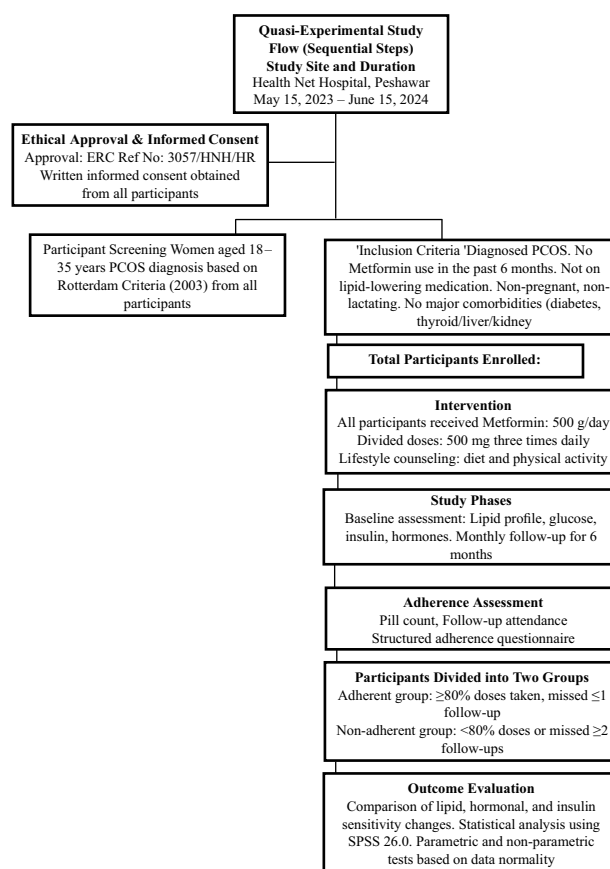


Figure 1: Methods Used for This Research

RESULTS

The study included 110 women diagnosed with PCOS. The mean age was 25.15 ± 3.61 years, and the average BMI was 29.51 ± 4.97 kg/m². The average duration of PCOS is approximately four years. More than half of the participants (55.5%) were single, and a majority (81.8%) reported menstrual irregularities. A family history of PCOS and diabetes, or dyslipidemia was present in about 49% of participants. Only 6.4% of women reported smoking, while 39.1% engaged in regular physical activity (Table 1).

Table 1: Demographic and Clinical Characteristics (n=110)

Study Indicators		n (%)
Age	Years	25.15 ± 3.61
BMI	kg/m ²	29.51 ± 4.97
Duration of PCOS	Years	4.12 ± 2.02
Marital Status	Single	61 (55.5%)
	Married	49 (44.5%)
Menstrual Irregularities	Yes	90 (81.8%)
	No	20 (18.2%)
Reported Family Occurrence of PCOS	Yes	54 (49.1%)
	No	56 (50.9%)
Family Incidence of Diabetes	Yes	54 (49.1%)
	No	56 (50.9%)
Smoking Status	Yes	7 (6.4%)
	No	103 (93.6%)

Regular Physical Activity	Yes	43 (39.1%)
	No	67 (60.9%)

Following six months of Metformin therapy, there were significant improvements in lipid profile, hormonal balance, and insulin sensitivity. Total cholesterol decreased from 199.43 to 167.60, LDL-C from 131.71 to 111.20, and triglycerides from 178.15 to 149.66 mg/dL ($p < 0.001$ for all comparisons). HDL-C levels significantly increased. Androgen levels, including testosterone and DHEA-S, showed marked reductions, while SHBG levels increased, indicating improved hormonal regulation. Fasting insulin, HOMA-IR, and HbA1c also improved significantly, reflecting enhanced insulin sensitivity (Table 2).

Table 2: Comparison of Key Metabolic and Endocrine Variables Before and After Metformin Administration

Measured Parameters	Before Treatment (Mean $\pm$ SD)	After Treatment (Mean $\pm$ SD)	p-value
Cholesterol – Total (mg/dL)	199.43 $\pm$ 26.84	167.60 $\pm$ 29.38	<0.001 *
LDL-C (mg/dL)	131.71 $\pm$ 24.24	111.20 $\pm$ 26.52	<0.001 *
HDL-C (mg/dL)	39.70 $\pm$ 7.60	45.24 $\pm$ 8.77	<0.001 *
Triglycerides (mg/dL)	178.15 $\pm$ 47.26	149.66 $\pm$ 42.82	<0.001 *
VLDL-C (mg/dL)	35.72 $\pm$ 8.51	30.03 $\pm$ 8.04	<0.001 *
LH (mIU/mL)	9.67 $\pm$ 3.20	8.11 $\pm$ 2.78	<0.001 *
Serum FSH Concentration	5.73 $\pm$ 1.24	5.52 $\pm$ 1.19	0.040 *
LH-to-FSH Proportion	1.59 $\pm$ 0.51	1.34 $\pm$ 0.47	<0.001 *
Serum Testosterone Level	66.78 $\pm$ 17.80	55.93 $\pm$ 16.05	<0.001 *
SHBG (nmol/L)	34.91 $\pm$ 7.80	42.16 $\pm$ 9.70	<0.001 *
DHEA-S (μ g/dL)	208.12 $\pm$ 45.61	175.08 $\pm$ 45.01	<0.001 *
Fasting Glucose (mg/dL)	95.21 $\pm$ 12.86	80.09 $\pm$ 14.68	<0.001 *
Fasting Insulin (μ U/mL)	18.65 $\pm$ 5.93	13.66 $\pm$ 4.85	<0.001 *
HOMA-IR	4.25 $\pm$ 1.65	3.15 $\pm$ 1.49	<0.001 *
HbA1c (%)	5.90 $\pm$ 0.86	4.97 $\pm$ 0.99	<0.001 *

*Statistically significant ($p \leq 0.05$) Shapiro-Wilk test was used to assess data normality. Paired Sample t-test was applied to normally distributed variables (Total Cholesterol, LDL-C, HDL-C, Serum FSH, Serum Testosterone, SHBG, Fasting Glucose, Fasting Insulin, HbA1c). Mann-Whitney U test was applied to non-normally distributed variables (Triglycerides, VLDL-C, LH, LH/FSH Ratio, DHEA-S, HOMA-IR).

Comparison between adherent and non-adherent participants revealed significantly better metabolic and hormonal outcomes in the adherent group. Fasting insulin was significantly reduced in the adherent group (11.48 vs. 16.27 μ U/mL, $p < 0.001$), LDL-C values were also lower (95.76 vs. 129.72, $p < 0.001$), and SHBG levels were elevated (44.71 vs. 39.09 nmol/L, $p = 0.002$) (Table 3).

Table 3: Comparison of Adherent vs. Non-Adherent Participants

Parameter	Adherent Participants	Non-Adherent Participants	p-value
LH (mIU/mL)	7.40 $\pm$ 2.53	8.96 $\pm$ 2.85	0.003 *
LH-to-FSH Proportion	1.18 $\pm$ 0.37	1.54 $\pm$ 0.49	<0.001 *
Serum FSH Concentration	51.67 $\pm$ 11.76	61.04 $\pm$ 18.91	0.002 *

SHBG (nmol/L)	44.71 $\pm$ 9.18	39.09 $\pm$ 9.50	0.002 *
Cholesterol (mg/dL)	150.27 $\pm$ 21.39	188.38 $\pm$ 23.67	<0.001 *
LDL-C (mg/dL)	95.76 $\pm$ 17.28	129.72 $\pm$ 23.74	<0.001 *
HDL-C (mg/dL)	46.83 $\pm$ 8.67	43.34 $\pm$ 8.59	0.037 *
Triglycerides (mg/dL)	134.69 $\pm$ 37.13	167.62 $\pm$ 42.60	<0.001 *
Fasting Glucose (mg/dL)	71.25 $\pm$ 9.28	90.69 $\pm$ 12.86	<0.001 *
Fasting Insulin (μ U/mL)	11.48 $\pm$ 3.94	16.27 $\pm$ 4.58	<0.001 *
HbA1c (%)	4.35 $\pm$ 0.69	5.71 $\pm$ 0.75	<0.001 *

*Statistically significant ($p \leq 0.05$). Normality was assessed using the Shapiro-Wilk test. Independent Sample t-test was used for normally distributed variables (e.g., LDL-C, HDL-C, SHBG, Fasting Glucose, Fasting Insulin, HbA1c). The Mann-Whitney U test was used for non-normally distributed variables (LH, Serum FSH, LH/FSH Ratio).

Categorical comparisons further revealed that a family history of PCOS was significantly associated with better adherence ($p = 0.012$). No significant associations were found for physical activity or family history of diabetes. Adverse effects were reported with similar frequency in both groups and were not statistically significant. Most participants (66.7% adherent vs. 62.0% non-adherent) reported no side effects (Table 4).

Table 4: Categorical Variables and Adverse Effects by Adherence Status

Variable / Adverse Effects	Adherent n (%)	Non-Adherent n (%)	p-value
Physical Activity (Regular)	23 (38.3%)	20 (40.0%)	0.858
Physical Activity (No)	37 (61.7%)	30 (60.0%)	
Family History of PCOS (Yes)	36 (60.0%)	18 (36.0%)	0.012 *
Family History of PCOS (No)	24 (40.0%)	32 (64.0%)	
Family History of Diabetes (Yes)	33 (55.0%)	21 (42.0%)	0.174
Family History of Diabetes (No)	27 (45.0%)	29 (58.0%)	
Abdominal Discomfort	5 (8.3%)	5 (10.0%)	0.961
Diarrhea	6 (10.0%)	6 (12.0%)	
Nausea	9 (15.0%)	8 (16.0%)	
No Adverse Effects	40 (66.7%)	31 (62.0%)	

*Statistically significant ($p \leq 0.05$). Chi-square test was used for comparisons of categorical variables (physical activity, family history, adverse effects).

The chart illustrates significant lipid profile improvements after Metformin therapy, with reductions in total cholesterol, LDL-C, triglycerides, and VLDL-C, and an increase in HDL-C, indicating reduced cardiovascular risk (Figure 2).

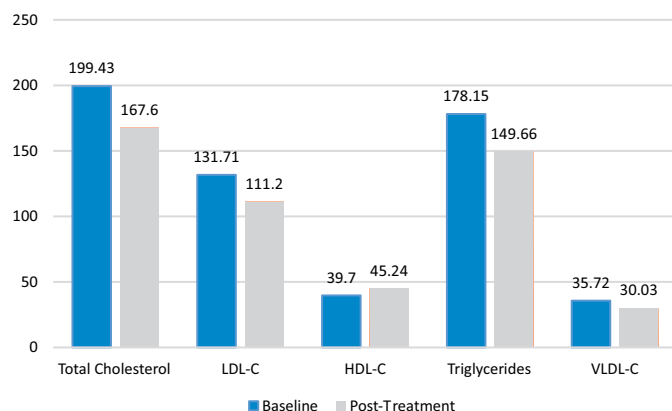


Figure 1: Comparison of Lipid Profile Before and After Metformin Treatment

DISCUSSION

This study reinforces the role of Metformin as a first-line therapy in managing both metabolic and reproductive features of PCOS. Significant improvements in lipid profile were observed, with reductions in total cholesterol, LDL-C, triglycerides, and VLDL-C, along with increased HDL-C levels. These findings were consistent with previous studies demonstrating Metformin's lipid-lowering effects, which may reduce cardiovascular risk in women with PCOS [8, 15]. Notably, these changes occurred independent of significant weight loss, supporting the hypothesis that Metformin directly influences lipid metabolism [16]. Metformin improved hormonal markers by lowering LH, LH/FSH ratio, and testosterone, while increasing SHBG, indicating better control of hyperandrogenism [17]. These changes support enhanced menstrual regularity and ovulation, with reduced symptoms like acne, hirsutism, and infertility [18]. Testosterone, thus further alleviating symptoms like acne, hirsutism, and infertility. Metformin improved glycemic control by reducing fasting glucose, insulin, HOMA-IR, and HbA1c, reflecting enhanced insulin sensitivity [19]. By targeting insulin resistance, a core feature of PCO, it offers dual benefits for metabolic and endocrine regulation. Adherence significantly influenced outcomes, with adherent women showing greater improvements in hormonal, lipid, and insulin parameters. This aligns with previous research linking long-term Metformin use to sustained metabolic and reproductive benefits, emphasizing the need for ongoing patient education and support [20]. Although mild gastrointestinal side effects such as nausea and diarrhoea were reported, the frequency of these events showed no meaningful statistical difference was observed between the adherent and non-adherent groups. This suggests that such side effects were not a major deterrent to treatment. Similar studies report that these symptoms usually subside with continued use [21, 22], reinforcing Metformin's favourable safety profile. Being a single-centre study, generalizability is limited, particularly to rural settings. Reliance on self-reported adherence and a short follow-up may affect

accuracy and overlook long-term outcomes.

The single-center design limits the generalizability of findings, particularly to diverse or rural populations. Additionally, reliance on self-reported adherence and short follow-up duration may affect accuracy and limit assessment of long-term outcomes. Future multicenter studies with longer follow-up and objective adherence measures are recommended to better evaluate the sustained effects of Metformin in PCOS.

CONCLUSIONS

It was concluded that Metformin improves lipid regulation, enhances hormonal activity, and promotes better glucose-insulin balance in females diagnosed with PCOS. Patients who adhered to medication experienced optimal results, demonstrating the need for greater focus on compliance towards treatment plans. These results further confirm Metformin's prescription validity regarding the patient's PCOS metabolic and reproductive complexities. Additional measures to improve patient education and support are necessary to increase treatment adherence and maximize prolonged therapeutic outcomes.

Authors' Contribution

Conceptualization: SA²

Methodology: SS, SFF, FN, SA¹, AS

Formal analysis: SFF, FN, SA¹

Writing and Drafting: SA¹, SS, SFF, FN, SA², AS

Review and Editing: SA¹, SS, SFF, FN, SA¹, SA², AS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency and Risk Factors Associated with Postoperative Sore Throat (POST) in Adults Undergoing General Anesthesia during ENT and Eye Surgery: A Cross-Sectional Study

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ABSTRACT

Postoperative Sore Throat and hoarseness are two common complications after intubation during general Anesthesia. It is crucial to understand the frequency and associated risk factors of POST to improve patients' outcomes and reduce its incidence in patients of ENT and eye surgeries undergoing General Anesthesia (GA). **Objectives:** To emphasize the frequency and risk factors of POST after endotracheal intubation in patients undergoing GA for elective ear, nose, throat (ENT) and eye surgeries. **Methods:** A DHQ Hospital hosted this cross-sectional study from August 2024 to October 2024. The number of participants was 215. A consecutive non-probability sampling technique was used for patient selection. The ASA tool was used to assess the health status of patients undergoing GA. All participants were observed perioperatively, including for 10 minutes in the Post Anesthetic Care Unit (PACU). This was not a blinded study. **Results:** In this study, female subjects comprised 62.8% of the total sample. Complications included sore throat in 102 patients (47.4%) and hoarseness in 25 (24.2%). After the surgeries lasting for 31-60 minutes (51 cases, $p=0.01$) and in throat surgeries (89 cases, $p=0.006$), the sore throat was more common. **Conclusions:** Sore throat and Hoarseness are two common complications reported postoperatively with high frequency. The problem may arise more frequently during long surgical procedures; other factors may include the type of surgery, use of an NG tube, and large diameter ETT size. Knowing these hazards makes it clear that the best airway management techniques are required to reduce patient discomfort and enhance recovery.

INTRODUCTION

General anesthesia with endotracheal intubation is associated with the occurrence of Postoperative Sore Throat (POST), which is common and unwanted [1]. The globally reported incidence of POST ranges from 21% to 65% [2], with findings from India showing rates as high as 54.25% in patients undergoing general anesthesia with endotracheal intubation [3]. The incidence may depend on various factors, including gender, age, size of the endotracheal tube (ETT), tube cuff pressure, duration of

the tube insertion, number of tube insertion attempts, the number of suctioning of the tube, cuff design, and intraoperative tube movement, etc [4]. A study conducted in Pakistan reported an incidence rate of 38.9% of POST, with higher prevalence in females (45.9%) compared to males (30.5%) and a significant increase when using larger ETT sizes (63.6% for size 7.5 tubes) [5]. Zhu et al., findings clearly state that during emergency patient awakening and changes in intracuff pressure are the two most significant



factors that may be associated with increased incidence of POST and hoarseness [6]. An endotracheal tube cuff pressure of less than 20 centimeters of water is the risk factor identified by Obsa *et al.*, to be substantially linked with the development of hoarseness [7]. Intraoperatively, cuff pressure should be monitored regularly [8]. In Azad Kashmir, local studies show that preoperative dexamethasone administration significantly reduces POST incidence, lowering rates from 54.5% to 16.4%, suggesting a potential preventive strategy [9]. The use of tracheal tube stylet for difficult airways has been demonstrated widely in clinical practice. However, this technique for difficult intubation may have some other stylet-related complications, including subglottic injury, palatal perforations, postoperative pharyngeal pain, and oropharyngeal injury [10]. According to an international study, the incidence of sore throat and hoarseness is significantly lower in patients intubated with a laryngeal mask airway (LMA) than in patients intubated with ETT as a result of follow-up for one hour postoperatively [11]. However, the incidence of hoarseness may rise when using a double lumen endobronchial tube (DLT) for one lung ventilation in thoracic surgeries instead of an endobronchial blocker. When hoarseness occurs as a result of using DLT for one lung ventilation, it does not last for more than three days [12]. The incidence and severity of hoarseness and sore throat associated with tube size can be minimized by using a small-sized endotracheal tube [13]. When compared to an endotracheal tube with a cylindrical cuff, intubation with a tapered cuff reduced the incidence and severity of POST as well as the incidence of hoarseness after surgery [14]. Before induction of anesthesia, a prophylactic intravenous injection of dexamethasone 8 mg reduces the incidence and severity of postoperative sore throat and hoarseness [15, 16]. To minimize the chances of airway difficulty and sore throat, the airway scope (video laryngoscope) has been used extensively for orotracheal intubation in patients with difficult airways [16]. Currently, there are no universally effective medications for preventing postoperative painful throat or hoarseness in patients, particularly when a DLT is used during surgery [2]. In contrast to IV dexamethasone, using betamethasone gel on tracheal tubes effectively reduces postoperative sore throat [17]. According to Mohseni and Christiansen *et al.*, applying betamethasone gel to the tracheal tube reduces the incidence of postoperative sore throat, cough, and hoarseness of voice [18, 19]. An article published in the Society of Ambulatory Anesthesiology suggested that spraying benzydamine hydrochloride on the ETT cuff reduces the incidence and severity of POST simply and effectively [20]. Despite these findings, Liu *et al.*, state that: 'use of ketamine (50 mg) and magnesium sulphate (500 mg) just 15 minutes before induction of anesthesia and endotracheal intubation reduces the incidence of

Postoperative sore throat (POST) in patients undergoing general anesthesia [21]. While there are several studies conducted on POST during general anesthesia. The research, especially focusing on ENT and eye surgeries, is limited. In multiple studies, there are generalized findings of POST in different surgeries, which may not accurately determine the unique risk factors and frequency of POST in ENT and eye surgeries during general anesthesia [14].

This study aims to provide a focused analysis of post-incidence and risk factors in ENT and eye surgeries, helping to enhance surgical and anesthetic practices for better patient outcomes. The objectives of this study were to determine the frequency of postoperative sore throat (POST) in adults undergoing general anesthesia with endotracheal intubation (ETT) in Ear, Nose, Throat, and Eye surgical procedures and to evaluate its associated risk factors.

METHODS

This cross-sectional study was conducted in the District Quarter Hospital Buner, Pakistan, from August 2024 to October 2024. After taking approval from the hospital ethical committee (IRB Ref # REC-UOL-/306/08/24), ensuring compliance with ethical standards for human research. The data were then collected through a questionnaire, and patients were examined during the perioperative period. The study adhered to ethical principles, ensuring patient confidentiality and voluntary participation. The formula used for sample size calculation was $n = p(1-p)(Z/E)^2$. Putting the values in the formula, we get $n = 0.5(1-0.5)(1.96/0.07)^2$. $n = 196$ Since an estimated 10% of non-subjects' rate will be added, an additional margin of 19% was taken. Thus $n = 196 + 19 = 215$. For this study, we consecutively enrolled 215 elective patients from the ENT and Eye Department who underwent general anesthesia requiring endotracheal intubation (ETT), having ASA Physical status class I and II, aged 15 years and older. Patients excluded from this study were; patients with the age of less than 15 years, patients with emergency surgery, cigarette smokers, preoperative history of any upper respiratory tract infection, pre-identified sore throat and hoarseness and surgical time more than 2-hours as these are the confounding factors which increases the risk of the occurrence of post operative sore throat that's why such patients were excluded from the study. Confounding factors were controlled by applying strict exclusion criteria. Statistical adjustments were not applied, as confounders were minimized at the study design stage through specific patient selection criteria. All patients were anesthetized by experienced anesthetists at the hospital. We recorded all the patient's personal information, including age, gender, weight, and airway management tools like endotracheal tube size, Nasogastric Tube (Yes/No), and type and duration of the procedure. Cormack-Lehane Grading was used for the

laryngeal view during direct laryngoscopy. For the determination of the frequency and risk factors of sore throat and hoarseness, patients were followed throughout the surgery and in the anesthetic Care Unit (PACU) for 10 minutes, because sore throat and hoarseness are the immediate side effects of extubation following tracheal intubation and peak within the first few minutes of recovery. Anesthesia management tools were well-ordered; no other premedications were administered to any patient except tramadol 1mg/ kg was administered for relieving intraoperative pain and atropine was administered to every patient for reducing the bradycardic effects just before the administration of IV anesthetic propofol (2mg /kg), followed by mask ventilation (combination of 100% oxygen and sevoflurane as inhalational anesthetic), muscle paralysis was achieved with 0.5mg/kg atracurium. After 3-5 minutes of mask ventilation, the endotracheal intubation was performed by an expert anesthetist with a Macintosh laryngoscope. The tube was inflated with 3-5 ml of air. The largest tube sizes of 7.0 mm of internal diameter for women and 8.0 mm of internal diameter for men were used. Maintenance of anesthesia was done with atracurium of 0.1mg/kg and isoflurane. At the end of every procedure, patients were administered a combination of neostigmine (0.04 to 0.08mg/kg) for the reversal of neuromuscular blocking agents and together with 1mg of atropine (for reducing the bradycardic effects of neostigmine). The ETT cuff was then completely deflated, and extubation was performed after suctioning the tube. Verbal consent was obtained from each research respondent, and only the participants who agreed were included in this study. All the important aspects of the research were discussed with the participants. All the data of the participants were then statistically analyzed to determine the frequency of sore throat in them. For this statistical analysis, SPSS version 22.0 was used. The p-value ≤ 0.050 was taken as significant. Chi-square test statistics were applied for comparing sore throat incidence with associated risk factors.

RESULTS

The results contain the data about the sociodemographic characteristics of the participants of the study. In total, 215 elective patients from the ENT and Eye departments, most of them were female, 62.8%, while the male ratio was 37.2%. Other variables mentioned in the table below are the ASA physical status of the study participants, with 56.7% of ASA class 1 and 43.3% of ASA class 2. The frequency of patients with diabetes was 2.8%, while the remaining 97.2% of participants were nondiabetic. Most of the participants were candidates for throat surgery (41.4%), while the patients of the nose (28.8%), ophthalmic (21.4%), and ear surgery (8.4%) also participated in the study. The nasogastric tube was only used in 1.9% of patients. In 82.8% of patients, the ETT size with the internal diameter

of 5 and 6 was used, while the ETT size of 7 (10.7%) and 8 (6.5%) was used in the remaining participants of the study. In 97.2% of patients, the intubation was done on the first attempt, while the intubation was done on the second attempt in the remaining 2.8% of patients. In 48.8% of patients, the duration of surgery was less than 30 minutes, while in 42.3% of patients, the surgical duration was 30-60 minutes, and in 8.8% of patients, the surgical duration was 1-2 hours. Most of the patients (52.6%) were classified as the Cormack Lehane Grade 2a, while the remaining 44.7% were classified as grade 1, and 2.8% of patients were of the grade 2b. There was no hoarseness in 75.8% of patients, while in the remaining 24.2% of patients, hoarseness was present at the PACU. Further, 52.6% of participants suffered from a sore throat, while there was no sore throat in the remaining 47.4% of participants (Table 1).

Table 1: Socio-demographic Characteristics of Participants

Variables	Categories	%
Gender	Female	62.8%
	Male	37.2%
ASA Physical Status	ASA Class-1	56.7%
	Asa Class-2	43.3%
Presence of DM	No	97.2%
	Yes	2.8%
Surgery Type	Ophthalmic Surgery	21.4%
	Throat Surgery	41.4%
	Ear Surgery	8.4%
	Nose Surgery	28.8%
NG Tube Used	No	98.1%
	Yes	1.9%
ETT Size	5-6 mm ID	82.8%
	7 mm ID	10.7%
	8 mm ID	6.5%
Intubation Attempt	First Attempt	97.2 %
	Second Attempt	2.8 %
Surgery Duration	≤ 30 Minutes	48.8 %
	31-60 Minutes	42.3 %
	1 - 2 Hours	8.8 %
Cormack_Lehane_Grade	Grade1	44.7 %
	Grade-2a	52.6 %
	Grade-2b	2.8 %
Hoarseness at PACU	No	75.8 %
	Yes	24.2 %
Sore Throat	No	52.6 %
	Yes	47.4 %

The study contains the details about the risk factors and their association with sore throat, as considered by the p-value of 0.050 significant. According to the data, there was no notable correlation between gender and the occurrence of sore throat, with 68.6% of females and 31.4% of males reporting sore throat, with a p-value of 0.093. Age is also not a crucial factor, as comparable high rates of sore throat were reported across age categories (15-30 years: 95.1%,

31–45 years: 3.9%, >45 years: 1.0%), with a p-value of 0.870. Furthermore, there was no notable difference between the ASA physical status classes and the occurrence of sore throat (p-values of 0.559 for ASA Class 1 and Class 2). In terms of the presence of diabetes, most of the non-diabetic patients reported sore throat (98.0%), but this was statistically insignificant (p=0.483). However, the POST was significantly linked with the type of surgery, particularly the throat surgery (42.2%) and ear surgery (14.7%), with a notable p-value of 0.006, indicating that the post-operative sore throat is significantly linked with the type of surgery. The association between the type of surgery and POST is statistically significant and suggests that ENT surgeries may carry a high risk of POST during these surgeries due to the manipulation of the airway. For the exploration of specific techniques that could mitigate this risk, further research is needed. The use of NG tubes showed an insignificant association (p=0.364), as well as the Cormack-Lehane grading system (p-values ranging from 0.450 to 0.611) was also not a significant factor. Likewise, the intubation attempts were also an insignificant influencer of the sore throat occurrence (p=0.483). While the above factors (age, ASA physical status, diabetes, NG tubes, and intubation attempts) did not reach statistical significance (p>0.050), their influence on POST cannot be entirely ruled out in this study. However, the surgical duration was significantly linked to POST, with a p-value of <0.001 for procedures of more than 30 minutes, indicating that longer surgeries are linked with the increased risk of POST. The

strong statistical association of longer surgical duration with POST suggests that, when clinically feasible, minimize the surgical time could be a strategy to reduce the POST's risk in ENT and eye surgery patients. Finally, all the patients in the PACU with the complaint of hoarseness also experienced a sore throat (51.0%) with a p-value of 0.000. Our results indicate a highly significant correlation between surgical duration and sore throat occurrence (p=<0.001). Longer surgical duration (≥30 minutes) showed that the POST incidence was high and notable. This suggests that the airway irritation is increased with longer intubation time, which can lead to sore throat and hoarseness. While the duration of surgery is often dictated by the complexity of the procedure and the patient's condition. Some strategies like optimizing the anesthetic techniques, procedural efficiency improvements like pre-operative planning, team coordination, minimizing unwanted airway manipulation, and using protective airway devices may help decrease the surgical time and the POST risk in such surgeries. Importantly, although not all cases allow for reduction in surgical duration due to the complex nature of the surgery, our findings suggest that targeting the surgeries with a duration of ≥30-minute threshold-where feasible-could be a practical focus for quality improvement initiatives in ENT and eye surgeries. Further research is required to determine which specific surgical or anesthetic alterations are most effective in mitigating surgical time and subsequent post-incidence in this patient population (Table 2).

Table 2: Risk Factors and Their Association with Sore Throat

Variables	Categories	Sore Throat		Total	p-value
		No	Yes		
		Frequency (%)			
Gender	Female	65 (57.5%)	70 (68.6%)	135 (62.8%)	0.093
	Male	48 (42.5%)	32 (31.4%)	80 (37.2%)	
Age (Years)	15-30	106 (93.8%)	97 (95.1%)	203 (94.4%)	0.870
	31-45	5 (4.4%)	4 (3.9%)	9 (4.2%)	
	>45	2 (1.8%)	1 (1.0%)	3 (1.4%)	
ASA Physical Status	ASA Class-1	62 (54.9%)	60 (58.8%)	122 (56.7%)	0.559
	ASA Class-2	51 (45.1%)	42 (41.2%)	93 (43.3%)	
Presence of Diabetes Mellitus	No	109 (96.5%)	100 (98.0%)	209 (97.2%)	0.483
	Yes	4 (3.5%)	2 (2.0%)	6 (2.8%)	
Type of Surgery	Ophthalmic Surgery	30 (26.5%)	16 (15.7%)	46 (21.4%)	0.006
	Throat Surgery	46 (40.7%)	43 (42.2%)	89 (41.4%)	
	Ear Surgery	3 (2.7%)	15 (14.7%)	18 (8.4%)	
	Nose Surgery	34 (30.1%)	28 (27.5%)	62 (28.8%)	
Nasogastric Tube Used	No	110 (97.3%)	101 (99.0%)	211 (98.1%)	0.364
	Yes	3 (2.7%)	1 (1.0%)	4 (1.9%)	
Cormack-Lehane Grade	Grade- 1	46 (40.7%)	50 (49.0%)	96 (44.7%)	0.450
	Grade- 2a	64 (56.6%)	49 (48.0%)	113 (52.6%)	
	Grade- 2b	3 (2.7%)	3 (2.9%)	6 (2.8%)	
Endotracheal Tube Size in millimeter Internal Diameter)	5-6 mm ID	93 (82.3%)	85 (83.3%)	178 (82.8%)	0.611
	7 mm ID	11 (9.7%)	12 (11.8%)	23 (10.7%)	
	8 mm ID	9 (8.0%)	5 (4.9%)	14 (6.5%)	

Intubation Attempt	First Attempt	109 (96.5%)	100 (98.0%)	209 (97.2%)	0.483
	Second Attempt	4 (3.5%)	2 (2.0%)	6 (2.8%)	
Surgery Duration	≤30 minutes	73 (64.6%)	32 (31.4%)	105 (48.8%)	<0.001
	31-60 minutes	40 (35.4%)	51 (50.0%)	91 (42.3%)	
	1-2 Hours	0 (0.0%)	19 (18.6%)	19 (8.8%)	
Hoarseness at PACU	No	113 (100.0%)	50 (49.0%)	163 (75.8%)	<0.001
	Yes	0 (0.0%)	52 (51.0%)	52 (24.2%)	

The study shows the overall incidence of sore throat in the study participants, where 60 patients suffered from sore throat, and 155 participants did not face this post-operative complication (Figure 1).

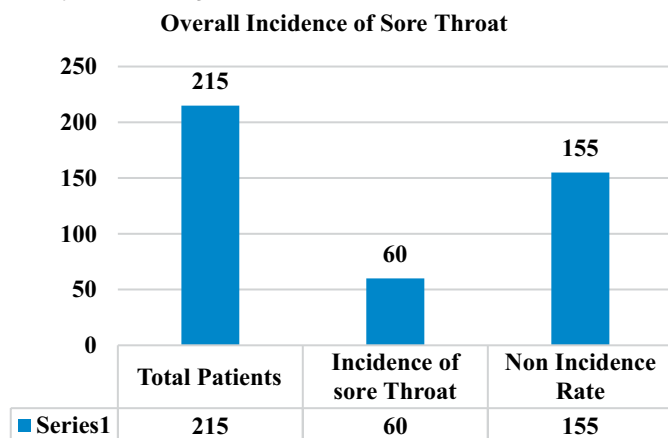


Figure 1: Incidence of Sore Throat

The study shows the overall incidence of sore throat in the study participants, where 60 patients suffered from sore throat, and 155 participants did not face this post-operative complication (Figure 1).

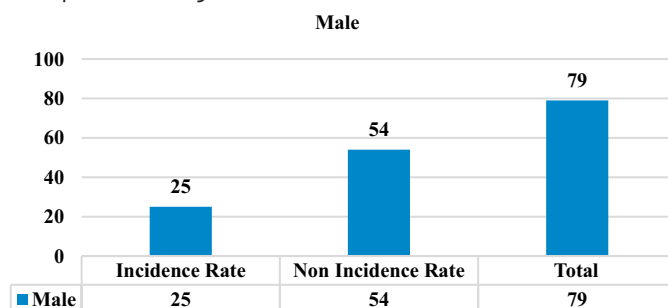


Figure 2: Post-surgical Incidence Among Male Participants

There was information about the female participants of the study, where the incidence of POST was in 35 patients, and the ratio of patients who did not suffer from POST was 101 out of a total of 136 female participants (Figure 3).

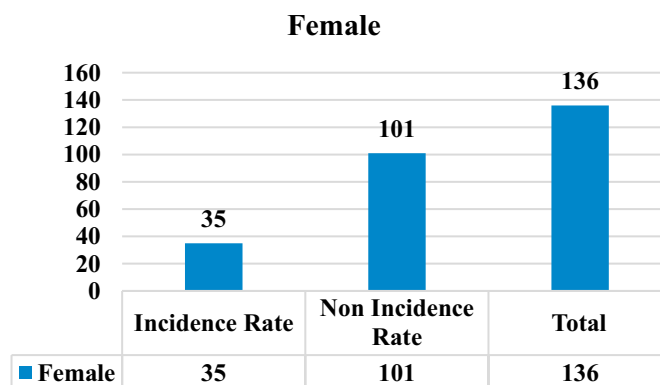


Figure 3: POST in Female Participants of the Study

DISCUSSION

Hoarseness and sore throat are the most common complications arising postoperatively after general anesthesia. Studies are available on these potential complications only in children, but not enough to illustrate these two complications in adult patients. Current study has enough description of these two complications among the adult population. During data collection from participants of this study, we found that the occurrence of sore throat was 102 (47.4%) and that hoarseness was 52 (24.2%). Some of the studies on postop hoarseness and sore throat may support this study, as a clinical report of Stout *et al.*, reveals the occurrence of postoperatively sore throat in a range of 22% to 48% for varying use of ETT sizes [22]. They demonstrated that a small diameter of ETT has less chance to produce postop sore throat than does by large diameter of ETT. Likewise, gender differences also the statistically different incidences of sore throat, 68.6% in female and 31.4% in male patients, and we found the greatest identical relation with Tsukamoto *et al.*, for male patients, 32%, whereas many great differences we found with their analysis for female patients (37%) [23]. The different statistical results among female participants may be the reasons involved: the use of different techniques or the use of dissimilar ETT sizes. Our observations are in line with Amin *et al.*, as there was no such statistically significant difference in sore throat in males and females because both groups suffered identically [16]. Among those patients who responded 'Yes' when questions were asked about hoarseness at PACU, nearly all the patients also suffered from a sore throat. We found a strong association of sore throat with long surgical procedures of intubated patients, which was statistically significant,

whereas no association occurred with the use of an NG tube and multiple attempts of ETT intubation. This evidence and findings are in-streak with Wallen *et al.*, findings of 'postoperative throat complications after tracheal intubation [24]. Current results showed high statistical significance (<0.001) when we compared the duration of surgery with a sore throat, as increased duration of the surgery will lead to increased chances of occurrence of postop sore throat and hoarseness. This finding was not in line with other studies, and the reasons might be the use of dexamethasone injections or local anesthetic gel on the tube [25]. In present study, all those patients who were complaining of sore throat had common signs and symptoms (i.e., pain or a scratchy sensation in the throat, hoarseness of voice, and their pain was exacerbated with swallowing or talking). While surgical duration cannot always be mitigated due to the demand of the procedure, certain measures may help decrease this effect. These include careful selection of endotracheal tube (ETT) size, use of humidified oxygen, and pharmacological interventions such as corticosteroids or local anesthetic applications.

Our study has multiple strengths. These include tracheal intubations performed by experienced anesthetists, less frequency of failed intubations, cost-effectiveness, good control over the work, and fewer available studies on POST in adults, which are the main strengths of this study. Future research should focus on identifying optimal anesthesia management techniques to minimize POST risk in prolonged surgeries.

CONCLUSIONS

It was concluded that hoarseness and sore throat after ETT intubation are the two most common complications during emergence from general anesthesia. We found the strongest association of postoperative sore throat (POST) with the duration of surgery. Many other risk factors may contribute; these include: type of surgery, the large size of ETT, more than one attempt for intubation, and use of an NG-tube. All these are of increased concern for an anesthetist to consider before the anesthesia. Therefore, care must be taken for these potential risk factors, and if possible, appropriate preventive measures should be applied before long surgical procedures.

Authors' Contribution

Conceptualization: AK

Methodology: AZK, AB

Formal analysis: TRU

Writing and Drafting: AK, IU, SS, NA

Review and Editing: AK, IU, AZK, AB, TRU, SS, NA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Outcomes in Conservative Versus Surgical Treatments in Ludwig's Angina Cases: A Comparative Study

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ABSTRACT

Rapid airway impairment brought on by Ludwig's angina may require careful antimicrobial treatment or surgery. **Objective:** To compare the airway compromise and hospital stay in conservative versus surgical approach in cases with Ludwig's Angina. **Methods:** This experiment was conducted at Liaquat University using a non-probability consecutive sampling technique to recruit 76 patients, aged 18 to 40, diagnosed with early-stage Ludwig's angina without airway obstruction. Quasi-experimental study. There were 38 patients in each group, and participants were randomized to either the surgery group or the conservative treatment group. Outcomes such as airway compromise and length of hospital stay were recorded and compared between groups using t-tests and Fisher's exact tests. **Results:** The conservative group's mean age was 30.58 ± 5.52 years, while the surgical group's was 31.34 ± 5.92 years. There were 11 females (28.95%) and 27 males (71.05%) in the conservative group and 8 females (21.05%) and 30 males (78.95%) in the surgical group. There was a statistically significant difference ($p < 0.001$) in the length of hospital stay between the surgical group (6.97 ± 1.10 days) and the conservative group (5.05 ± 0.89 days). Five patients (13.16%) in the surgical group and three patients (7.89%) in the conservative group experienced airway impairment; however, this difference was not statistically significant ($p = 0.706$). **Conclusion:** Conservative treatment, being less invasive, can be effective in mild cases, leading to shorter hospital stays and a reduced risk of airway compromise.

INTRODUCTION

The severe ailment known as Ludwig's angina, or "Angina Ludovici," is characterized by extensive cellulitis that affects the neck, the floor of the mouth, and the submandibular areas on both sides, which may restrict the airway [1]. Ludwig's angina, also known as "Angina Maligna" or "Morbus Strangularis," gets its name from the Latin verb "angere," which means to strangle, and reflects the feeling of choking it induces. Ironically, it was first documented by German physician Wilhelm Frederick Von Ludwig in 1836.

However, he passed away in 1865 from inflammation in his neck, which was thought to be related to the illness. It has a notoriously high mortality rate due to its rapid progress and because of this airway may very quickly become compromised if acute treatment is not given [2]. Patients with a history of dental infections, mainly from the lower second and third molars, are more likely to develop Ludwig's angina [3]. Additionally, it can exacerbate diseases like sialolithiasis, peritonsillar and



parapharyngeal abscesses, or submandibular gland sialadenitis [4]. Mandibular trauma, penetrating injuries to the floor of the mouth, oral malignancies, lymphangiomas, and cultural customs such as tongue piercing are additional contributing factors [5]. The swelling that results may cause the tongue to move backward and upward, which could restrict the airway and cause asphyxiation. The infection usually starts in one side but quickly spreads to both sides causing very quick swelling of tissue that can block the airway and manage saliva [6, 7]. The identification and treatment for Ludwig's angina urgently is important as delayed intervention may increase morbidity considerably with a 10 % to the 50 % reported case fatality rates [8]. The management of Ludwig's angina most commonly involves two principal routes, as follows: conservative treatment and surgery [9]. The conservative treatment mainly depends on broad-spectrum intravenous antibiotics, supportive care and close airway status monitoring [10]. This approach is one used to successfully control the infection, reduce immediate complications and provide an avenue for spontaneous resolution of swelling. The 2022 study on Ludwig's angina found that 20% of patients required tracheostomy and 10% experienced mortality despite aggressive treatment, emphasizing the importance of early surgical intervention [11]. However, surgery is typically recommended for significant risk of airway involvement or when conservative measures are inadequate. Surgical therapy may include drainage of any abscesses, submandibular space decompression and for severe cases tracheostomy to secure the airway [12]. The choice of the best treatment is still a matter for discussion in medical schools, although these treatments appear to be available. The decision depends on the severity of infection, clinical status of patient as well as risks and benefits associated with both. Clearly there are theoretical implications for patient outcome, most importantly time to first waking and therefore length of stay in hospital stress has been placed on having a secure airway at the end of surgery. To compare conservative and surgical interventions for hospital stay in patients with Ludwig's angina, this randomized controlled trial was conducted that included the airway compromise at some point during treatment as an additional important outcome measure. Through a systematic analysis of these important variables, the study aims to provide evidence that allow clinicians to make data-driven decisions based on individual patient situations. Ultimately, the purpose of this research was to inform on how management strategies for Ludwig's angina can progress so patients receive best and timely care when required without significant complications that arise with such a critical condition.

METHODS

Using a non-probability successive sampling technique, this quasi-experiment was carried out in the Department of Oral and Maxillofacial Surgery, Institute of Dentistry, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad, from January 27, 2024, to October 1, 2024. Following an explanation of the study's goals, all participants provided written informed permission, and CPSP and the hospital's ethical review committee granted their ethical approval (CPSP/REU/DSG-2020-166-32240). The WHO calculator was used to determine the sample size using the following formula:

$$n = 2 \times (Z_{\alpha/2} + Z_{\beta})^2 \times \frac{\delta^2}{\alpha^2}$$

Parameters included a 90% confidence level, 5% alpha error, an anticipated proportion of airway compromise in the conservative group of 26.3%, and 2.9% in the surgical group [13]. A total of 76 Ludwig's angina patients were included in the study, with 38 instances per group being the determined sample size. Included were patients with Ludwig's angina of either sex, ages 18 to 40, who had early-stage symptoms such as neck pain, neck erythema or swelling, swollen jaw, cheeks, or tongue, painful tongue, or an abscessed tooth. Patients with a history of maxillofacial trauma or prior submandibular surgery, those with systemic diseases such as diabetes mellitus or immunosuppression, and individuals unable to provide informed consent at the time of the procedure were excluded. Using the lottery approach, patients who met the aforementioned criteria were chosen and split into two groups: Group A (conservative treatment) and Group B (surgical treatment), each of which had 38 patients. Each patient gave their informed written consent, with translations available upon request. All procedures were performed by a resident maxillofacial surgeon under the supervision of a consultant, and study variables were recorded on a standardized proforma. Patients with early-stage Ludwig's angina, in which the airway was uncompromised, made up the sample; patients with airway blockage were not included. Without any concurrent infections, all groups were given the same antibiotics for the same amount of time. Airways were assessed through clinical examination and pulse oximetry, with respiratory compromise identified by symptoms such as anxiety, cyanosis, stridor, tachypnea, low oxygen saturation level, unable to lie supine, alar flariness, and intercostal or supraclavicular indrawing. For five days, Group A was given intravenous cefotaxime (1g twice day) and metronidazole (500 mg three times daily), with dosages modified in accordance with culture findings. Group B underwent surgical decompression with stab incisions and drain placement in the submandibular and submental spaces. Monitoring was done for patients for the airway compromise, and if needed emergency tracheostomy was

performed. Outcomes, including airway compromise, mortality, and length of hospital stay, were assessed over a 15-day follow-up. Inter observer variability in airway compromise assessment was minimized using standardized protocols, with good agreement observed ($k = 0.91$). SPSS version 22.0 was used to analyze the data. While categorical data, such as gender and airway impairment, were presented as frequencies and percentages, continuous data, like age and length of stay, were summarized as means and standard deviations. Both the t-test and Fisher's exact test were used to compare the outcome variables (length of stay and airway compromise) between the two groups. The length of hospital stay was evaluated using the Shapiro-Wilk test, which revealed that it was regularly distributed ($p=0.16$). Statistical significance was defined as a p-value of less than 0.05.

RESULTS

Patients in the surgery group were 31.34 ± 5.92 years old on average, compared to 30.58 ± 5.52 years old in the conservative group. The conservative group included 11 females (28.95%) and 27 males (71.05%), while the surgical group comprised 8 females (21.05%) and 30 males (78.95%) (Table 1).

Table 1: Age and Gender Distribution of Conservative and Surgical Approaches (n = 76)

Characteristic	Conservative Mean $\pm$ SD/Frequency (%)	Surgical Mean $\pm$ SD /Frequency (%)
Age (Years)	30.58 ± 5.52	31.34 ± 5.92
Gender		
Female	11 (28.95)	8 (21.05)
Male	27 (71.05)	30 (78.95)

The average length of stay was 5.05 ± 0.89 days in the conservative group and 6.97 ± 1.10 days in the surgical group, indicating a statistically significant difference ($p < 0.001$). Five patients (13.16%) in the surgical group and three patients (7.89%) in the conservative group had airway impairment; however, the difference was not statistically significant ($p=0.706$) (Table 2).

Table 2: Comparison of Length of Stay and Airway Compromise between Two Approaches in Ludwig's Angina (n = 76)

Characteristic	Conservative Mean $\pm$ SD/Frequency (%)	Surgical Mean $\pm$ SD /Frequency (%)	p-Value
Length of Stay (Days)	5.05 ± 0.89	6.97 ± 1.10	$<0.001^*$
Airway Compromise			0.706**
No	35 (92.11)	33 (86.84)	
Yes	3 (7.89)	5 (13.16)	

*Student t test; **Fisher test

DISCUSSION

There is a debate regarding treatment of Ludwig's angina, with the primary goal being to secure the airway and control the spread of infection. The purpose of this study is to evaluate the results of treating Ludwig's angina conservatively versus surgically [14]. According to this research, early-stage Ludwig's angina can be effectively treated conservatively—with antibiotics, corticosteroids, and close observation—to prevent surgery and associated side effects. However, surgical intervention is essential for advanced cases with airway obstruction or rapid disease progression, as it reduces mortality and prevents severe complications, especially when conservative methods fail. Difference in length of hospital stay was statistically significant. The mean LOS for Group A was shorter (5.05 days (SD = 0.89)) compared to Group B (6.97 days (SD = 1.10)) suggesting faster recovery for less severe cases using conservative treatment [15, 16]. Results of the present study indicated that airway compromise was more (13.2%) common in Group B than Group A (7.9%), suggesting vital role of surgical interventions towards better managing cases of Ludwig's angina. The reason for this higher rate of airway compromise in the surgical group may be because by presenting with more advanced stage, patients in this group had already undergone initial conservative measures requiring surgical management. Airway compromise in Ludwig's angina occurs due to swelling and cellulitis of submandibular, sublingual, submental space due to the obstruction of airway [17]. As the extent of Ludwig's angina progresses, there is increased risk of airway compromise [18]. In these cases, it is, therefore, necessary to perform an incision and drainage to relieve the pressure, remove the pus, and to secure the airway. This is in consonance with other researches indicating that it is only advisable to operate to treat severe cases of such insulinomas [18, 19]. However, it may be seen that Group A presented with comparatively less airway compromise implying that the clinical management through antibiotics, corticosteroids and monitoring may therefore be appropriate in early, less severe or localized infection where the airway is not at an imminent risk. Nonetheless, any instance of airway compromise was seen in the conservative group, and therefore underscores on the need to monitor patients closely and not hesitate to move to surgery if needed [20].

The study's limited sample size and potential baseline differences in disease severity between groups may affect the comparability of outcomes. Additionally, the lack of long-term follow-up restricts assessment of recurrence and delayed complications. Future studies should involve larger, multicenter cohorts with standardized severity grading and extended follow-up to better guide management strategies for Ludwig's angina.

CONCLUSIONS

Conservative treatment, being less invasive, may be effective in managing milder cases of Ludwig's angina, and is associated with shorter hospital stays and a reduced risk of airway compromise. However, each patient requires an individualized treatment plan, tailored to their clinical presentation and physician's judgment.

Authors' Contribution

Conceptualization: MS, SS

Methodology: FI, MM, JNG

Formal analysis: SS

Writing and Drafting: FI, MS, ZHC, UB, SS

Review and Editing: FI, MS, ZHC, MM, UB, JNG, SS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison between Oral Nifedipine and Intravenous Labetalol in Managing Severe Preeclampsia

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ABSTRACT

Hypertensive disorders contribute to significant maternal morbidity and mortality in pregnancy. Immediate treatment is required to avoid serious complications. **Objectives:** To compare the mean time taken to achieve the target BP with oral nifedipine versus intravenous labetalol in patients with severe preeclampsia. **Methods:** This quasi-experimental study was conducted at Lady Willingdon Hospital, Lahore, over six months after taking approval from CPSP, involving 100 patients diagnosed with severe preeclampsia. Participants were divided into two equal groups: Group oral nifedipine and IV labetalol. Study outcome time taken to reach target BP <140/90 mmHg was compared among groups using an independent sample test, with a p-value ≤ 0.05 as significant. **Results:** Target BP was achieved earlier at 43.96 ± 5.93 minutes with oral nifedipine compared to IV labetalol at 48.60 ± 6.80 minutes (p < 0.001). **Conclusions:** It was concluded that the findings strongly support the use of nifedipine as a more effective option for rapidly lowering blood pressure compared to labetalol. Its faster onset of action makes it the preferred choice for achieving timely blood pressure control in patients with severe preeclampsia.

INTRODUCTION

Preeclampsia is a significant pregnancy-related complication, characterized by high blood pressure and proteinuria developing in previously normotensive women [1]. It complicates about 5-7% of first-time pregnancies and 1-3% of subsequent pregnancies, posing severe risks to both maternal and fetal health [2]. A review conducted between 1969 and 2019, encompassing data from 30 countries, found 291,247 cases of preeclampsia, prevalence of preeclampsia/eclampsia (PE/E) noted as 6.7%. This highlights the worldwide burden of PE/E over five decades and emphasizes the need for continued

monitoring and intervention strategies targeting this high-risk population [3]. Severe hypertension is a frequent complication in pregnancy-associated hypertensive disorders, and there is no clear consensus on the preferred first-line antihypertensive drug for emergency use [4]. Blood pressure ≥160/110 mmHg, requires prompt intervention to prevent severe maternal complications of preeclampsia such as hypertensive encephalopathy, cerebrovascular accidents, and eclampsia and neonatal complications including intrauterine growth retardation, prematurity, and death [5]. Among the various



antihypertensive agents available, oral nifedipine, labetalol, and hydralazine are commonly recommended for the management of severe hypertension in pregnancy [6]. Both nifedipine and labetalol are FDA-approved for managing hypertension in pregnancy. Despite nifedipine being cost-effective and easy to administer, healthcare providers often prefer labetalol, although this preference is not consistently supported by robust evidence [7, 8]. In terms of adverse reactions, nifedipine may cause reflex tachycardia, headache, and flushing, while labetalol is more commonly associated with bradycardia, fatigue, and potential fetal growth concerns when used long-term. Both drugs are generally well tolerated in acute settings and are considered safe in pregnancy when used appropriately. Some clinical trials, particularly in low- and middle-income countries, have shown that oral nifedipine lowers blood pressure more rapidly and effectively than labetalol [9]. Conversely, studies from high-income settings suggest there is no significant difference in efficacy or safety profiles between the two agents [10]. This variability in results across different healthcare systems, resource availability, and patient populations explains the absence of a clear global consensus on the preferred first-line agent. Therefore, more context-specific research is essential to establish definitive guidelines that are adaptable across varying clinical environments.

This study aims to address this gap by comparing the effectiveness of oral nifedipine and IV labetalol in achieving target BP in women with severe preeclampsia. This provides valuable insights into the optimal management of severe preeclampsia, potentially influencing clinical practice and guidelines. By determining the more effective and safer option between the two drugs, healthcare providers can make informed decisions that enhance maternal and fetal outcomes, especially in resource-limited settings where cost and ease of administration are critical considerations.

METHODS

This quasi-experimental study was conducted at Lady Willington Hospital, Lahore, from August 2021 to February 2022 after taking approval from CPSP (REU No: 40385). 100 participants, 50 cases in each group, were determined based on a 95% confidence level and 80% power of the test. This determination considered the mean time required to achieve the target BP (40 ± 10 minutes for oral nifedipine and 60 ± 11.25 minutes for intravenous labetalol) [11]. Non-probability consecutive sampling method was utilized for this study. Participants were chosen based on specified selection criteria. The inclusion criteria consisted of females with severe preeclampsia (BP $\geq 160/110$ mmHg with proteinuria $>+1$ on dipstick method), aged 20-40 years, with parity less than 5, gestational age over 24 weeks determined by LMP or dating scan. Exclusion criteria included females with chronic hypertension, eclampsia (BP

$\geq 160/110$ mmHg with convulsions), diabetes (random BSL ≥ 186 mg/dl), abnormal placenta conditions (as determined on ultrasound), multiple pregnancies, those who had taken antihypertensive treatment within past 24 hours, and those with unsuccessful medical management as noted in medical records. One hundred females meeting the selection criteria were recruited from the Emergency Obstetrics and Gynaecology Department of Lady Willington Hospital, Lahore. Informed consent was obtained from all participants. Demographic information was recorded. Participants were assigned to two groups using the lottery method. Nifedipine Group, in which females received 10 mg oral nifedipine up to 5 doses repeated every 30 minutes and Labetalol Group, in which females received IV labetalol injection up to 5 doses in an escalating dose regimen of 20 mg, 40 mg, 80 mg, 80 mg, and 80 mg repeated every 30 minutes. This is by ACOG guidelines; a slight modification was made in labetalol, repeated every 30 minutes instead of 20 minutes. [10] All female was monitored in Gynaecology wards until the target BP ($<140/90$ mmHg) was achieved, and the time between administration of the first dose and to time when the target BP was achieved was noted in minutes, and also several doses required to achieve the target BP was noted. This information was collected using a pre-designed proforma. Analysis was done using SPSS version 26. Normality of the quantitative data was assessed using the Shapiro-Wilk test. Mean and standard deviation were calculated for quantitative variables, and frequency/percentage for qualitative variables. Outcome was compared among groups using an independent samples t-test, considering p-value ≤ 0.050 as significant.

RESULTS

The mean age of participants was comparable between the Nifedipine group (25.3 ± 4.8 years) and the Labetalol group (24.9 ± 4.3 years, $p=0.661$). Parity was also similar between groups ($p=0.511$). Regarding residence, 46% of patients in the Nifedipine group and 48% in the Labetalol group were from rural areas, whereas 54% in the Nifedipine group and 26% in the Labetalol group were from urban areas. Mean gestational age was 37.3 ± 3.4 weeks and 37.4 ± 3.1 weeks in Nifedipine and Labetalol groups, respectively ($p=0.878$) and mean BMI was 28.5 ± 5.4 kg/m² and 27.6 ± 5.4 kg/m², respectively ($p=0.406$). Baseline systolic BP was 180.40 ± 5.48 mmHg in the Nifedipine group and 182.30 ± 6.43 mmHg in the Labetalol group ($p=0.115$), while diastolic BP was 116.80 ± 5.92 mmHg and 115.60 ± 7.33 mmHg, respectively ($p=0.370$) (Table 1).

Table 1: Demographics and Baseline Characteristics

Characteristics		Nifedipine Group (n=50)	Labetalol Group (n=50)	p-Value
Age	Years	25.3 ± 4.8	24.9 ± 4.3	0.661
Parity	—	1.7 ± 0.94	1.6 ± 0.52	0.511
Residence	Rural (%)	23 (46%)	24 (48%)	—
	Urban (%)	27 (54%)	52 (26%)	—
Gestational Age	—	37.3 ± 3.4	37.4 ± 3.1	0.878
BMI	—	28.5 ± 5.4	27.6 ± 5.4	0.406
Baseline BP (mmHg)	Systolic	180.40 ± 5.48	182.30 ± 6.43	0.115
	Diastolic	116.80 ± 5.92	115.60 ± 7.33	0.370

Patients in the oral nifedipine group have achieved the target BP in 43.96 ± 5.93 minutes, compared to 48.67 ± 6.8 minutes in IV labetalol group ($p < 0.001$). Mean doses required to achieve target BP were also less for the nifedipine group as compared to the labetalol group, 2.20 ± 1.24 and 2.75 ± 1.43 , $p = 0.04$, and this difference was statistically significant (Table 2).

Table 2: Comparison of Study Outcome

Outcomes	Nifedipine Group (n=50)	Labetalol Group (n=50)	p-Value
Time Taken to Achieve Target BP (Minutes)	43.96 ± 5.93	48.67 ± 6.80	< 0.001
Doses Required to Achieve the Target BP	2.20 ± 1.24	2.75 ± 1.43	0.040

DISCUSSION

Hypertensive emergencies in pregnancy require prompt and effective management to prevent fetomaternal complications. Antihypertensive agents are commonly used to achieve rapid blood pressure control, each with varying efficacy and time to reach target levels [12]. The choice of medication depends on factors such as onset of action, safety profile, and clinical response, making it essential to evaluate their comparative effectiveness in different settings [13]. Current study found that average time to reach target BP of $< 140/90$ mmHg was less for nifedipine 43.96 ± 5.93 minutes for and 48.67 ± 6.80 minutes for labetalol, ($p < 0.001$) and mean doses required to achieve target BP was also less for nifedipine group as compared to labetalol group, $p = 0.040$. These findings align with Li *et al.*, where the time taken to achieve target BP was significantly less with nifedipine than IV labetalol [14]. Sahai *et al.*, also reported similar findings. However, the mean time taken by nifedipine in their study was shorter than the current observation (34.67 minutes), while the time taken by labetalol was longer (52.00 minutes), $p < 0.001$ [15]. In contrast, Kaur *et al.*, found that IV labetalol is more effective in terms of achieving target BP in less time as compared to nifedipine (48.67 ± 17.80 minutes' vs 64.33 ± 9.81 , $p < 0.001$) [16]. Furthermore, Nivethana *et al.*, found both drugs safe, but IV labetalol has taken less time in lowering BP [17]. Upendra *et al.*, however, concluded that both drugs are equally effective in lowering BP [18]. A trial conducted in 2022 found that the effectiveness of nifedipine, labetalol, and hydralazine in achieving a 20% reduction in MAP varied with dosage [19]. In contrast, a locally conducted trial by Wasim *et al.*, found both drugs equally effective in terms of achieving the target BP and several doses required to achieve that [20]. One meta-

analysis recommends nifedipine as the preferred strategy for BP management in pregnant women with severe hypertension. While labetalol and hydralazine remain conventional treatment options, their efficacy appears more limited and also stated that clinicians should be mindful of hydralazine's inconsistent blood pressure-lowering effects and need for higher doses of labetalol to achieve optimal benefits [21].

The relatively small sample size and single-center design may limit the generalizability of the findings. Additionally, the study did not assess long-term maternal and fetal outcomes or potential adverse effects beyond initial blood pressure control. Future large-scale, multicenter studies with extended follow-up are recommended to compare long-term safety and efficacy of antihypertensive agents in hypertensive emergencies of pregnancy.

CONCLUSIONS

It was concluded that the findings strongly support the use of nifedipine as more effective option for rapidly lowering blood pressure compared to labetalol. Its faster onset of action makes it preferred choice for achieving timely BP control in patients with severe preeclampsia.

Authors' Contribution

Conceptualization: AS¹

Methodology: AS¹, AS², NS, FB, HR, HZ

Formal analysis: AS¹

Writing and Drafting: NS, FB

Review and Editing: AS¹, AS², NS, FB, HR, HZ

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article



Primary Cesarean Section: A Gateway to Repeat Surgery

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ABSTRACT

The rising rate of Cesarean Sections (CS) is a significant concern globally. While C-sections are lifesaving in many cases, an increasing number of unnecessary procedures pose risks to both mothers and babies. It has been found that the most common indication of CS is previous CS. **Objective:** To assess the indications and the factors leading to primary CS. **Methods:** The study was conducted at a tertiary care hospital of Pakistan employing non-probability consecutive sampling. A detailed history of participants revolving around their first CS was taken including indication and the associated demographics. All the information was entered on a specific proforma. Data analysis was conducted using SPSS software version 26.0. The primary outcome variable was the indication for primary cesarean section, while the secondary variables included factors contributing to the procedure. **Results:** A total of 264 women who had CS for at least one of their pregnancy were considered. The vast majority (n=195, 73.9%) were primigravida, had 4-6 antenatal visits (n=174, 65.9%) and underwent CS at term (180, 68.2%). There were more emergency CS (n=140, 53%) performed at private clinics/hospitals (n=201, 57.4%). Regarding the indications of primary CS, the most prevalent was failed progress of labour, followed by oligohydramnios, breech presentation/transverse lie, fetal distress, reduced fetal movements and maternal request. **Conclusion:** It is need of time to scrutinize the indications of primary CS and to adopt potential strategies to minimize its number with the aim to lower overall CS rate.

INTRODUCTION

Cesarean Section (CS) has been an integral constituent of Obstetrics over the last so many decades. It is the surgical procedure frequently employed to salvage the lives of mothers and fetuses [1]. Its fetal indications comprise a long list, including failure to progress in labour, malpresentation, abnormal fetal heart rate, oligohydramnios, macrosomia, cord prolapse [2]. The maternal indications include previous CS, medical disorder like hypertension or cardiac disease, placenta previa, infections like HIV or active genital Herpes Simplex virus. The proven role of C section delivery in dealing with the complicated childbirth and saving the lives of mothers as well as babies is of no doubt. However, the rise in the CS rates over the last few years has raised many concerns. In 1985, a panel of experts of WHO concluded the remarks that 'there is no justification for any region to have a Caesarean section rate higher than 10-15% [3]. Nevertheless, the

whole globe is witnessing the continuous rise in the rates of CS and it has become a matter of concern for the health experts as well as the expecting mothers. In year 2000, estimated CS rate was 12% [4]. The worldwide current estimated CS rate is 21.1% [5]. It is relatively higher in developed countries (27.2%), lower in less developed countries (24.2%) and lowest in least developed countries (8.2%)[6]. It has been predicted that by year 2030, CS rate will reach 28.5% with more than 38 million deliveries ending up in CS [7]. In Pakistan, a tremendous rise has been observed in CS rate from 3.2% in 1990 to 19.6% in 2018 [8]. The increasing trend of CS rate has prompted health professionals to investigate the various indications of CS. Some indications like malpresentation, previous C section, abnormal fetal heart rate, oligohydramnios, macrosomia, cord prolapse and hypertensive disorders are quite justifiable on medical grounds [9]. Certain demographic



features like socio-economic status, education level and occupation are also linked to high CS rate [10]. An important factor contributing to continuously rising CS rate is the medicalization of the childbirth procedure [11]. Instead of being a physiological process, delivery has been commercialized by the mal-practicing doctors who opt for CS for their own convenience and time saving along with financial benefits. The use of social media has also played a pivotal role in this rising trend of CS. The expecting mothers watch the videos of normal delivery, becoming horrified by the pains of labour process, and resort directly to C section, thus contributing to high C section rate [12]. The unawareness of expecting mothers regarding Caesarean delivery complications also make them vulnerable for CS as this procedure is related to baby safety by the doctors, which is infact not always the case. An overview of the common indications of CS reveals that the most common indication is previous CS [13]. The ascending trend of CS can be turned to descending trend by critically reviewing the indications of primary CS. By doing so, non-genuine indications can be brought under the audit process, with the hope that that primary CS are performed only for authentic and legitimate reasons. The extensive online search revealed paucity of such studies in Pakistan. It prompted us to assess the indications and the circumstances or factors leading to primary CS.

Despite the rising global and national rates of cesarean section (CS), there is limited local evidence critically evaluating the indications and contributing factors leading to primary CS, particularly in Pakistan where rates are increasing rapidly. This lack of context-specific data restricts efforts to identify non-medically justified procedures and implement strategies to reduce unnecessary CS. By collecting and reviewing such data, initiatives can be taken to pare down the incidence of primary CS and thus minimizing the most common indication of repeat CS.

METHODS

This retrospective descriptive study was conducted in the Obstetrics Department of Nishtar Hospital, Multan, Pakistan, from November 2024 to February 2025, after receiving ethical approval from the Institutional Review Board of Nishtar Medical University (Ref. No. 18991/NMU). A non-probability consecutive sampling technique was employed, and the sample size was calculated to be 264 using the formula

$$n = Z^2 \times p \times (1-p) / d^2$$

Where:

Confidence level = 95% ($Z = 1.96$)

Proportion (p) [14] = 22% (0.22)

Margin of error (d) = 5% (0.05)

Women with a history of cesarean section (CS) between 28 and 40 weeks of gestation during any pregnancy in the last

5 years, who had documented discharge records specifying the indication and procedure of the CS, were included after providing informed consent. Exclusion criteria included women with a history of myomectomy prior to CS or CS performed before 28 weeks of gestation. Primary CS was defined as a cesarean section performed on a gravid woman with no prior CS history. Data were collected using a structured proforma through participant interviews and verification of discharge cards. Variables assessed included maternal age at the time of primary CS, socio-economic status (classified as low, middle, or high based on residence ownership and monthly income), gravidity, gestational age (categorized as very preterm: 28–34 weeks, preterm: 34–36 weeks, and term: 37–40 weeks), and the number of antenatal visits (1–3, 4–6, 7–9). The nature of the CS was categorized as either emergency (unplanned due to maternal or fetal risk) or elective (planned before labor), and the healthcare facility was identified as public or private sector. The surgeon's qualification was recorded as either a graduate (MBBS without specialization) or consultant gynecologist (with postgraduate specialization in Obstetrics and Gynecology). The primary outcome was the indication for primary CS, while secondary variables included maternal and obstetric factors. BMI data at the time of surgery could not be included due to the retrospective design. Data were analyzed using SPSS version 26.0, with frequencies and percentages reported for categorical variables, and means with standard deviations for numerical variables. A p -value of ≤ 0.050 was considered statistically significant.

RESULTS

A total of 264 women who had CS for at least one of their pregnancy were considered. The vast majority ($n=252$, 95.45%) was in the age range of 15–35 years. Those having 4–6 antenatal visits ($n=174$, 65.9%) had the maximum chance of CS. Most of them ($n=195$, 73.9%) were primigravida and a large bulk of them (180, 68.2%) had their CS at term. There were more cases ($n=140$; 53%) of emergency CS. A great preponderance ($n=201$; 57.4%) was performed at private clinics/hospitals.

Table 1: Demographics Regarding Primary Caesarean Section ($n=264$)

Variables	Subgroups	Frequency (%) / Mean $\pm$ SD	P-Value
Maternal Age at the Time of Surgery	15–25 Years	125 (47.34)	*0.036
	25–35 Years	127 (48.11)	
	35–45 Years	12 (4.55)	
	Mean $\pm$ SD	26.63 $\pm$ 4.88	
Socio-Economic Status	Low	201 (76.1)	-
	Middle	60 (22.7)	
	High	03 (0.1)	
Number of Antenatal Visits	1–3	52 (19.7)	0.080
	4–6	174 (65.9)	

Gravidity at the Time of CS	7-9	38 (14.4)	*0.030
	Mean $\pm$ SD	5.04 $\pm$ 2.57	
	Primigravida	195 (73.9)	
	Multigravida	69 (26.1)	
Gestational Age	Mean $\pm$ SD	1.27 $\pm$ 0.495	*0.001
	28-34 Weeks	10 (3.7)	
	35-36 Weeks	74 (28.1)	
	37-40 Weeks	180 (68.2)	
Nature of CS	Emergency	140 (53)	*0.001
	Elective	124 (47)	
Designation of Surgeon	Graduate Doctor	114 (43.2)	*0.001
	Consultant Gynecologist	150 (56.8)	
Place of Surgery	Government Hospital	149 (42.5)	*0.001
	Private Hospital	201 (57.4)	

Note: *Indicates Statistically Significant p-Value

Regarding the indications of primary CS, the most prevalent is failed progress of labour, followed by oligohydramnios, breech presentation/transverse lie, fetal distress, reduced fetal movements and maternal request. The other indications included hypertension, failed induction of labour, bad obstetrical history, placenta previa and twin pregnancy.

Table 2: Indications of Primary Caesarean Section (n=264)

Indication of primary CS	Frequency (%)
Failed progress of labour	65 (24.6)
Oligohydramnios	43 (16.3)
Breech presentation/ transverse lie	26 (9.8)
Cephalopelvic disproportion	9 (3.4)
Fetal distress/ meconium	19 (7.2)
Reduced fetal movements	18 (6.8)
Maternal request	17 (6.4)
Hypertension	13 (4.9)
Failed induction of labour	11 (4.2)
Bad obstetrical history	13 (4.9)
Placenta previa	15 (5.7)
Twin pregnancy	15 (5.7)

DISCUSSION

Though the CS is considered a safe mode of delivery for the fetus at institutions where logistics and skill are available, it's not the same at all health facilities where safe conduct of CS along with management of complications is still in jeopardy. Also this mode of confinement has its own implications ranging from short term health issues to increased morbidity and even mortality in some cases [14, 15]. In this study, 264 women who had at least one CS for any of their pregnancy were recruited. Regarding the indications of primary CS, the most frequent is failed progress of labour which was reported by 24.6%. These results are quite close to that reported by Saraya et al.,

(22.5%) in Saudi Arabia [16]. However, this is high when compared with the study conducted by Kanji et al. in Pakistan in 2018, where 12.9% had CS for failed progress of labour [16, 17]. Kanji studied the CS performed at a government hospital. The high rate in this study might be due to the fact that we included all cases whether done at government or private health facility. The failed progress of labour is the favourite indication by the obstetricians of private sector as they opt for early CS for their own convenience and mostly do not fulfill the criteria of failure to progress in labour especially in the light of new labour care guide. Also the overall CS rate is increasing with each passing year. There is need of institutional protocol change to allow sufficient time for slow progress in the first and second stage according to labour care guide. It will definitely reduce the rate of cesarean delivery in nulliparous women. In this study, 43 (16.3%) CS were performed for the indication of oligohydramnios. Kanji et al., found reduced liquor as the indication in 0.4% and Saraya et al., in 0.5% of the cases [16, 17]. The resultant figure in this study is comparatively very high. It can be explained by the fact that 57.4% of these procedures were performed at private hospitals, again reflecting the commercialization of the parturition procedure. Lack of proper antenatal care can also be a contributory factor as improper control of hypertension along with timely non-detection and mismanagement of liquor abnormality can be a reason for this high figure. Also less resort to induction of labour for minor liquor abnormalities can be an explanation, which again is in the hand of obstetrician. Proper counselling along with proper monitoring of labour induction can help in reducing the number of CS for this indication. The next common indication (7.2%) was fetal distress with or without meconium-stained liquor. It is close to that concluded by Idris et al., (5.9 %) [18]. Kanji et al., also reached the same result (8.2%) [17]. Fetal distress proved by abnormal cardiotocography or fetal blood sampling is the most authentic indication of CS. This study revealed that 9.8% had CS for breech presentation. Aftab et al., conducted a study in Pakistan regarding indications of primary CS and found breech presentation as an indication in 4% of the cases [19]. The explanation of higher rate in our study is that the art of breech vaginal delivery is vanishing with the passage of time. The obstetricians of today are not competent for this delivery. Also the fear of litigation in case of any morbidity or mortality hinders the doctors from risk taking attitude. Same applies to twin vaginal delivery as this study cases have this indication in 5.7%. Maternal request accounted for 6.4% of the cases. It approximates that estimated by Trahan MJ (5.4%) [20]. The fear of pain associated with vaginal delivery, the risk of fetal compromise and the fright of pelvic area damage are the myths for this indication of CS. Proper education of antenatal mothers regarding benefits of normal vaginal

delivery can help to narrow down this inciation of CS. Another absolute indication in this study was placenta previa and twin pregnancy with non-cephalic first twin (each 5.7%). Both these indications were counted as 2% by Saraya et al., [16]. The analysis of demographics in the study highlights important trends related to primary CS. There is high proportion of primigravida women undergoing Primary CS (73.9%). This aligns with Birla's study in India, which reported a 65% prevalence of primary CS among primigravida women [21]. Emergency CS at private hospitals were seen outnumbering elective CS at public hospitals. The study suggests that most women attended moderate antenatal care visits. This would have contributed to high CS rate due to lack of proper antenatal education and diagnosis of complications. This study has certain limitations. The retrospective design doubts the authenticity of certain subjective findings like fetal distress and failed progress of labour. As the participants were the patients attending a government hospital for free medical care, so most of them belonged to low socio-economic status. Thus it was not representative of whole population. Also the indications would have been classified according to Robson Ten Group Classification System which is an internationally accepted standard for analyzing and comparing cesarean section rates. This system enhances audit and benchmarking by identifying which groups contribute most to the CS rate, allowing targeted interventions to reduce unnecessary procedures.

This study has certain limitations. The retrospective design doubts the authenticity of certain subjective findings like fetal distress and failed progress of labour. As the participants were the patients attending a government hospital for free medical care, so most of them belonged to low socio-economic status. Thus it was not representative of whole population. Also the indications would have been classified according to Robson Ten Group Classification System which is an internationally accepted standard for analyzing and comparing cesarean section rates. This system enhances audit and benchmarking by identifying which groups contribute most to the CS rate, allowing targeted interventions to reduce unnecessary procedures. Future studies should adopt prospective designs and utilize standardized tools like the Robson Ten Group Classification System for more accurate and generalizable comparisons.

CONCLUSIONS

The primary CS is the most common indication for repeat CS. Considering the high CS rates in the developing nations, like Pakistan, this study contributed to research on maternal health by offering a deeper understanding of the indications of primary CS in the developing world. Regular evaluation of these indications can help ensure appropriate use and avoid unnecessary procedures. Continued audit and adherence to standardized guidelines

are essential to optimize maternal and neonatal outcomes.

Authors' Contribution

Conceptualization: ST

Methodology: FS

Formal analysis: AUT, SAR

Writing and Drafting: ST

Review and Editing: ST, FS, AUT, SAR

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Perceptions of Artificial Intelligence in Medical Education: A Cross-Sectional Study Among Students and Faculty at HBS Medical and Dental College, Islamabad

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ABSTRACT

As artificial intelligence (AI) continues to transform healthcare, its integration into medical education is increasingly critical. However, many institutions lack formal AI curricula, leaving students and faculty underprepared for the digital demands of clinical practice. **Objectives:** To assess awareness, familiarity, perceived benefits, and concerns regarding AI among medical students and faculty, and to explore training preferences and barriers to AI integration in academic settings. **Methods:** A descriptive cross-sectional survey was conducted at HBS Medical and Dental College, with a total of 100 participants (76 students and 24 faculty). A questionnaire assessed demographic characteristics, AI familiarity, perceived benefits and concerns, and interest in formal training. Chi-square tests and logistic regression were used to analyse group differences and predictors of training interest. **Results:** Most participants (60%) were under 25 years old, and 76% were students. While 68% had heard of AI, only 43% reported basic familiarity. Interest in AI training was high (87%). Commonly cited benefits included faster knowledge access and personalized learning, while concerns focused on ethical issues and misinformation. A significant association was found between academic role and perceived lack of training ($p=0.041$). Logistic regression showed a non-significant trend linking prior AI exposure with interest in training ($p=0.125$). **Conclusions:** It was concluded that there is strong enthusiasm for AI in medical education among both students and faculty. However, limited familiarity and perceived barriers highlight the need for structured training and targeted curriculum reforms to build digital competence in future healthcare professionals.

INTRODUCTION

The rapid advancement of artificial intelligence (AI) is revolutionizing healthcare, introducing innovations in diagnostics, therapeutics, and education that were once the domain of science fiction. AI technologies such as image recognition, predictive analytics, natural language processing, and intelligent tutoring systems are now being applied across various healthcare sectors, including radiology, pathology, and surgical planning, to enhance

clinical accuracy and efficiency [1, 2]. AI-based models like DeepMind's diagnostic tools have demonstrated performance comparable to human radiologists in detecting eye disease [3], while chatbots such as ChatGPT are increasingly explored for virtual patient simulation and self-directed learning in medical education [4, 5]. As healthcare becomes more digitally integrated, medical professionals need to understand and ethically engage



with these technologies. However, despite global momentum, the incorporation of AI into undergraduate medical curricula remains inconsistent and underdeveloped. According to recent surveys, fewer than 20% of medical schools globally have formal AI instruction, and the majority of students report inadequate training in digital competencies [6]. The gap is particularly notable in low- and middle-income countries (LMICs), including Pakistan, where infrastructural limitations and lack of faculty readiness present additional barriers [7]. Most prior research has focused on clinical applications of AI or physician attitudes, with limited exploration of how medical students and educators perceive its role in teaching and learning. Moreover, faculty-specific challenges such as resistance to digital tools, concerns over role redundancy, and lack of training opportunities have received minimal attention [8, 9]. In South Asian contexts, cultural and systemic factors further compound the gap in understanding how educators and learners are preparing for an AI-integrated future [10].

To address this knowledge gap, the present study assesses the familiarity, attitudes, perceived benefits, and concerns regarding AI among medical students and faculty at a private institution in Pakistan. This dual-perspective approach enables a nuanced understanding of both learner readiness and institutional barriers. The study also aims to identify interest in AI training as a key outcome variable, to inform future educational strategies and curriculum development tailored to the local context. This study aims to explore the familiarity, attitudes, and concerns related to artificial intelligence in medical education, focusing on both learners and educators. It seeks to bridge the gap between technological innovation and educational readiness, ensuring that future healthcare professionals are equipped not just with clinical skills, but with digital competence as well.

METHODS

This descriptive cross-sectional survey was conducted to examine the challenges and opportunities associated with the use of artificial intelligence (AI) in medical education. The study took place at HBS Medical and Dental College, Islamabad, which offers undergraduate and postgraduate programs in medical and dental sciences. The study was conducted over six months, from March to August 2024, following ethical approval. The Institutional Review Board (IRB) of HBS Medical and Dental College approved the research protocol under Reference No. App#EC02/4. Participation was voluntary, and written informed consent was obtained from all participants. Anonymity and confidentiality were maintained throughout. The target population included both faculty members and students currently affiliated with the institution. Participants were selected through convenience sampling. Inclusion criteria

required participants to be aged 18 years or older, currently enrolled or employed at the institution, and willing to participate. Administrative staff and those with incomplete responses were excluded. The final sample comprised 100 participants, including 76 students and 24 faculty members. This distribution allowed for group-based comparisons. The primary outcome variable for this study was interest in receiving formal AI training, assessed using a binary (Yes/No) response item. The sample size was calculated using the standard formula for estimating a single population proportion: $n = (Z^2 \times p \times (1 - p)) / d^2$. Where: n = required sample size, $Z = 1.96$ (corresponding to 95% confidence level), p = estimated proportion (0.06), based on Civaner et al., [11], who reported 6% of medical students felt confident in communicating AI-related risks to patients and d = desired margin of error (0.05). Thus, the minimum required sample was 87 participants. To allow for potential non-response or incomplete data, the target was increased by approximately 15%, yielding a final sample size of 100 participants. The structured questionnaire used in this study was adapted from previously validated tools, including the needs assessment framework by Civaner et al., [11], titled "Artificial Intelligence in Medical Education: A Cross-Sectional Needs Assessment". The questionnaire consisted of 28 structured items distributed across five key domains: Demographics (4 items): age group, gender, academic role (faculty/student), and prior exposure to AI. Awareness and Familiarity with AI (5 items): including binary questions like "Have you heard about AI?" and multi-level self-reported familiarity (None, Basic, Intermediate, Advanced). Perceived Benefits of AI (5 items): Likert-style and Yes/No questions on benefits such as faster access to knowledge, personalized learning, diagnostic support, engagement, and grading assistance. Concerns Regarding AI (5 items): binary (Yes/No) items assessing ethical dilemmas, misinformation, job replacement, and devaluation of clinical judgment. Training Interest and Perceived Barriers (9 items): questions on preferred learning modes (workshops, online, curriculum-based), interest in formal AI training (primary outcome variable), and barriers such as lack of training, infrastructure, and resistance. The primary outcome variable was interest in formal AI training, measured by a binary item: "Are you interested in receiving formal training in AI applications for medical education?" The questionnaire was reviewed by three experts for content validity and underwent pilot testing with 10 participants (excluded from final analysis). Reliability was assessed using Cronbach's alpha, which yielded a value of 0.81, indicating high internal consistency. To ensure content validity, the questionnaire was reviewed by a panel of three medical education and informatics experts. Their feedback was used to refine language clarity, item relevance, and domain coverage. A pilot test was conducted on 10 participants, and results informed

minor revisions (rewording unclear terms). These pilot responses were excluded from the final data analysis. Internal consistency reliability was assessed using Cronbach's alpha, which yielded a score of 0.81, indicating high reliability of the instrument across domains. Data analysis was performed using IBM SPSS Statistics version 23. Descriptive statistics (frequencies and percentages) summarized participant characteristics and survey responses. Inferential statistics included Chi-square (χ^2) tests to assess associations between academic role (faculty vs. student) and other categorical variables. Cramér's V was used to evaluate effect size. A p-value of <0.05 was considered statistically significant. Binary logistic regression was used to identify predictors of interest in formal AI training. Independent variables included gender, role, AI exposure, familiarity level, awareness of AI, and use of AI tools. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Model fit was assessed using the Hosmer-Lemeshow test and Nagelkerke R^2 . This approach allowed for both group-wise comparisons and multivariate analysis to assess independent predictors of the primary outcome.

RESULTS

The study included 100 participants, with the majority (60%) under 25 years, 31% aged 25–30, and 9% over 30. Females slightly outnumbered males (54% vs. 46%). Most respondents were students (76%), while faculty comprised 24%. Only 30% reported prior exposure to AI tools or concepts, indicating limited hands-on familiarity. The demographic profile shows that younger individuals,

particularly students, formed the bulk of the sample. The near-equal gender distribution and low overall exposure to AI highlight a foundational gap in digital preparedness among future and current medical educators (Table 1).

Table 1: Demographic Characteristics of Participants (n=100)

Variables	Frequency (%)
Age Group	
<25	60 (60.0%)
25–30	31 (31.0%)
>30	9 (9.0%)
Gender	
Female	54 (54.0%)
Male	46 (46.0%)
Role	
Student	76 (76.0%)
Faculty	24 (24.0%)
Previous Exposure to AI	
Yes	30 (30.0%)
No	70 (70.0%)

Study compares faculty and students' awareness and engagement with AI. The proportion of those who had heard about AI was similar across both groups ($p=0.872$), indicating no significant difference in general awareness. When evaluating familiarity levels, students showed greater representation in intermediate and advanced familiarity; however, the difference was not statistically significant ($\chi^2=6.382$, $df=3$, $p=0.094$). Regarding actual use of AI tools such as ChatGPT, faculty and students differed slightly, but the difference was not statistically significant ($p=0.304$) (Table 2).

Table 2: Familiarity with AI by Academic Role (n=100)

Variables		Faculty (n=24)	Student (n=76)	χ^2 (df)	p-Value	Cramér's V
Heard About AI	Yes	16	52	0.026 (1)	0.872	0.016
	No	8	24			
Familiarity Level	Advanced	0	4	6.382 (3)	0.094	0.253
	Intermediate	1	18			
	Basic	13	30			
	Non	10	24			
Use of AI Tools	Yes	13	50	1.057 (1)	0.304	0.103
	No	11	26			

Findings summarise participants' perceptions of AI's potential benefits in medical education. Overall, both faculty and students strongly agreed on the positive impact of AI. The most commonly endorsed benefits were faster access to information, personalized learning, and diagnostic support. However, none of the comparisons between faculty and students reached statistical significance. The closest was in the area of personalized learning, suggesting a trend toward stronger endorsement by faculty, but the difference was not statistically significant ($\chi^2=1.170$, $p=0.279$). These results reflect a shared optimism about AI's value, regardless of academic role. Results explore the concerns expressed by faculty and students regarding AI integration in medical education. While concerns such as ethical dilemmas, misinformation, and the threat to traditional teaching roles were common, no statistically significant differences were found between faculty and students. The concern that came closest to significance was the risk of misinformation, although students expressed slightly higher concern, the difference was not statistically significant ($\chi^2=2.602$, $p=0.107$). The overall similarity in concern levels points to shared anxieties (Table 3).

Table 3: Perceived Benefits and Concerns Regarding AI by Academic Role

Perceived Benefits	Faculty (Yes/No)	Student (Yes/No)	χ^2 (df)	p-Value	Cramér's V
Perceived Benefits					
Faster Knowledge Access	21 / 3	60 / 16	0.867 (1)	0.352	0.093
Personalized Learning	20 / 4	55 / 21	1.170 (1)	0.279	0.108
Enhanced Diagnostics	16 / 8	51 / 25	0.002 (1)	0.968	0.004
Student Engagement	13 / 11	38 / 38	0.127 (1)	0.722	0.036
Grading Assistance	9 / 15	26 / 50	0.087 (1)	0.768	0.029
Concerns Regarding AI in Medical Students					
Ethical Dilemmas	14 / 10	56 / 20	2.047 (1)	0.153	0.143
Threat to Teaching Roles	14 / 10	36 / 40	0.877 (1)	0.349	0.094
Risk of Misinformation	6 / 18	33 / 43	2.602 (1)	0.107	0.161
AI Replacing Teachers	10 / 14	27 / 49	0.295 (1)	0.587	0.054
Devaluation of Clinical Judgement	12 / 12	47 / 29	1.057 (1)	0.304	0.103

Results compare faculty and student perspectives regarding AI training preferences and perceived barriers to integration. A large majority in both groups expressed interest in AI training, but the difference was not statistically significant ($p=0.191$). Most participants preferred workshops or curricular integration over online modules. Among perceived barriers, only "lack of training" showed a significant difference ($\chi^2 = 4.176$, $p=0.041$), with faculty members more frequently citing it as a constraint. Other barriers, including infrastructure limitations and faculty resistance, did not show meaningful differences between groups. These findings suggest a general openness to AI training, with targeted faculty development needed to address capacity gaps (Table 4).

Table 4: AI Integration Preferences and Barriers by Academic Role (n=100)

Variables		Faculty	Student	χ^2 (df)	p-Value	Cramér's V
Interested in Training	Yes	19	68	1.713 (1)	0.191	0.131
	No	5	8			
Preferred Learning Mode	Curriculum	9	20	1.113 (2)	0.573	0.106
	Online	6	23			
	Workshops	9	33			
Lack of Training	Yes	21	50	4.176 (1)	0.041	0.204
	No	3	26			
Limited Infrastructure	Yes	15	44	0.160 (1)	0.689	0.040
	No	9	32			
Faculty Resistance	Yes	7	29	0.640 (1)	0.424	0.080
	No	17	47			

Findings present a logistic regression analysis assessing predictors of interest in formal AI training. Although several variables showed elevated odds, none reached statistical significance ($p>0.05$). Participants with prior AI exposure had higher odds of expressing interest in training (OR=2.80, 95% CI: 0.75–10.47, $p=0.125$). Similarly, those who had heard about AI were more likely to be interested (OR=2.08, $p = 0.361$), though not significantly so. Familiarity level also showed trends: intermediate familiarity was associated with increased interest (OR=3.08, $p=0.187$), while basic familiarity showed decreased odds (OR=0.15, $p=0.168$) compared to those with no familiarity. Gender, academic role, and AI tool usage were not significant predictors. The model demonstrated acceptable fit (Hosmer-Lemeshow $p=0.54$) and explained 12% of the variance in training interest (Nagelkerke $R^2=0.12$) (Table 5).

Table 5: Logistic Regression Predicting Interest in AI Training (n=100)

Predictor Variables	B	OR (Exp B)	95% CI for OR	p-Value
Gender (Male vs Female)	-0.367	0.69	0.16–3.05	0.627
Role (Student vs Faculty)	-1.016	0.36	0.08–1.58	0.177
Previous Exposure to AI	1.030	2.80	0.75–10.47	0.125
Heard About AI	0.730	2.08	0.43–9.92	0.361
Familiarity Level (overall)	—	—	—	0.237

Basic vs None	-1.875	0.15	0.01–2.20	0.168
Intermediate vs None	1.125	3.08	0.58–16.41	0.187
Advanced vs None	0.319	1.38	0.19–9.78	0.750
Use of AI Tools (Yes vs No)	-0.970	0.38	0.10–1.52	0.170
Constant	1.714	5.55	—	0.117

DISCUSSION

This study examined the perceptions, familiarity, and attitudes of medical students and faculty toward artificial intelligence (AI) in medical education. Despite the increasing integration of AI technologies in healthcare, findings indicate limited hands-on experience and moderate familiarity among participants, particularly among faculty members. This trend aligns with previous research highlighting a general awareness of AI but a lack of deep understanding and practical application among educators [12, 13]. While this study revealed most participants reported having heard of AI, the difference in awareness between faculty and students was not statistically significant. Students showed slightly higher self-reported familiarity and usage of tools like Chat-GPT, though these differences were not statistically significant. Comparable results were noted in studies by Buabbas *et al.*, and Sami *et al.*, which highlighted that while students are more open to AI, both groups lack structured training and often use AI informally without institutional guidance [8, 14]. Respondents across roles recognized AI's benefits, including faster access to knowledge, personalized learning, and diagnostic support. These perceptions align with findings from Civaner *et al.*, and Yañez *et al.*, who reported general optimism toward AI integration among learners and educators alike [11, 15]. Nonetheless, the present study, like others, found no statistically significant role-based differences in perceived benefits, which may reflect a shared but superficial engagement with AI's potential. Concerns such as ethical dilemmas, misinformation, and the potential erosion of traditional teaching roles were frequently cited by both groups, with no statistically significant differences observed. This mirrors the observations of Saleh *et al.*, and Abouammoh *et al.*, who documented widespread concern about AI's implications for teaching quality, academic integrity, and professional boundaries [16, 17]. Faculty in particular noted the threat of being replaced or undervalued, a sentiment echoed by Nevárez Montes and Elizondo-Garcia, who emphasized faculty apprehension in integrating generative AI tools into their educational practices [18]. A statistically significant association was found between academic role and perceived lack of training, with faculty more likely to cite this as a barrier. This suggests a need for faculty development programs tailored to digital competencies. Although logistic regression analysis did not identify any statistically significant predictors of interest in formal AI training, participants with prior exposure to AI were nearly three times more likely to show interest. Similar trends were observed by Kong *et al.*, and Yilmaz *et al.*, suggesting that even limited interaction with AI may enhance motivation to pursue structured learning [19, 20]. It is also worth noting that the model explained 12% of the variance in training interest, suggesting other unexplored factors

may contribute. This aligns with findings from Al-Qahtani *et al.*, and Khlaif *et al.*, who underscored the complexity of AI adoption in educational settings and recommended multi-level frameworks for successful integration [21, 22].

The cross-sectional design limits the ability to establish causality, and findings rely on self-reported data, which may introduce response bias. Additionally, the single-institution setting restricts the generalizability of results to other academic environments. Future multicenter studies incorporating objective assessments and intervention-based designs are recommended to better evaluate AI integration in medical education.

CONCLUSIONS

AI is widely recognized as a transformative force in medical education. Our study showed that familiarity, practical use, and structured training remain limited among both students and faculty. There was a clear enthusiasm for AI's potential benefits, but also shared concerns and barriers, particularly the lack of formal training. Structured curriculum development, targeted faculty workshops, and more widespread exposure to practical AI tools may bridge this gap and foster responsible integration of AI in medical education.

Authors' Contribution

Conceptualization: SA

Methodology: SA, RF, KA, SAK

Formal analysis: SA, SS, RF, KA

Writing and Drafting: SS, KA, RS

Review and Editing: SA, SS, RF, KA, RS, SAK

All authors approved the final manuscript and take responsibility for the integrity of the work

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All the authors declare no conflict of interest.

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Original Article



Hepatitis B and C Infections in Pregnant Women Undergoing Chorionic Villus Sampling in Pakistan (2023–2024)

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ABSTRACT

Pregnant women with high viral loads of HBV and HCV are at increased risk of vertical transmission and long-term complications. **Objectives:** To determine the disease burden of hepatitis B and C infections in pregnant women who underwent chorionic villus sampling (CVS). **Methods:** A comparative cross-sectional study was done in MINAR Cancer Hospital, Multan, from January 2023 to June 2024 for eighteen months using a non-probability purposive sampling technique. 1000 pregnant ladies who were scheduled for CVS were included after fulfilling the exclusion and inclusion criteria. Participants were divided into two age groups: 16–25 years and 26–50 years. Blood samples were taken and tested for HBV and HCV infections using commercial kits. The data were recorded and explored using SPSS version 24. **Results:** The participants had an average age of 27.78 ± 4.93 years (range: 16–46 years). HBV DNA was detected in 21 women (2.1%), while 66 (6.6%) tested positive for HCV RNA, leading to a total infection rate of 8.7%. Participants were divided into two age groups: 16–25 years ($n=370$) and 26–50 years ($n=630$). HBV infection rates were 1.6% and 2.38% in younger and older groups, respectively ($P=0.418$), while HCV infection rates were significantly higher in the older group (7.77% vs. 4.59%, $p=0.04$). **Conclusion:** It was concluded that the study highlights a significant prevalence of HBV and HCV infections in pregnant women undergoing CVS, emphasizing the need for routine screening and preventive strategies to reduce vertical transmission.

INTRODUCTION

The hepatitis B (HBV) and hepatitis C virus (HCV) are major global health concerns [1]. Viral hepatitis during pregnancy is commonly caused by HBV and HCV. It can vary from mild or asymptomatic to severe liver damage. The primary worry is the potential for maternal-to-child transmission [2]. Serious side effects from HBV include liver cancer and cirrhosis. Chronic HBV infection can also result in risks for both the mother and fetus [3]. During pregnancy, HCV increases the likelihood of low birth weight, preterm delivery, gestational diabetes, and, in rare cases, stillbirth [4]. Chorionic villus sampling (CVS), a prenatal diagnostic

procedure, may potentially facilitate the transmission of these viruses [5]. Universal HBV screening during pregnancy is widely recommended, with many organizations also advising HCV screening [6]. Tenofovir is the preferred antiviral for managing chronic HBV during pregnancy. Alternatives like Lamivudine and Telbivudine are less commonly used due to concerns about efficacy [1]. HBV and HCV infection in pregnant female has also been examined in female with COVID-19 [7]. A total of 152 studies on HBV prevalence among pregnant women found a global pooled prevalence of 4.8% (3.8–5.8%). The Solomon



Islands had the highest prevalence at 13.6%, while North America had the lowest at 0.6%. Low-income countries had the highest prevalence at 6.6%. HBV prevalence was highest in studies from 2001-2010 (8.7%) and lowest from 2011-2020 (4.8%). The highest prevalence was observed in women aged 21-30 (4.0%). For HCV, 58 studies reported a global prevalence of 1.0%. Sub-Saharan Africa had the highest prevalence at 3.7%, with the highest prevalence among women aged 21-30 (2.2%) [8].

Despite the importance of this issue, there is a paucity of research on hepatitis B and C infections in pregnant women undergoing CVS. The lack of data on the prevalence, transmission dynamics and outcomes of these infections in this population hinders the development of evidence-based guidelines for screening, diagnosis and management in women undergoing CVS. This study aims to illuminate the intersection of Hepatitis B and Hepatitis C and CVS in pregnant women, with the focus on the risks, consequences and potential interventions to enhance the maternal and child health outcomes in this vulnerable population

METHODS

It was a descriptive cross-sectional study done in MINAR Cancer Hospital, Multan, from January 2023 to June 2024 for eighteen months using a non-probability purposive sampling technique. The study was approved by MINAR Cancer Hospital's local ethical committee (Ref.No.M-3(13)/2018). Inclusion criteria were pregnant women who were willing to participate, with ages ranging from 16 to 46 years, undergoing chorionic villus sampling, primigravida and multigravida (upto 3) and singleton pregnancy at gestational age 10-14 weeks, assessed by ultrasound. Women with multiple pregnancies, Women with medical disorders like diabetes, Hypertension, hypothyroidism, Hyperthyroidism, bleeding disorders, history of preterm births, Ischemic heart disease, Valvular heart disease, and Malignancy were precluded from the study. A total of 1000 pregnant ladies were included. The formula used for sample size calculation was $n = Z^2 * p * q / d^2$, where $Z = 1.96$ (95% confidence interval), $p = 0.054$ (5.4% prevalence of hepatitis B in pregnant women presenting in first trimester; taken from previous study) [4]. $q = 1 - p$ and $d = 1.4\%$ (margin of error). Participants were divided into two age groups, 16-25 years and 26-50 years, because of different exposure risks and behaviours. Women in the younger age group might be more likely to have received the vaccination for hepatitis B, which could impact the prevalence rate. Hepatitis B surface antigen (HBs Ag) and Anti-HCV screening samples were collected for patients referred to the Punjab Thalassemia Prevention Program (PTPP) of Nishtar Hospital, Multan, for chorionic villus sampling. Blood samples were taken in K2-EDTA vials. Screening for hepatitis B and hepatitis C was performed through SD (Standard Diagnostics, South Korea) ICT screening kits.

Antigen, antibody, and viral DNA detection by PCR were all part of the hepatitis B confirmatory tests, while antibody and viral RNA identification by PCR were part of the hepatitis C confirmatory tests. The data were recorded and explored using SPSS version 24. Descriptive statistics were used to summarize data. Frequencies and percentages were calculated for categorical variables like maternal age, gestational age at the time of CVS, parity, socio-economic status, level of education, occupation and hepatitis B and C infection in pregnant women undergoing CVS. Mean or median, with respective measures of dispersion, was calculated for quantitative variables like age. Effect modifiers like age, gestational age and parity were controlled by stratification. Post-stratification Chi-square test was applied to see their effect on the outcome. All tests were two-sided and judged statistically significant at $p < 0.05$.

RESULTS

A total of 1000 pregnant women whose ages ranged from 16 to 46 years were included. There were two age groups in the data: 370 female aged 1-25 (Group 1) and 630 female aged 26-50 (Group 2). The mean age of Group 1 was 22.81 ± 1.98 years, and Group 2 was 30.70 ± 3.64 years. Out of 1000 women, 913 (91.3%) were found negative for viral infections (hepatitis B and C virus). 21 (2.1%) were found positive for HBs Ag, and 66 (6.65%) were positive for Anti-HCV. All cases remained positive after ELISA testing for both viruses. In group 1, 6 (1.6%) had hepatitis B, and 17 (4.59%) cases were having hepatitis C. In Group 2, there were 49 (7.77%) Hepatitis C positive cases and 15 (2.38%) Hepatitis B positive cases. All the other socio-demographic variables are mentioned (Table 1).

Table 1: Socio-Demographic Variables among the Participants

Variables	Categories	Group 1	Group 2
Gestational Age at the Time of CVS	10-12 Weeks	75 (20.2%)	195 (30.9%)
	13-14 Weeks	295 (79.8%)	435 (69%)
Parity	<3	16 (4.3%)	188 (29.8%)
	>3	354 (95.7%)	442 (70.2%)
Level of Education	1 st -5 th Standard	284 (76.8%)	295 (46.8%)
	5 th -10 th Standard	49 (13.2%)	300 (47.6%)
	>10 th Standard	37 (10%)	35 (5.6%)
Residential Status	Rural	250 (67.6%)	467 (74.1%)
	Urban	120 (32.4%)	163 (25.9%)
Socioeconomic Status (Monthly Family Income)	<Rs.15,000	208 (56.2%)	267 (42.4%)
	Rs. 15,000-30,000	143 (38.6%)	300 (47.6%)
	>Rs.30,000	19 (5.1%)	63 (10%)

Patients with HBS/HCV aged 16-25 are analyzed (Figure 1).

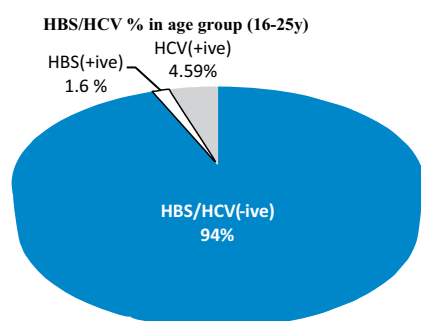


Figure 1: HBV and HCV Infections in Pregnant Women Aged 16-25 Years

Patients with HBS/HCV aged 26-50 are analyzed (Figure 2).

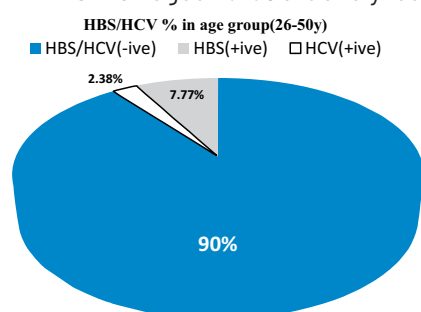


Figure 2: HBV and HCV Infections in Pregnant Women Aged 26-50 Years

There was an increased frequency of hepatitis C in group 2 (7.77%) as compared to Group 1, where the frequency was 4.59%. The frequency of Hepatitis B was also increased in Group 2. The chi-square test was applied, and a comparison of different variables was done. In doing a comparison of the frequency of hepatitis C between both groups, it was found that there was a statistically significant variance ($p=0.040$) while HBV infection did not reveal any significant variance ($p=0.418$) between the two groups (Table 2).

Table 2: HBV and HCV Infections in Pregnant Women Presenting for CVS

Outcomes	Group 1 (16-25 years)	Group 2 (26-50 years)	p-Value
Hepatitis B Positive	6 (1.6%)	15 (2.38%)	0.418
Hepatitis C Positive	17 (4.59%)	49 (7.77%)	0.040

The stratification of the frequency of hepatitis C by demographics is shown. There was a statistically significant variance while comparing the level of education with hepatitis C prevalence between both groups ($p=0.030$) (Table 3)

Table 3: Stratification of Hepatitis C with Regards to Socio-Demographic Variables

Variables	Categories	Hepatitis C	Group 1	Group 2	p-Value
Age Groups	—	Yes	17	49	0.040
		No	353	581	
Parity	<3	Yes	13	116	0.344
		No	3	72	

Level of Education	>3	Yes	208	191	0.135
		No	146	251	
	Matric	Yes	65	8	0.030
		No	219	287	
	Graduation	Yes	3	258	0.336
		No	46	42	
	Masters	Yes	4	1	0.382
		No	33	34	

DISCUSSION

Many researchers have investigated the frequency and risk factors of hepatitis B and C virus infections in pregnant women. This study examined these infections within a more targeted cohort in our research, which included 1,000 pregnant women who had chorionic villus sampling after dividing them into two age groups. The study compared the prevalence of hepatitis B and hepatitis C in both groups. Notably, the study concluded that Hepatitis B and C were more prevalent in older women presenting for CVS. This could be due to increased lifetime exposure in older women and vaccination for hepatitis B in younger female. Furthermore, current study concluded that there was a significant association between education level and hepatitis C frequency, as education may influence awareness about prevention, mode of transmission and early detection. Our findings highlighted the varying prevalence rates of HBV and HCV in pregnant women with different demographics. Present finding has important implications for screening policies among women undergoing CVS. A large-scale study conducted in China analyzed data from over 4 million pregnant women across 20 provinces. The findings revealed that HBV infection was significantly linked to a history of abortion and prior hospitalizations requiring intravenous medication [9]. According to this study, there is an importance of examining both clinical and demographic factors for a better understanding of the transmission dynamics of HBV and HCV in the pregnant population. In Italy, a study tested 6,896 pregnant women for HBV and HCV from 2016 to 2019. The infection rate was higher in foreign women (2.1% for HBs Ag and 0.7% for HCV). Although Italy is among high-income countries, but results are close to our study, possibly because most of the foreign women belong to low or middle-income countries [10]. In another study, where the sample size was close to our study, among 966 pregnant women, 96.7% underwent prenatal HBs Ag screening in the first trimester, with a 2% positive rate, and women over 25 years were at greater risk of HBs Ag positivity, close to our results. All infants born to HBs Ag-positive mothers received the hepatitis B vaccine and hepatitis B immunoglobulin. These findings emphasize the importance of universal HBS Ag screening and standardizing post-exposure prophylaxis to reduce perinatal disease transmission [11]. In a systematic review of 31 studies involving 33,967 pregnant women in Africa.

The pooled prevalence of HBV was reported as 6.77% [12]. This is because most low-income countries are in Africa. There is an urgent need for improved surveillance and targeted interventions in these countries. In Spain, among 21,870 women screened for HBV (prevalence: 0.42%) and 7,659 for HCV (prevalence: 0.26%), lower than our results [13]. A study done among pregnant female in Northern Ethiopia showed that 8.1% of women were HBs Ag positive and 3.2% were anti-HCV positive [14]. In the UK, estimates of chronic hepatitis B prevalence ranged from 0.27% to 0.73%, while more recent data reported ~0.05% prevalence, attributed to under-reporting in vulnerable groups [15]. In the previous literature, researchers looked at how invasive testing performed during pregnancy and delivery affected the likelihood of hepatitis B virus (HBV) transmission from mother to child (MTCT). Amniocentesis is generally considered safe for pregnant women; however, it may raise the risk of MTCT for women with positive HBs Ag status [16]. Moreover, another study showed no risk of MTCT in infants of women undergoing amniocentesis, if infants received standard immunoprophylaxis [17, 18]. No conclusive results have been drawn from data collected from other methods, including intrapartum testing, cordocentesis, or chorionic villus sampling (CVS) [19]. A review of 50 international clinical guidelines revealed a lack of clear recommendations for managing HBV in pregnant women undergoing these procedures, with notable inconsistencies among existing guidelines. This underscores the need for standardized clinical guidance and further research [20].

The study's single-center design and specific cohort (women undergoing CVS) may limit the generalizability of findings to the broader pregnant population. Additionally, potential confounding factors such as vaccination status, prior exposures, and socioeconomic variables were not fully controlled. Future multicenter studies with broader populations and detailed risk factor assessment are needed to better inform screening and prevention strategies for HBV and HCV in pregnancy.

CONCLUSIONS

It was concluded that the study highlights the importance of considering age and education level when screening for viral hepatitis in CVS patients as these factors affect the incidence. The study will raise awareness about regular antenatal screening programs for viral infections specially in women undergoing CVS. It will also contribute to improve public health policies.

Authors' Contribution

Conceptualization: SP

Methodology: SP, BK, AA

Formal analysis: RS

Writing and Drafting: SP, BK, AA, TR, RM

Review and Editing: SP, BK, AA, TR, RS, RM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Causative Organisms and Antimicrobial Sensitivity Pattern in Patients with Urinary Tract Infection

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ABSTRACT

Patterns of pathogens in urinary tract infection (UTI) and antibiotic sensitivity have been scarcely studied in the recent past in local settings. Hence, the study has been planned to address the knowledge gap arising from the non-availability of recent data. **Objectives:** To evaluate the causative organisms and antimicrobial sensitivity patterns in patients with urinary tract infections. **Methods:** This descriptive cross-sectional study was carried out at the Medicine Department of Khyber Teaching Hospital, Peshawar, during the period 1st July 2022 till 31st December 2022. Male and female patients aged 20 to 80 years with culture-proven urinary tract infections were enrolled. Pathogens isolated were noted their sensitivity to antibiotics was assessed. Data were analyzed using SPSS version 26.0. **Results:** The majority of study participants were aged more than 50 years (n=92, 51.4%). 109 patients (60.9%) were male, and 85 patients (47.5%) were diabetic. 89 patients (49.7%) were enrolled from the Outpatient Department. The most common pathogen was E coli, recorded in 48 patients (26.8%). Isolates in 154 (86.0%) out of 179 participants were susceptible to nitrofurantoin, followed by meropenem in 151 (84.3%). **Conclusions:** It was concluded that people of all ages can be affected by urinary tract infection. The most common bacterial cause of UTI is E coli. Nitrofurantoin and meropenem are the most effective antibiotics against uropathogens.

INTRODUCTION

Urinary tract infections (UTI) range in clinical manifestation from subclinical to catastrophic sepsis, are among the most prevalent bacterial infections in regular healthcare settings [1]. UTIs rank second in terms of hospitalizations and are among the leading causes of illness in people of all ages [2]. In numerous medical facilities, it serves as an extremely prevalent nosocomial illness, accounting for around 35% of all infections contracted in hospitals [3]. This expense has a major negative influence on people's financial lives and contributes significantly to the usage of antibacterial medications [4]. A novel category of infectious diseases caused by resistance to medication

was once more exemplified by the microbes that continued to transmit diseases despite the use of these more recent antibiotics [5]. As a result of their novel genetic changes, bacteria are expected to ultimately acquire greater resistance. A variety of pathogens have been isolated, leading to UTIs in both the community and hospitals. The majority of them constitute the normal flora of the human gut, making it simple to colonize the urinary system. The majority of community-acquired UTIs are mild, optimally occupying the bladder and leading to cystitis [6]. Microbial resistance to medications is a major problem in the management of infectious illnesses worldwide. The



improper application of antibiotics in medical care has led to an increase in microbial resistance [7]. The ensuing proliferation of bacterial resistant strains is a serious healthcare concern. The risk of severity is decreased by early UTI therapy, indicating that empirical antibiotic prescription is usually given. Providing an efficient empirical regimen requires knowledge of the main bacteria frequently linked to urinary tract infections and their distinctive forms of antibiotic resistance [8]. This procedure makes it possible to restrict the spread of resistant bacterial strains and the worldwide public health concern of antibiotic resistance [9]. Updated knowledge about the pattern of pathogens and antibiotic sensitivity is vital for improved outcomes without increasing the risk of antibiotic resistance. In a study by Gul et al., the most frequent symptoms included fever, loin discomfort, and uneasiness brought on by pain. *E. coli* accounted for 65.1% of all isolated organisms, with *E. fecalis* coming in second (20.8%). Vancomycin, Amikacin, Nitrofurantoin, and imipenim had strong sensitivity in terms of sensitivity pattern, but Ceftriaxone and Ampicillin displayed the highest resistance [10]. In another study by Anwar et al., *E. Coli* was the most common cause of UTIs (40.6%), followed by *Actinobacter* spp, *Staph aureus*, *Klebsiella* spp and *Enterococcus* spp. Ceftriaxone, moxifloxacin, ampicillin and cefazolin were most effective against *E. coli*. Other sensitive antibiotics included sulzone, fosfomycin and imipenim group [11].

The spectrum of bacterial pathogens and antibiotic sensitivity in patients with urinary tract infection is very broad. Moreover, the pattern of pathogens and antibiotic sensitivity has seldom been studied in the recent past in local settings. Hence, the study has been planned to address the knowledge gap arising from the non-availability of recent data. Moreover, the study would provide useful information regarding the bacterial agent's patterns and trends in antibiotic sensitivity among patients with urinary tract infections. The study aims to evaluate the causative organisms and antimicrobial sensitivity patterns in patients with urinary tract infections.

METHODS

This descriptive cross-sectional study was carried out at the Department of Medicine, Khyber Teaching Hospital, Peshawar, during the period 1st July 2022 till 31st December 2022, after taking approval from the hospital IRB vide no: 36/DME/KMC. Male and female patients in the age range of 20 to 80 years diagnosed with urinary tract infection were enrolled. Patients with a history of antibiotic intake in the last 4 weeks, immune-compromised patients, and patients with KUB stones, chronic kidney disease on ultrasound, catheterized patients and pregnant females were excluded. Urinary tract infection was defined when the patient was complaining of fever (body temperature

>38.0°C on thermometer) and urine R/E showing more than 10 pus cells/mm³ or more than 5 red cells/mm³. Bacterial pathogens were broadly classified as gram-negative pathogens, including *E. coli*, *Proteus*, *P. aeruginosa* and *Klebsiella*, and gram-positive pathogens included *Staphylococcus* species, *Enterococci* and *Streptococcus* species. Antibiotic spectrum included Penicillins, cephalosporins, macrolides, fluoroquinolones and nitrofurantoin. Antibiotic sensitivity was assessed using the minimum inhibitory concentration (MIC) test. Antibiotics were said to be sensitive when MIC inhibit the growth of pathogens, and failure to inhibit the growth of pathogens was called resistance. The sample size was 179, calculated using an anticipated value for *E. coli* as the cause of UTI=65.1%, margin of error=7% and confidence level=95% [10]. Participants were enrolled using a non-probability convenience sampling method. Informed consent was obtained from patients satisfying selection criteria and willing to participate in the study. Participants were enrolled from the indoor and out departments. Baseline characteristics like age, gender, BMI, duration of fever (days), comorbidities like diabetes and hypertension, residence, education, profession and SE status were noted. A 10cc mid-urine sample was collected in an air-tight plastic container. The sample was sent to the hospital lab for culture and sensitivity. Culture was grown using various media. Any growth was recorded. The organisms were exposed to various antibiotics at various amounts, and inhibition/non-inhibition of colony growth in the culture was noted to record the sensitivity pattern of antibiotics. Data were recorded and analyzed using SPSS version 26.0. Means $\pm$ SD were recorded for continuous data, and frequencies and percentages were recorded for categorical data. Bacterial pathogens and patterns of antibiotic sensitivity were recorded. Contingency table analysis was carried out between pathogens and antibiotic sensitivity. Bacterial pathogens were stratified by various clinic-demographic parameters to control for effect modifiers. Post-stratification chi-square test was applied at a 5% level of significance.

RESULTS

The mean age of the participants was 49.93 ± 16.03 years, the mean BMI was 23.941 ± 1.702 kg/m², and the mean complaints duration was 8.043 ± 1.480 days. The majority of study participants were aged more than 50 years (n=92, 51.4%). 109 patients (60.9%) were male, and 85 patients (47.5%) were diabetic. 89 patients (49.7%) were enrolled from the Outpatient Department (Table 1).

Table 1: Descriptive Statistics and Baseline Features of the Study Cohort (n=179)

Parameters	Subgroups	Frequency (%)
Age (Years)	50 or Below	87 (48.6%)
	Above 50	92 (51.4%)
BMI (kg/m ²)	24.0 or Below	101 (56.4%)
	More Than 24.0	78 (43.6%)
Gender	Male	109 (60.9%)
	Female	70 (39.1%)
Diabetes	Yes	85 (47.5%)
	No	94 (52.5%)
Disease Duration (Days)	7 Or Below	48 (26.8%)
	More Than 7	131 (73.2%)
Department	IPD	90 (50.3%)
	OPD	89 (49.7%)

The most common pathogen was E coli, recorded in 48 patients (26.8%), and the least common isolated pathogen was S aureus (n=9, 5.0%) (Table 2).

Table 3: Susceptibility Pattern of Pathogens to Various Antibiotics (n=179)

Antibiotics		Pathogens							Total
		E coli	Proteus	Pseudomonas	Klebsiella	Strep	Enterococci	Staph	
Ampicillin	S	28 (29.8%)	16 (17.0%)	23 (24.5%)	11 (11.7%)	8 (8.5%)	5 (5.3%)	3 (3.2%)	94 (100.0%)
	R	20 (23.5%)	17 (20.0%)	11 (12.9%)	19 (22.4%)	7 (8.2%)	5 (5.9%)	6 (7.1%)	85 (100.0%)
Amikacin	S	29 (25.0%)	24 (20.7%)	26 (22.4%)	21 (18.1%)	6 (5.2%)	4 (3.4%)	6 (5.2%)	116 (100.0%)
	R	19 (30.2%)	9 (14.3%)	8 (12.7%)	9 (14.3%)	9 (14.3%)	6 (9.5%)	3 (4.8%)	63 (100.0%)
Ceftriaxone	S	35 (28.2%)	22 (17.7%)	24 (19.4%)	21 (16.9%)	10 (8.1%)	5 (4.0%)	7 (5.6%)	124 (100.0%)
	R	13 (23.6%)	11 (20.0%)	10 (18.2%)	9 (16.4%)	5 (9.1%)	5 (9.1%)	2 (3.6%)	55 (100.0%)
Cefixime	S	26 (23.4%)	24 (21.6%)	21 (18.9%)	21 (18.9%)	9 (8.1%)	5 (4.5%)	5 (4.5%)	111 (100.0%)
	R	22 (32.4%)	9 (13.2%)	13 (19.1%)	9 (13.2%)	6 (8.8%)	5 (7.4%)	4 (5.9%)	68 (100.0%)
Cotrimoxazole	S	26 (31.7%)	9 (11.0%)	17 (20.7%)	14 (17.1%)	8 (9.8%)	6 (7.3%)	2 (2.4%)	82 (100.0%)
	R	22 (22.7%)	24 (24.7%)	17 (17.5%)	16 (16.5%)	7 (7.2%)	4 (4.1%)	7 (7.2%)	97 (100.0%)
Clindamycin	S	25 (27.2%)	22 (23.9%)	12 (93.0%)	15 (16.3%)	8 (8.7%)	6 (6.5%)	4 (4.3%)	92 (100.0%)
	R	23 (26.4%)	11 (12.6%)	22 (25.3%)	15 (17.2%)	7 (8.0%)	4 (4.6%)	5 (5.7%)	87 (100.0%)
Cloxacillin	S	29 (24.8%)	26 (22.2%)	18 (15.4%)	20 (17.1%)	12 (10.3%)	6 (5.1%)	6 (5.1%)	117 (100.0%)
	R	19 (30.6%)	7 (11.3%)	16 (25.8%)	10 (16.1%)	3 (4.8%)	4 (6.5%)	3 (4.8%)	62 (100.0%)
Erythromycin	S	24 (23.8%)	22 (21.8%)	17 (16.8%)	17 (16.8%)	10 (9.9%)	7 (6.9%)	4 (4.0%)	101 (100.0%)
	R	24 (30.8%)	11 (14.1%)	17 (21.8%)	13 (16.7%)	5 (6.4%)	3 (3.8%)	5 (6.4%)	78 (100.0%)
Meropenem	S	39 (25.8%)	28 (18.5%)	30 (19.9%)	26 (17.2%)	14 (9.3%)	7 (4.6%)	7 (4.6%)	151 (100.0%)
	R	9 (32.1%)	5 (17.9%)	4 (14.3%)	4 (14.3%)	1 (3.6%)	3 (10.7%)	2 (7.1%)	28 (100.0%)
Ofloxacin	S	28 (26.9%)	15 (14.4%)	23 (22.1%)	20 (19.2%)	10 (9.6%)	4 (3.8%)	4 (3.8%)	104 (100.0%)
	R	20 (26.7%)	18 (24.0%)	11 (14.7%)	10 (13.3%)	5 (6.7%)	6 (8.0%)	5 (6.7%)	75 (100.0%)
Ciprofloxacin	S	25 (30.5%)	10 (12.2%)	15 (18.3%)	16 (19.5%)	7 (8.5%)	6 (7.3%)	3 (3.7%)	82 (100.0%)
	R	23 (23.7%)	23 (23.7%)	19 (19.6%)	14 (14.4%)	8 (8.2%)	4 (4.1%)	6 (6.2%)	97 (100.0%)
Nitrofurantoin	S	40 (26.0%)	28 (18.2%)	28 (18.2%)	28 (18.2%)	15 (9.7%)	7 (4.5%)	8 (5.2%)	154 (100.0%)
	R	8 (32.0%)	5 (20.0%)	6 (24.0%)	2 (8.0%)	0 (0.0%)	3 (12.0%)	1 (4.0%)	25 (100.0%)

S=sensitive, R=resistant

No statistically significant association was observed between pathogens and baseline parameters (p>0.05) (Table 4).

Table 2: Various Pathogens Isolated in the Study Cohort (n=179)

Pathogens	Frequency (%)
E coli	48 (26.8%)
Proteus	33 (18.4%)
Pseudomonas	34 (19.0%)
Klebsiella	30 (16.8%)
Strep	15 (8.4%)
Enterococci	10 (5.6%)
Staph	9 (5.0%)

Isolates in 154 (86.0%) out of 179 participants were susceptible to nitrofurantoin followed by meropenem in 151 (84.3%), ceftriaxone (69.2%) and amikacin in 116 (64.8%) respectively (Table 3).

Table 4: Stratification of Pathogens with Various Clinic-Demographic Parameters (n=179)

Variables		Pathogens							Total	p-value
		E coli	Proteus	Pseudomonas	Klebsiella	Strep	Enterococci	Staph		
Age (Years)	≤50	20 (23.0%)	18 (20.7%)	16 (18.4%)	17 (19.5%)	7 (8.0%)	3 (3.4%)	6 (6.9%)	87 (100.0%)	0.571
	>50	28 (30.4%)	15 (16.3%)	18 (19.6%)	13 (14.1%)	8 (8.7%)	7 (7.6%)	3 (3.3%)	92 (100.0%)	
BMI (kg/m ²)	≤24.0	28 (27.7%)	19 (18.8%)	20 (19.8%)	15 (14.9%)	9 (8.9%)	7 (6.9%)	3 (3.0%)	101 (100.0%)	0.750
	>24.0	20 (25.6%)	14 (17.9%)	14 (17.9%)	15 (19.2%)	6 (7.7%)	3 (3.8%)	6 (7.7%)	78 (100.0%)	
Gender	M	30 (27.5%)	19 (17.4%)	22 (20.2%)	20 (18.3%)	8 (7.3%)	7 (6.4%)	3 (2.8%)	109 (100.0%)	0.621
	F	18 (25.7%)	14 (20.0%)	12 (17.1%)	10 (14.3%)	7 (10.0%)	3 (4.3%)	6 (8.6%)	70 (100.0%)	
DM	Yes	24 (28.2%)	11 (12.9%)	17 (20.0%)	15 (17.6%)	6 (7.1%)	7 (8.2%)	5 (5.9%)	85 (100.0%)	0.477
	NO	24 (25.5%)	22 (23.4%)	17 (18.1%)	15 (16.0%)	9 (9.6%)	3 (3.2%)	4 (4.3%)	94 (100.0%)	
Complaint Duration (Days)	Yes	11 (22.9%)	11 (22.9%)	11 (22.9%)	8 (16.7%)	6 (12.5%)	1 (2.1%)	0 (0.0%)	48 (100.0%)	0.262
	NO	37 (28.2%)	22 (16.8%)	23 (17.6%)	22 (16.8%)	9 (6.9%)	9 (6.9%)	9 (6.9%)	131 (100.0%)	
Department	IPD	25 (27.8%)	18 (20.0%)	16 (17.8%)	13 (14.4%)	9 (10.0%)	6 (6.7%)	3 (3.3%)	90 (100.0%)	0.809
	OPD	23 (25.8%)	15 (16.9%)	18 (20.2%)	17 (19.1%)	6 (6.7%)	4 (4.5%)	6 (6.7%)	89 (100.0%)	

DISCUSSION

The mean age of the participants was 49.93 ± 16.03 years. The majority of study participants were aged more than 50 years (n=92, 51.4%). 109 patients (60.9%) were male, and 85 patients (47.5%) were diabetic. 89 patients (49.7%) were enrolled from the Outpatient Department. The most common pathogen was E coli, recorded in 48 patients (26.8%), and the least common isolated pathogen was S aureus (n=9, 5.0%). Nitrofurantoin was the most effective. Isolates in 154 (86.0%) out of 179 participants were susceptible to nitrofurantoin, followed by meropenem in 151 (84.3%), ceftriaxone (69.2%) and amikacin in 116 (64.8%), respectively. The majority of isolates in this study were obtained from male patients. Isolation rate concerning gender was statistically insignificant in a study by Patel *et al.*, which was in contrast to our findings [12]. A higher proportion of female patients was reported in other studies, including George *et al.*, and Singhal *et al.*, [13, 14]. Our study results are, however, similar to those reported by Mehboob *et al.*, where 57.0% of the study cohort comprised male patients [15]. This difference in the results may be explained by the fact that female patients tend to seek treatment at the loco-regional level and seldom report to tertiary care centers like ours due to socio-cultural and financial reasons. Moreover, time-consuming tests such as culture are not preferred on the part of the patient, particularly female, owing to the delay in result availability and delayed initiation of treatment. The most common isolate from our study cohort was E coli, followed by Pseudomonas, Proteus and Klebsiella. Staph group and enterococci constituted the least commonly retrieved pathogens. The bacterial spectrum in isolates in Patel *et al.*, in descending order, was E coli, Candida and Klebsiella [12]. Bhargava *et al.*, reported E coli as the most common pathogen, followed by Proteus, Klebsiella and Pseudomonas [16]. In another study by Al-Awkally *et al.*, E coli was the most common causative agent of urinary tract infection in their study participants, and Enterococci and

Staphylococcus species were the least prevalent uropathogens [17]. Mehboob *et al.*, and Said *et al.*, reported similar findings concerning the distribution of uropathogens [15, 18]. Our results are in agreement with these studies' findings. E coli accounts for more than three-fourths of all urinary tract infections globally and more than 50.0% of complicated infections requiring hospitalization. The higher incidence of E coli-related UTIs may be because of the increased pathogenicity of E coli and increased susceptibility of urinary tract mucosa towards invasion by E coli [19]. Nitrofurantoin was the most effective antibiotic against uropathogens isolated from our study participants, followed by meropenem and third-generation cephalosporins. The least susceptibility was observed towards older antibiotics such as ampicillin. Ciprofloxacin susceptibility was disappointing. Girma *et al.*, reported nitrofurantoin as the most effective antibiotic in urinary tract infections in their study. Ceftriaxone and norfloxacin were shown to have adequate sensitivity [20]. Lowest resistance to nitrofurantoin and ceftriaxone was reported in a study by Majumder *et al.*, [21]. In studies by Patel *et al.*, AND Adugna N *et al.*, 100% susceptibility was observed with meropenem [12, 22]. Nitrofurantoin was shown to be slightly inferior to meropenem in a study by Bhargava *et al.*, [16]. In a study by Madeeha *et al.*, nitrofurantoin and meropenem were the most effective antibiotics against uropathogens obtained in the culture isolate [15]. Ciprofloxacin though routinely and most often empirically prescribed in urinary tract infections, but resistance is now increasingly reported, as evident from this study and the results of the study by Said *et al.*, [18]. Increased resistance to ciprofloxacin was reported by Girma A *et al.*, urinary tract infections [20]. Fluoroquinolones like ciprofloxacin, once effective in UTI, have had their efficacy reduced over the years. It may be because of the rampant and empirical administration of ciprofloxacin in various infections. Overall, the study provided valuable insights into microbial

trends and sensitivity patterns in patients with urinary tract infections.

This was a single-center study with a relatively limited sample size, which may restrict the generalizability of the findings. Additionally, potential selection bias and lack of detailed data on prior antibiotic use could have influenced the observed resistance patterns. Multicenter studies with larger cohorts and inclusion of antibiotic usage history are recommended to better understand evolving resistance trends and guide empirical therapy.

CONCLUSIONS

It was concluded that people of all ages can be affected by urinary tract infection; however, elderly male patients are more frequently affected. The most common pathogen leading to urinary tract infection isolated in culture is *E. coli*. Currently, nitrofurantoin and meropenem are the most effective antibiotics against uropathogens. Sensitivity pattern of antibiotics and pathogen distribution is not affected by patient baseline clinic-demographic parameters.

Authors' Contribution

Conceptualization: MZ

Methodology: MZ, SA, FA, RG

Formal analysis: MZ

Writing and Drafting: MZ, SA, NI, FA, SN

Review and Editing: MZ, SA, NI, FA, SN, RG

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Investigating Motorcycle Accident Risk Factors among Educated Riders: Associations with Driver Behaviour, Road Conditions, and Vehicle Safety Concerns

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ABSTRACT

Motorcycle accidents pose a significant threat to public health and often present as serious medicolegal challenges, particularly in developing countries. **Objectives:** To identify and analyze key risk factors, over speeding, poor driving sense, lighting defects, and mirror faults, associated with motorcycle accidents among an educated population comprising students and faculty. Also, to explore the association of these factors with demographic characteristics and varying road conditions. **Methods:** A cross-sectional study was conducted using a self-administered questionnaire to gather data on participants' demographics, motorcycle usage patterns, self-reported safety concerns, and perceived road hazards. Chi-square tests were used to assess associations between variables. **Results:** Over-speeding emerged as the most frequently reported safety concern, especially among younger riders and during peak traffic hours. Although notable trends were observed across different age groups, professions, and road conditions, none of the associations reached statistical significance ($p > 0.05$). **Conclusions:** It was concluded that although over-speeding was consistently reported as the most frequent safety concern among students and faculty, statistical analysis revealed no significant associations between reported concerns and demographic or road condition variables. These findings suggest that motorcycle safety risks are broadly distributed across rider categories. Institutional interventions such as safety awareness programs, infrastructure improvements, and strict enforcement of traffic laws may still be beneficial in promoting safer riding practices within the academic community.

INTRODUCTION

Motorcycle accidents represent a growing public health concern, particularly in developing countries where rapid urbanization and inadequate traffic infrastructure contribute to increased road risk [1]. These accidents account for a significant proportion of trauma-related injuries and deaths, especially among young, economically active males [2]. When such incidents are brought before legal authorities, they often involve complex medicolegal

consequences and prolonged court proceedings [3]. In countries like Pakistan, motorcycles are one of the most common modes of transport due to their affordability and convenience [4]. However, riders often operate in high-risk environments with limited protective measures, weak enforcement of traffic laws, and poor road conditions. This makes motorcyclists more vulnerable to accidents compared to users of other transportation modes [5, 6].



While various studies have explored factors such as helmet use, alcohol consumption, and collision mechanics in the general population, limited attention has been given to risk behaviours and perceptions among educated individuals, university students and academic staff who are assumed to have better awareness yet still engage in unsafe practices[7-9].

This study aims to address this gap by investigating the relationship between driver characteristics (age, gender, marital status, and literacy level) and specific problems encountered by students and faculty while riding motorcycles, including over-speeding, poor driving sense, and issues with lights or mirrors. It also explores the association between various road conditions (peak hours, traffic jams, routine hours, and low visibility) and the type of safety concerns reported by motorcyclists.

METHODS

This cross-sectional study was conducted to investigate the factors contributing to motorcycle accidents among students and faculty members of Sahara Medical College, Narowal, from 6th June 2021 to 6th November 2021. The study aimed to explore the association between driver characteristics, road conditions, and reported motorcycle safety concerns within this academic population. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Sahara Medical College under reference number No. 83/FMT/SMC. The approved study period extended from 06 June 2021 to 06 November 2021. The study was conducted by ethical guidelines, ensuring informed consent, voluntary participation, and confidentiality of all participants. The target population included all male students and faculty members of Sahara Medical College. A convenience sampling technique was employed to recruit participants who were accessible and willing to participate. The inclusion criteria specified participants aged 18 years or older, who used motorcycles as their primary mode of commuting and voluntarily provided informed consent. Exclusion criteria included female individuals, minors (under 18 years), non-motorcycle users, and those unwilling to consent. The final sample comprised 250 participants, including 123 MBBS students, 80 Allied Health Sciences students (from disciplines such as Pharmacy, Medical Lab Technology, Information Technology, Microbiology, and Biotechnology), and 47 faculty members. The sample size was determined using a 95% confidence level and a 5% margin of error to ensure statistical representativeness. Data were collected using a self-administered questionnaire distributed in both print and digital formats. Printed copies were made available in classrooms, department offices, and faculty lounges. The questionnaire gathered information on four key areas: (1) demographic characteristics (age, marital status, profession), (2) motorcycle riding habits (frequency

of riding, safety practices), (3) driving experiences (problems encountered while riding), and (4) perceptions of road conditions (traffic congestion, visibility issues, infrastructure). To ensure anonymity, all responses were de-identified before analysis. Data were entered and analyzed using SPSS version 22. Descriptive statistics were used to summarize participant characteristics and response frequencies. Chi-square tests were applied to evaluate associations between driver characteristics, road conditions, and reported motorcycle safety concerns. A p-value of <0.05 was considered statistically significant.

RESULTS

The majority of participants aged 18-25 and 26-32 years identified over-speeding as their primary concern (53.6% and 55.4%, respectively). Older age groups, particularly those above 46 years, showed a broader distribution across issues, including driving sense (32.4%), lighting problems (13.5%), and mirror faults (16.2%). Notably, the youngest group (18-25 years) reported the lowest concern for driving sense, reinforcing the idea that younger riders may underestimate behavioural factors. However, the chi-square test result ($\chi^2=13.432$, Degrees of Freedom (df)=12, $p=0.338$) suggests no statistically significant relationship between age and safety concerns. Single participants more frequently reported over-speeding (52.1%) and driving sense (30.3%) issues compared to married individuals (48.2% and 24.7%, respectively). Interestingly, married riders expressed greater concern for mirror faults (11.8%), more than double the percentage among singles (4.2%). Despite these differences, the chi-square result ($\chi^2=5.608$, $df=3$, $p=0.132$) indicates that the association is not statistically significant. The findings may still hint at subtle behavioural distinctions based on marital responsibility or maturity, even if not statistically proven (Table 1).

Table 1: Association Between Age Group, Marital Status, and Reported Motorcycle Safety Concerns (n=250)

Groups	Over Speeding	Driving Sense	Front/Back Lights	Side Mirror	Total	Pearson Chi-Square Value	df	p-value
Age								
18–25 Years	59 (53.6%)	27 (24.5%)	19 (17.3%)	5 (4.5%)	110	13.432	12	0.338
26–32 Years	36 (55.4%)	19 (29.2%)	6 (9.2%)	4 (6.2%)	65			
33–39 Years	2 (40.0%)	2 (40.0%)	0 (0.0%)	1 (20.0%)	5			
40–46 Years	16 (48.5%)	11 (33.3%)	5 (15.2%)	1 (3.0%)	33			
Above 46 Years	14 (37.8%)	12 (32.4%)	5 (13.5%)	6 (16.2%)	37			
Total	127 (50.8%)	71 (28.4%)	35 (14.0%)	17 (6.8%)	250			
Marital Status								
Single	86 (52.1%)	50 (30.3%)	22 (13.3%)	7 (4.2%)	165	5.608	3	0.132
Married	41 (48.2%)	21 (24.7%)	13 (15.3%)	10 (11.8%)	85			
Total	127 (50.8%)	71 (28.4%)	35 (14.0%)	17 (6.8%)	250			

Among MBBS students, over-speeding was the most reported issue (52.8%), while AHS students exhibited a comparatively higher concern for driving sense (36.3%), indicating more emphasis on behavioural risks. Faculty members displayed a similar trend to students, with over-speeding leading (51.1%), but also a noticeable concern for mirror and lighting issues. Despite visible distribution differences, the chi-square result ($\chi^2=5.690$, $df=6$, $p=0.459$) implies no significant statistical relationship between profession and the type of safety concern reported (Table 2).

Table 2: Association Between Profession and Reported Motorcycle Safety Concerns (n=250)

Professions	Over Speeding	Driving Sense	Front/Back Lights	Side Mirror	Total	Pearson Chi-Square Value	df	p-value
MBBS Students	65 (52.8%)	28 (22.8%)	21 (17.1%)	9 (7.3%)	123	5.690	6	0.459
AHS Students	38 (47.5%)	29 (36.3%)	9 (11.3%)	4 (5.0%)	80			
Faculty Members	24 (51.1%)	14 (29.8%)	5 (10.6%)	4 (8.5%)	47			
Total	127 (50.8%)	71 (28.4%)	35 (14.0%)	17 (6.8%)	250			

Over-speeding was the most frequently cited issue across all road conditions, particularly under low visibility (67.9%) and peak hours (51.1%), highlighting the dangers of fast riding when visibility or traffic density is poor. Routine hours showed a relatively even concern for various issues. Although these patterns are meaningful from a public safety standpoint, the statistical analysis ($\chi^2=11.125$, $df=12$, $p=0.518$) showed no significant association. However, the data still reinforces the importance of improving behaviour during high-risk road conditions like traffic congestion or smog (Table 3).

Table 3: Association Between Road Conditions and Reported Motorcycle Safety Concerns (n=250)

Road Condition	Over Speeding	Driving Sense	Front/Back Lights	Side Mirror	Total	Pearson Chi-Square Value	df	p-value
Peak Hours	67 (51.1%)	39 (29.8%)	16 (12.2%)	9 (6.9%)	131	11.125	12	0.518
Traffic Jams	21 (41.2%)	18 (35.3%)	10 (19.6%)	2 (3.9%)	51			
Routine Hours	4 (44.4%)	3 (33.3%)	2 (22.2%)	0 (0.0%)	9			
Low Visibility	19 (67.9%)	4 (14.3%)	2 (7.1%)	3 (10.7%)	28			
Other Causes	16 (51.6%)	7 (22.6%)	5 (16.1%)	3 (9.7%)	31			
Total	127 (50.8%)	71 (28.4%)	35 (14.0%)	17 (6.8%)	250			

The highest rate of over-speeding (73.3%) was reported in accidents caused by animal crossings, likely due to sudden, unpredictable road events. In contrast, collision-related accidents showed a more balanced distribution with concerns for lighting (15.6%) and mirrors (7.8%). Riders involved in slip/skid and overturn incidents also emphasized over-speeding and driving sense, but with varied percentages. Despite these variations, the chi-square value ($\chi^2=7.658$, $df=9$, $p=0.569$) suggests that the type of accident does not significantly influence the specific safety concern identified (Table 4).

Table 4: Association Between Accident Type and Reported Motorcycle Safety Concerns (n=250)

Type of Accident	Over Speeding	Driving Sense	Lighting Issues	Mirror Fault	Total	Pearson Chi-Square Value	df	p-value
Collision	70 (49.6%)	38 (27.0%)	22 (15.6%)	11 (7.8%)	141	7.658	9	0.569
Slip/Skid	31 (47.0%)	21 (31.8%)	10 (15.2%)	4 (6.1%)	66			
Overturn	15 (53.6%)	10 (35.7%)	1 (3.6%)	2 (7.1%)	28			

Animal Crossing	11(73.3%)	2(13.3%)	2(13.3%)	0(0.0%)	15			
Total	127(50.8%)	71(28.4%)	35(14.0%)	17(6.8%)	250			

Over-speeding is the most dominant safety concern across all age groups, with the highest frequency reported among riders aged 18–25 years ($n=59$) and 26–32 years ($n=36$). This trend aligns with earlier findings that younger riders tend to exhibit more aggressive riding behaviour and risk-taking tendencies. As age increases, concern shifts gradually toward driving sense, particularly in the above 46 years' group, where 12 participants reported it as a primary issue. Equipment-related concerns lighting problems and mirror faults were less commonly reported but more prominent in older groups than younger ones, possibly due to increased attention to safety with age. Notably, mirror issues were least reported overall, except in the above 46 group, suggesting a general lack of emphasis on visual safety aids among younger riders. These patterns underscore the importance of age-specific road safety education, particularly targeting youth with behaviour-focused interventions to mitigate over-speeding risks (Figure 1).

Distribution of Reported Motorcycle Safety Concerns by Age Group

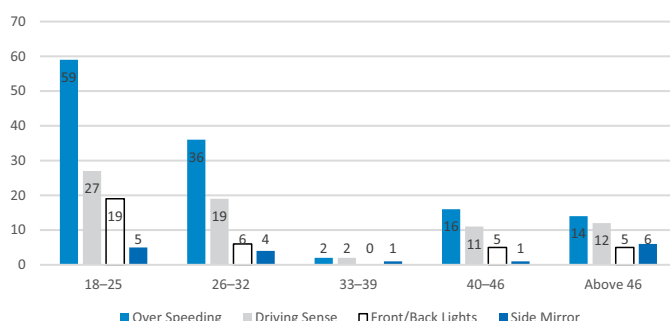


Figure 1: Distribution of Reported Motorcycle Safety Concerns by Age Group ($n=250$)

This bar chart presents the frequency of self-reported motorcycle safety concerns, such as over speeding, poor driving sense, front/backlighting issues, and side mirror faults, among different age groups of participants. The 18–25 and 26–32-year groups reported the highest rates of over speeding, while older age groups (40 and above) expressed relatively higher concern regarding driving sense and mirror-related issues.

DISCUSSION

This study explored key risk factors contributing to motorcycle accidents among an educated population, specifically students and faculty members of Sahara Medical College. It focused on analyzing associations between rider characteristics, road conditions, and reported safety concerns such as speeding, poor driving sense, and vehicle issues. Consistent with global trends, over-speeding emerged as the predominant safety concern reported by participants, particularly among younger motorcyclists aged 18–32 years. Similar findings were observed by Kumar et al., who highlighted over-speeding as a major contributor to accidents among

younger riders due to their higher risk-taking tendencies and overconfidence on the road [7]. This behavioural pattern was also supported by Sumit et al., who reported that younger riders underestimate hazards, thereby increasing their vulnerability to accidents [10]. Interestingly, despite observable trends linking rider age to safety concerns, the statistical tests in our study showed no significant association ($p=0.338$). A similar outcome was reported in a Malaysian study by Zaki et al., who identified distinct behavioural trends without statistically significant differences, suggesting widespread risky riding practices across various age groups [11]. Profession-wise analysis revealed MBBS students primarily reporting over-speeding, whereas Allied Health Sciences (AHS) students demonstrated higher concerns regarding driving sense. These findings align with previous research by Champahom et al., in Thailand, where variations in risk perception among university students were observed based on their educational background and exposure to safety training [12]. However, our findings did not show statistically significant differences ($p=0.459$), similar to Nurain and Razelan's (2022) Malaysian study, which found no significant differences despite noticeable patterns [13]. The reported safety concerns varied slightly with road conditions, although again not significantly ($p=0.518$). Peak hours and low visibility conditions were predominantly associated with over-speeding concerns. Similar findings were documented by Pervez et al., in Pakistan, who identified over-speeding as exacerbated by environmental factors such as dense traffic and low visibility, highlighting the importance of targeted safety measures during specific road conditions [14]. Equipment-related concerns, including issues with mirrors and lighting, were less frequently reported, especially among younger riders. Sunnud et al., investigating older Thai riders, noted that younger riders typically neglect routine maintenance and safety checks, reflecting their limited understanding of pre-ride safety protocols. This insight complements the observations from this current study [15]. Our findings support global research stressing the importance of educational programs targeted toward younger, educated populations. Rankin et al., observed positive outcomes from structured educational interventions aimed at improving riding behaviours among young adults in developed settings [16]. Such educational initiatives could be adapted effectively within academic environments like Sahara Medical College. This study had certain limitations, notably the reliance on self-reported data, which potentially led to recall bias. Similar methodological limitations were identified in recent studies conducted by Beyera et al., and McCarty and Kim emphasizing the need for observational methods or mixed-method approaches

to validate findings further [5, 17]. Additionally, the lack of gender diversity in our sample limits the generalizability of results, an issue similarly discussed by Setyowati et al., in their review of African motorcycle studies [18]. Given the global relevance of motorcycle safety and the consistency in risk factors identified across studies, educational institutions must proactively implement comprehensive safety training programs. Such interventions have proven beneficial, as demonstrated by Hussain et al., and Amodu et al., who reported reduced risky riding behaviours following targeted awareness programs in university settings [19, 20].

This study relied on self-reported data, which may introduce recall and reporting bias. Additionally, the limited sample diversity, particularly in terms of gender and single-institution setting, restricts the generalizability of findings. Future studies should incorporate multicenter designs with observational or mixed-method approaches to validate and expand upon these findings.

CONCLUSIONS

This study identified over-speeding as the most frequently reported motorcycle safety concern among educated riders (students and faculty members). While younger age groups and certain road conditions, such as peak hours and low visibility, were associated with higher frequencies of safety concerns, no statistically significant associations were found across demographic factors, professional categories, or road conditions. These findings highlight a broad prevalence of risky riding behaviours, indicating a critical need for targeted educational interventions, improved road infrastructure, and stricter enforcement of motorcycle safety regulations within educational communities.

Authors' Contribution

Conceptualization: MH, MAS

Methodology: SK, RA, DZ, ZAB, MAS

Formal analysis: RA, DZ, ZAB, MAS

Writing and Drafting: MH, SK, RA, DZ, ZAB

Review and Editing: MH, SK, RA, DZ, ZAB, MAS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Role of a Teacher in Medical Education: A Faculty's Perspective from HBS

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ABSTRACT

Medical educators are vital in delivering knowledge and shaping students' professional behaviour and critical thinking. However, their effectiveness is influenced by institutional support, teaching training, and the ability to adapt to innovative methodologies. **Objectives:** To assess faculty members' perceptions, teaching practices, and institutional involvement in medical education and to explore the association between formal training and innovative teaching methods. **Methods:** A descriptive cross-sectional survey was conducted at HBS Dental College, Islamabad, including 85 faculty members. Data were collected using a structured questionnaire covering demographics, teaching methods, perceptions of educational roles, and barriers faced. Statistical analysis was performed using SPSS version 25.0, applying Chi-square, Mann-Whitney U, and Kruskal-Wallis tests. **Results:** Lecture-based teaching was universal, while small group teaching (68.2%) and PBL (41.2%) were also common. Only 35.3% of faculty had formal training in medical education. A significant association was found between training and the use of innovative methods ($p=0.001$). Reflective teaching scores were higher among trained faculty ($p=0.049$). Lack of time was the most reported barrier (69.4%). **Conclusions:** It was concluded that faculty with formal training were more likely to adopt innovative and reflective teaching practices. Addressing institutional barriers and investing in structured faculty development can significantly enhance the quality of medical education.

INTRODUCTION

Teachers are foundational to educational systems, and their role is especially pivotal in medical education, where they serve not only as knowledge providers but also as facilitators of clinical reasoning, role models for professional conduct, and mentors fostering lifelong learning [1]. With the global shift toward competency-based, student-centred education, medical faculty face increasing expectations to integrate diverse teaching methodologies, utilize digital tools, encourage critical

thinking, and actively engage students often within rigid institutional structures and considerable time limitations [2, 3]. While medical education has seen substantial innovation worldwide, the pace of adopting such innovative teaching and assessment approaches varies significantly across regions, notably in low- and middle-income countries, including Pakistan [4]. In South Asia, specifically Pakistan, medical educators frequently enter academia without formal pedagogical training, often relying



predominantly on traditional lecture-based methods. Challenges such as limited institutional resources, inadequate faculty development programs, and a lack of structured support systems further complicate the transition to modern, interactive teaching practices [4, 5]. Although various international studies have explored faculty perceptions and development in diverse settings, research [6], specifically addressing the perceptions, teaching roles, and challenges faced by medical and dental faculty within the unique educational context of Pakistan, remains limited. Particularly scarce are studies examining how formal educational training influences teaching methods, institutional involvement, and the practical barriers faculty encounter in private sector medical institutions.

This study aims to address these gaps by exploring faculty perceptions at Hazrat Bari Imam Sarkar (HBS) Medical and Dental College, Islamabad. Specifically, it investigates faculty teaching practices, institutional engagement, perceived barriers to effective teaching, and the role formal training plays in shaping educational approaches. By providing region-specific insights, the study intends to inform institutional policies, support targeted faculty development strategies, and enhance the overall quality of medical education delivery.

METHODS

This descriptive cross-sectional study was conducted among faculty involved in undergraduate and postgraduate teaching at HBS Medical and Dental College, Islamabad, from May 8, 2023, to October 30, 2023. The study aims to explore the role of teachers in medical education from the perspective of faculty members. The study was approved by the Institutional Research and Ethical Committee (Ref: 3 EC). Participation was voluntary, with informed consent obtained. Confidentiality and anonymity were assured. Data collection took place over one month between January 2023 and February 2023. The total faculty population was approximately 100. Sample size was calculated using Yamane's formula for a known population: $n = N \cdot 1 + N(e^2)$, where $N = 100$, $e = 0.05$ (margin of error). This yielded a minimum sample of 80. A total of 85 faculty members participated to accommodate potential non-responses. A similar approach was used by Bashir and McTaggart, for institutional-level faculty surveys [7]. Inclusion criteria were full-time faculty involved in teaching with voluntary participation. Exclusion criteria were visiting or part-time faculty, administrative staff, or incomplete responses. A structured, self-administered questionnaire was developed by adapting elements from validated instruments used in previous faculty perception studies [1, 7]. Items were tailored to suit the context of the medical and dental faculty in Pakistan. The tool included constructs commonly used to assess teaching practices,

institutional involvement, role perception, and barriers to effective teaching. The tool was reviewed by three medical educationists for content validity and piloted with 10 faculty members (excluded from final data). Feedback led to minor modifications. Reliability was confirmed using Cronbach's alpha: Perception of Teaching Role: $\alpha = 0.81$, Teaching Practice: $\alpha = 0.78$, Institutional Involvement: $\alpha = 0.73$ and Barriers to Teaching: $\alpha = 0.75$. Face validity and expert consensus supported the tool's overall clarity. The questionnaire included five sections: Demographics (age, gender, designation, experience) Teaching Practices (frequency and type of instructional methods), Institutional Involvement (committees, faculty development), Perceptions of Teaching Role (5-point Likert scale) Total score range: 4–20 (minimum per item=1, maximum=5) and Barriers to Teaching (Yes/No items on common challenges) Forms were distributed during meetings and also emailed to ensure maximum participation. Respondents completed them independently. Data were entered into SPSS version 25. Descriptive statistics included frequencies and percentages. Likert-scale responses were treated as ordinal and reported with median and interquartile ranges. The following inferential tests were applied: Chi-square test: Association between categorical variables, Mann-Whitney U test: Perception scores vs. training status. Kruskal-Wallis test: Differences across designations and Cramér's V strength of association between categorical variables. A $p\text{-value} \leq 0.05$ was considered statistically significant. All analyses were performed at a 95% confidence level.

RESULTS

The faculty members who participated in this study predominantly fell within the 25–35 year age group, representing nearly half of the sample (49.4%). Females slightly outnumbered males (52.9% vs. 47.1%). A large majority of respondents were married (75.3%). In terms of academic designation, assistant professors made up the highest proportion (32.9%), followed by associate professors (25.9%) and lecturers (24.7%). Professors accounted for 16.5% of participants. The distribution across departments showed a relatively balanced representation, with basic sciences faculty comprising 40%, clinical sciences 34.1%, and dental clinical faculty 25.9%. Teaching experience varied, with the largest group having over 10 years of experience (38.8%), followed by 5–10 years (31.8%), and less than five years (29.4%). Only a minority of faculty (35.3%) had formal training in medical education, while the majority (64.7%) reported having no such background. Involvement in institutional activities was moderately high, with 44.7% serving on curriculum committees. Regarding teaching load, most respondents taught between 4–6 classes weekly (42.4%), with others

handling either fewer (28.2%) or more (29.4%) sessions. Notably, engagement in faculty development was encouraging 35.3% had attended at least one development activity in the past year, while 41.2% had participated in multiple sessions, indicating a growing interest in professional development (Table 1).

Table 1: Demographic, Professional, and Institutional Characteristics of Faculty (n=85)

Variables	Category	Frequency (%)
Age (in Years)	25–35	42 (49.4%)
	36–45	21 (24.7%)
	46–55	14 (16.5%)
	>55	8 (9.4%)
Gender	Female	45 (52.9%)
	Male	40 (47.1%)
Marital Status	Married	64 (75.3%)
	Unmarried	21 (24.7%)
Designation	Assistant Professor	28 (32.9%)
	Associate Professor	22 (25.9%)
	Lecturer	21 (24.7%)
	Professor	14 (16.5%)
Departments	Basic Sciences	34 (40.0%)
	Clinical Sciences	29 (34.1%)
	Dental Clinical	22 (25.9%)
Teaching Experience (Years)	<5	25 (29.4%)
	5–10	27 (31.8%)
	>10	33 (38.8%)
Formal Training in Medical Education	Yes	30 (35.3%)
	No	55 (64.7%)
Curriculum Committee Membership	Yes	38 (44.7%)
	No	47 (55.3%)
Classes Taught per Week	1–3	24 (28.2%)
	4–6	36 (42.4%)
	>6	25 (29.4%)
Faculty Development Activities (Last Year)	None	20 (23.5%)
	Once	30 (35.3%)
	More than once	35 (41.2%)

*All values are shown in percentages.

Lecture-based teaching remained universally practised, with all respondents (100%) using this method. However, more interactive approaches were also commonly employed. Small group teaching was reported by 68.2% of faculty, followed by problem-based learning (41.2%) and case-based learning (32.9%). Simulation-based teaching and self-directed learning were less commonly used, cited by 17.6% and 25.9% respectively. A strong majority (78.8%) reported using teaching technology, suggesting increasing integration of digital tools into educational delivery. Among those using teaching technology, multimedia presentations were the most popular tool (60%), followed closely by learning management systems (56.5%) and online quizzes or Google Forms (48.2%). This highlights a

substantial reliance on digital platforms to support instructional strategies, particularly for content delivery and student engagement. The most frequently cited barrier was lack of time, reported by 69.4% of participants. Other notable barriers included limited institutional resources (38.8%), an overloaded curriculum (37.6%), and student disinterest (35.3%). Institutional constraints and lack of incentives were also noted by a significant portion (35.3% and 21.2%, respectively). These findings underscore the multifactorial challenges faced by educators in delivering effective instruction (Table 2).

Table 2: Teaching Methods, Technology Use, and Barriers to Effective Teaching

Category	Item	Frequency (%)
Teaching Methods	Lecture-Based	85 (100.0%)
	Small Group Teaching	58 (68.2%)
	Problem-Based Learning (PBL)	35 (41.2%)
	Case-Based Learning (CBL)	28 (32.9%)
	Simulation/Skill-Based Teaching	15 (17.6%)
	Self-Directed Learning (SDL)	22 (25.9%)
Technology Use (General)	Use of Teaching Technology	67 (78.8%)
	No Use of Technology	18 (21.2%)
Technology Tools	Multimedia Presentations	51 (60.0%)
	Learning Management System	48 (56.5%)
	Online Quizzes/Google Forms	41 (48.2%)
Barriers to Teaching	Lack of Time	59 (69.4%)
	Limited Resources	30 (35.3%)
	Overloaded Curriculum	33 (38.8%)
	Student Disinterest	30 (35.3%)
	Institutional Constraints	32 (37.6%)
	Lack of Incentives	18 (21.2%)

Nearly half the faculty (47.1%) strongly agreed they acted as facilitators in learning, and 70.5% viewed themselves as reflective practitioners. A majority also considered themselves role models. However, only 22.4% strongly felt institutionally supported (Table 3).

Table 3: Faculty Perceptions and Training-Linked Differences

Statements	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
I Serve as A Facilitator In Student Learning	47.1%	36.5%	10.6%	1.2%	4.7%
I Reflect To Improve My Teaching	37.6%	32.9%	14.1%	8.2%	7.1%
I Act As A Mentor And Role Model	41.2%	38.8%	8.2%	5.9%	5.9%
I Feel Institutionally Supported In My Role	22.4%	29.4%	34.1%	9.4%	4.7%

Faculty with formal training had significantly higher reflective practice scores ($U=621.000$, $p=0.049$), suggesting that training fosters self-improvement behaviours. While role model perception varied by designation, the differences were not statistically significant ($p=0.174$), although assistant and associate professors had relatively higher mean ranks (Table 4).

Table 4: Faculty Perceptions and Training-Linked Differences

Comparison	Groups	Mean Rank	p-value*	Test Statistic
Reflective Practice by Training Status	Trained Faculty	49.80	0.049*	U=621.000
	Untrained Faculty	39.29		
Role Model Perception by Designation	Lecturer	35.62	0.174	H=4.975
	Assistant Professor	48.64		df=3
	Associate Professor	46.18		N=85
	Professor	37.79		

*Statistically significant at $p \leq 0.050$

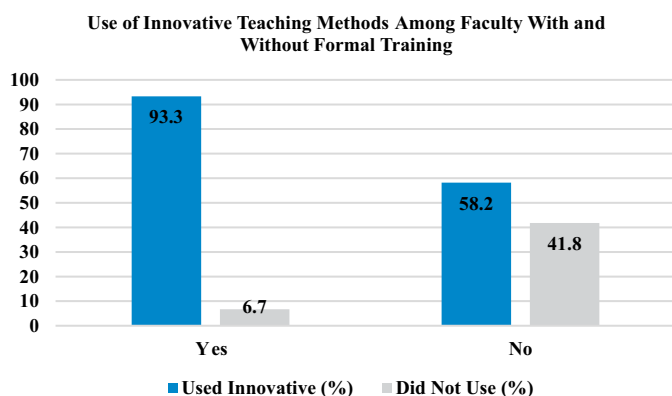
A statistically significant association was observed between formal training and the use of innovative teaching methods ($p=0.001$). Faculty with training were substantially more likely to adopt innovative strategies (93.3%) compared to those without training (58.2%). The strength of this relationship was moderate, as indicated by a Cramér's V value of 0.369. This finding underscores the value of structured training programs in enhancing teaching innovation (Table 5).

Table 5: Association Between Training and Use of Innovative Teaching Methods

Training Status	Used Innovative Methods (%)	Chi-square (χ^2)	p-value*	Cramér's V
Yes	30 (93.3%)	11.553	0.001*	0.369
No	55 (58.2%)			

*Statistically significant at $p \leq 0.050$. Cramér's V is a measure of the strength of association between categorical variables; 0.369 indicates a moderate relationship

The chart illustrates a clear disparity in the adoption of innovative teaching strategies based on formal training status. Among faculty who had received formal training, a significant majority (93.3%) reported using innovative methods, while only 6.7% did not. In contrast, among those without formal training, 58.2% employed such methods, whereas 41.8% did not. These findings indicate a strong positive association between faculty development and the application of contemporary teaching approaches, underscoring the value of structured training programs in enhancing pedagogical practices (Figure 1).

**Figure 1:** Comparison of innovative teaching method adoption among faculty with and without formal training in medical education ($n=85$)

DISCUSSION

This study explored the perceptions, practices, and challenges that faculty members face regarding their roles in medical education. The findings reveal that faculty at HBS Medical and Dental College exhibit a thoughtful understanding of teaching responsibilities, largely aligned with international literature, while also pointing toward institutional areas requiring improvement [8-10]. A balanced mix of junior and senior faculty was observed, with nearly half of the respondents aged 25-35 years. This demographic is encouraging, as younger faculty are often more open to adopting innovative teaching methods. At the same time, a substantial portion (38.8%) had over a decade of teaching experience, contributing to a culture of mentorship. This demographic pattern is consistent with findings from Qureshi et al., and Nawabi et al., who observed evolving faculty profiles in South Asian medical

colleges [11, 12]. Lecture-based instruction remained the dominant method, though interactive strategies like small group teaching, PBL, and CBL were also commonly used. However, modern techniques such as simulation and self-directed learning (SDL) were underutilized, likely due to resource limitations and insufficient faculty development infrastructure. Studies by Catanzano *et al.*, Hennessy *et al.*, and Widayati *et al.*, the importance of institutional investment in simulation labs, digital tools, and SDL frameworks to bridge these gaps [13-15]. One of the most significant findings was the strong association between formal training in medical education and the adoption of innovative teaching methods. Faculty who received such training were significantly more likely to implement diverse instructional approaches. These results align with studies by Challa *et al.*, and B. Hathur and P. Kulkarni *et al.*, which demonstrate that structured development programs not only increase educator confidence but also enhance teaching quality and student engagement [16, 17]. Successful faculty development strategies highlighted in global literature include longitudinal certificate or diploma programs in health professions education, institutional teaching fellowships, peer coaching, and micro-teaching workshops. For example, the Stanford Faculty Development Program (SFDP) and FAIMER fellowship models have shown measurable impact on teaching quality and leadership among faculty. In the local context, expanding short courses through PMDC/PMC or university-affiliated medical education departments could offer sustainable, scalable pathways for faculty growth. The faculty's self-perception was largely positive. Most saw themselves as facilitators and role models and reported practicing reflective teaching. However, institutional support appeared lacking only 22.4% of faculty strongly felt supported in their roles. This gap between individual motivation and institutional reinforcement has been observed in prior research and underlines the need for structured recognition systems such as teaching awards, reduced teaching loads for active contributors, and dedicated faculty development budgets [18-20]. Among reported barriers, lack of time was the most common, noted by nearly 70% of participants. Limited resources, overloaded curricula, and lack of incentives also featured prominently. These systemic challenges reflect a broader need for administrative planning and support. Streamlining academic workloads, introducing digital learning management systems, and incentivizing innovation can reduce faculty burnout and improve teaching effectiveness. Notably, while mentoring was perceived as a shared responsibility across ranks, mid-career faculty (assistant and associate professors) appeared more engaged in such roles. This may be due to their balance of experience and ongoing student contact. Though differences by rank were not statistically significant, the trend supports targeted mentorship initiatives led by mid-

career educators.

This study is limited by its single-institution design and reliance on self-reported data, which may introduce response bias and limit the generalizability of the findings. Additionally, the cross-sectional nature of the study restricts the ability to assess changes in faculty perceptions and practices over time. Future multicentred longitudinal studies incorporating objective teaching assessments are recommended to better evaluate the impact of faculty development programs on teaching practices and educational outcomes.

CONCLUSIONS

This study reinforces the critical role of faculty in shaping the direction and quality of medical education. From the perspective of teachers at HBS Medical and Dental College, it is evident that while faculty generally hold positive perceptions of their roles as facilitators, mentors, and reflective practitioners their ability to implement innovative teaching methods is significantly enhanced by formal training in medical education.

Authors' Contribution

Conceptualization: AHA

Methodology: SA, RS, YK, HA

Formal analysis: AHA, SA, YK

Writing and Drafting: AHA, SA, US, YK

Review and Editing: AHA, SA, US, RS, YK, HA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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**Original Article**

Differences in Depressive Symptoms, Perceived Social Support, and Quality of Life among Patients with Hepatitis C and Psychiatric Patients: A Cross-Sectional Study

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ABSTRACT

Hepatitis is a series of viral illnesses that can impact a person's health and social life. **Objective:** To investigate the differences in depressive symptoms, perceived social support, and quality of life among the normal population, patients with Hepatitis C, and patients with psychiatric disorders. **Methods:** 402 participants were taken from Faisalabad's different urban and rural areas. The participants' ages ranged from 25 to 54 years. The sample consisted of married participants (n=189, 47%) and unmarried participants (n=213, 53%). A purposive sampling technique was used to collect the data. The following measures were used to assess the findings: Demographic Form, Patient Health Questionnaire, Multidimensional Scale of Perceived Social Support, and World Health Organization Quality of Life-BREF scale. **Results:** The findings revealed that patients with hepatitis C and patients with psychiatric disorders perceived a high degree of depression as compared to individuals having no history of medical and psychiatric treatment. Similarly, patients with hepatitis C and patients with psychiatric disorders perceived a low degree of social support and quality of life as compared to individuals having no history of medical and psychiatric treatment. **Conclusion:** In this study, depression, perceived social support, and quality of life were found to significantly differ between the general population, Hepatitis C patients, and people with a mental health condition.

INTRODUCTION

Hepatitis C Virus (HCV) infection continues to be a substantial public health concern on a global scale, affecting millions of individuals through its chronic progression and long-term complications [1]. The disease, which is predominantly transmitted through blood-to-blood contact, can result in severe liver damage, such as cirrhosis and hepatocellular carcinoma [2]. Hepatitis C and

mental illnesses are both chronic health problems that can have a major impact on people's psychological well-being, social interactions, and general quality of life. The impact of HCV and its psychological effects are exacerbated when combined with pre-existing mental health issues. It is essential to comprehend how depression, psychiatric illness [3]. Patients with chronic HCV are more likely to



experience depressive symptoms, especially among those who contracted the virus through intravenous drug use or other marginalized behaviors, which are all responsible for this [4]. Furthermore, even though antiviral medications have revolutionized the treatment of HCV, the disease's psychological toll has not completely decreased. Compared to older treatments like interferon, newer direct-acting antiviral drugs have lessened neuropsychiatric side effects, although patients still experience a significant psychological burden [5]. It is commonly known that people with HCV have a comorbidity of mental illnesses. Anxiety, schizophrenia, personality disorders, and substance use problems have all been found to be more common in this group [6]. Depressive symptoms can exacerbate the social isolation that many patients already experience, interfere with coping strategies, and make it more difficult to start and finish HCV therapy. HCV may act as an extra stressor for people who already have psychiatric illnesses, aggravating pre-existing mental health issues and perhaps resulting in worse overall outcomes [7]. In contrast, the diagnosis of HCV in an individual with a psychiatric disorder may exacerbate psychological symptoms, especially if the disease is advanced or the individual is subjected to social stigma [8]. This cross-sectional study identified that sociodemographic, psychopathological, and psychiatric factors significantly impact the health-related quality of life in patients with chronic hepatitis C [9]. Addressing the trio of psychiatric diseases, HCV, and depression demands a holistic strategy that takes into account not just the medical bases of these disorders but also the social, psychological, and structural elements that determine health trajectories [10].

Despite known links between Hepatitis C, psychiatric disorders, and depression, limited studies have compared their combined impact on depression, social support, and quality of life with the general population, especially in Pakistan. This study addresses this gap by evaluating these outcomes across normal individuals, HCV patients, and psychiatric patients. The objectives of this study were to examine the differences in levels of depression, perceived social support, and quality of life among the normal population, patients with hepatitis C, and patients with psychiatric disorders.

METHODS

In this study, cross-sectional study design was used. This study was conducted from March 2023 to February 2024. The present study was approved by the Institutional Review Board of Government College University, Faisalabad (Ref/GCUF/ERC/4670, IRB No. 791). A total of 402 participants were taken from different tertiary care hospitals. The study sample size was extracted using G-Power Software and the estimated sample was below 400

participants; and a sample of 402 participants was collected. A convenient sample technique was used to collect the sample. The study sample consisted of three different participants general population (category=1), patients with hepatitis-C (category=2), and psychiatric patients (category=3). Psychiatric patients with infectious hepatitis C participated in the study. Patients with hepatitis were recruited from Faisalabad's public and private clinics and hospitals. Infectious hepatitis C patients with psychiatric problems were chosen from various Faisalabad neighborhood locations as well as rural and urban areas. Patients from all socioeconomic backgrounds were included (i.e., low, middle, high). The study did not include patients with hepatitis E or D. Participants were excluded if they had co-occurring diseases. Participants with viral hepatitis A, B, and C who were younger than 18 or older than 55 were excluded from the study. Patients who were not Faisalabad residents were excluded from the trial. The following instruments were used in the current study to measure the variables. Information such as personal details (name, age, education, legal status, and family status) and medical history (disease duration, severity, and length of therapy) were obtained using the demographic form. A popular, trustworthy, and validated self-report tool for screening, diagnosing, tracking, and assessing the severity of depression is the Patient Health Questionnaire-9 (PHQ-9). Using a four-point Likert scale from 0 ("Not at all") to 3 ("Nearly every day"), each item evaluates the frequency of depression symptoms during the last two weeks, including low mood, loss of interest or pleasure, exhaustion, sleep difficulties, and thoughts of self-harm. Higher scores indicate more severe depressive symptoms; the total score goes from 0 to 27. Minimal (0-4), mild (5-9), moderate (10-14), fairly severe (15-19), and severe (20-27) are the usual classifications for severity [11]. MPSS's twelve things' responses were on a seven-point Likert scale from very strongly disagree (1) to very strongly agree (7). To measure the perceived support from family, friends, and excellent friends, the twelve-item MPSS was created. In the original study Zimet et al., in 1998, 200 and seventy-five university undergraduate men and women completed the Hopkins symptoms list HSCL et al., in 1974 and MPSS [11]. The subscales and total scale had constant alphas 85 to 91, indicating good internal consistency [12]. Additionally, test-retest consistency values were 72 to 85, indicating sensible constancy. Major correlations between HSCL depression and anxiety subscales and MPSS subscales showed construct validity [12]. World Health Organization Quality of Life development began in 1991. WHOQOL-BREF has 4 domains. Four WHOQOL-BREF domains support twenty-six items: Domain one, physical health, covers daily activities, medication use, energy and tiredness, mobility,

pain and anxiety, sleep and relaxation, and workability. Physical appearance, bad thoughts, positive sentiments, shallowness, spiritual studies, religion, personal perspective, thinking, learning, memory, and a spotlight are in Domain 2. Personal relationships, social support, and gender are covered in Domain 3. Domain 4 evaluates economic resources, independence, physical protection and security, health and social care. This study collected data from infectious Hepatitis C and psychiatric patients. All subjects gave informed consent before data collection. Participants were briefed on the study's purpose and completed a self-developed demographic form and standardized instruments like PHQ-9, the Multidimensional Scale of Perceived Social Support (MSPSS), and the WHO-QOL in Urdu for clarity and accessibility. After months of data collecting, responses were coded and input into a computer for statistical analysis. Descriptive and inferential statistics provided insights, and the thesis was proofread, supervisor-reviewed, and submitted. Descriptive statistics were calculated to better summarise the statistical view of the sample demographics. In addition to the descriptive statistics, the inferential statistic was calculated to draw a meaningful conclusion from the data[13].

RESULTS

Individuals, 51.5% male ($n = 207$) and 48.5% female ($n = 195$). The plurality (38.3%) of participants is aged 25–34 ($n = 154$), followed by 33.1% aged 45–54 ($n = 133$), and 28.6% aged 35–44 ($n = 115$). Educational background: 29.6% had completed middle school ($n = 119$), 29.4% had completed matriculation ($n = 118$), 14.9% had an FA ($n = 60$), 16.9% had a BA ($n = 68$), and 9.2% had an MA ($n = 37$). The sample was 53%

single ($n = 213$) and 47% married ($n = 189$). Rural residents comprised 69.7% of the sample ($n = 280$), while urban residents comprised 30.3% ($n = 122$). 23.6% of participants were sick for less than 6 months ($n = 95$), 33.6% for 6 to 12 months ($n = 135$), and 42.8% for more than one year ($n = 172$).

Table 1: Demographic Characteristics of the study participants

Variables	Category	Frequency (%)
Gender	Male	207 (51.5)
	Female	195 (48.5)
Age	25-34	154 (38.3)
	35-44	115 (28.6)
	45-54	133 (33.1)
Education	Middle	119 (29.6)
	Metri	118 (29.4)
	FA	60 (14.9)
	BA	68 (16.9)
	MA	37 (9.2)
Marital Status	Single	213 (53.0)
	Married	189 (47.0)
Residence	Rural	280 (69.7)
	Urban	122 (30.3)
Duration of Illness	< 6 months	95 (23.6)
	6-12 months	135 (33.6)
	>1 year	172 (42.8)

Findings reveal (Table 2) that patients with hepatitis C and patients with psychiatric disorders perceived a high degree of depression as compared to the individuals having no history of medical and psychiatric treatment. Similarly, patients with hepatitis C and patients with psychiatric disorders perceived a low degree of social support and quality of life as compared to individuals having no history of medical and psychiatric treatment.

Table 2: Mean, Standard Deviation, ONE-WAY ANOVA Statistics among the General Population, Patients with Hepatitis C and Psychiatric Patients

Variables		N	Mean ± SD	Std. Error	MS	F	p	95% Confidence Interval for Mean	
								Lower Bound	Upper Bound
PHQ-9	1.00	116	38.16 ± 7.77	0.722	595.075	14.505	<0.001	36.72	39.59
	2.00	152	37.72 ± 7.01	0.569	41.025			36.59	38.84
	3.00	134	34.28 ± 3.86	0.334	-			33.62	34.94
	Total	402	36.70 ± 6.61	0.330	-			36.05	37.35
SOS	1.00	116	19.79 ± 3.38	0.31469	40.276	3.350	<0.036	19.1698	20.4164
	2.00	152	20.00 ± 3.42	0.27786	12.022			19.4510	20.5490
	3.00	134	20.84 ± 3.57	0.30919	-			20.2317	21.4548
	Total	402	20.22 ± 3.48	0.17394	-			19.8794	20.5633
FMS	1.00	116	19.87 ± 3.60	0.33491	71.542	5.907	<0.003	19.2159	20.5427
	2.00	152	20.04 ± 3.08	0.25019	12.112			19.5517	20.5404
	3.00	134	21.23 ± 3.77	0.32650	-			20.5855	21.8771
	Total	402	20.39 ± 3.52	0.17569	-			20.0476	20.7384
FRS	1.00	116	19.35 ± 3.94	0.36657	96.380	7.439	<0.001	18.6274	20.0795
	2.00	152	19.55 ± 3.31	0.26857	12.956			19.0220	20.0833
	3.00	134	20.92 ± 3.59	0.31077	-			20.3107	21.5401
	Total	402	19.95 ± 3.65	0.18238	-			19.5942	20.3113

MPSS	1.00	116	59.02 ± 9.31	0.86498	605.622	8.116	<0.001	57.3125	60.7392
	2.00	152	59.59 ± 7.57	0.61420	74.620			58.3851	60.8122
	3.00	134	63.00 ± 9.14	0.79040	-			61.4366	64.5634
	Total	402	60.56 ± 8.79	0.43842	-			59.7053	61.4290
Domain-1	1.00	116	20.53 ± 3.09	0.28753	172.947	26.984	<0.001	19.9649	21.1040
	2.00	152	21.23 ± 2.28	0.18546	6.409			20.8704	21.6033
	3.00	134	22.80 ± 2.23	0.19316	-			22.4239	23.1880
	Total	402	21.55 ± 2.69	0.13420	-			21.2934	21.8210
Domain-2	1.00	116	17.31 ± 2.83	0.26278	175.413	27.723	<0.001	16.7984	17.8395
	2.00	152	17.60 ± 2.30	0.18697	6.327			17.2359	17.9747
	3.00	134	19.44 ± 2.45	0.21202	-			19.0284	19.8671
	Total	402	18.13 ± 2.67	0.13356	-			17.8743	18.3994
Domain-3	1.00	116	9.06 ± 1.90	0.17732	38.313	14.462	<0.001	8.7177	9.4202
	2.00	152	9.66 ± 1.74	0.14155	2.649			9.3848	9.9442
	3.00	134	10.17 ± 1.15	0.09985	-			9.9816	10.3766
	Total	402	9.66 ± 1.68	0.08386	-			9.4993	9.8290
Domain-4	1.00	116	23.74 ± 3.91	0.36305	202.042	20.132	<0.001	23.0223	24.4605
	2.00	152	24.46 ± 3.06	0.24837	10.036			23.9764	24.9578
	3.00	134	26.18 ± 2.49	0.21585	-			25.7596	26.6135
	Total	402	24.8 ± 3.31	0.16537	-			24.5057	25.1559
QLS	1.00	116	76.0 ± 9.62	0.894	2460.570	50.834	<0.001	75.05	78.59
	2.00	152	79.16 ± 6.22	0.505	48.404			78.16	80.15
	3.00	134	85.29 ± 4.60	0.397	-			84.50	86.08
	Total	402	80.53 ± 7.77	0.388	-			79.77	81.29

Note: $p < .001$, MS= Mean Square, 1= General Population, 2= Patients with Hepatitis-C, 3= Psychiatric Patients, PHQ-9= Patients Health Questionnaire-9, SOS= Significant Others Subscale, FMS= Family Subscale, FRS= Friend Subscales, MPSS= Multidimensional Perceived Social Support

Post-hoc comparisons (Table 3) showed that patients with hepatitis C were found to be significantly different from patients with psychiatric disorders and individuals having no history of medical and psychiatric treatment on the scale of depression and social support. Similarly, on the quality-of-life scale, all groups, such as patients with hepatitis C, patients with psychiatric disorders, and individuals having no history of medical and psychiatric treatment, were found to be significantly different.

Table 3: Tukey Comparisons among the General Population, Patients with Hepatitis C and Psychiatric Patients

Dependent Variable	(I) A1.B2.C3	(J) A1.B2.C3	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Mean	
						Lower Bound	Upper Bound
PHQ-9	1.00	2.00	0.438	0.790	0.844	-1.42	2.30
		3.00	3.879*	0.812	<0.001	1.97	5.79
	2.00	1.00	-0.438	0.790	0.844	-2.30	1.42
		3.00	3.441*	0.759	<0.001	1.66	5.23
	3.00	1.00	-3.879*	0.812	<0.001	-5.79	-1.97
		2.00	-3.441*	0.759	<0.001	-5.23	-1.66
SOS	1.00	2.00	-.20690	0.42747	0.879	-1.2125	0.7987
		3.00	-1.05018*	0.43972	0.046	-2.0846	-0.0157
	2.00	1.00	0.20690	0.42747	0.879	-0.7987	1.2125
		3.00	-0.84328	0.41086	0.101	-1.8098	0.1233
	3.00	1.00	1.05018*	0.43972	0.046	0.0157	2.0846
		2.00	0.84328	0.41086	0.101	-0.1233	1.8098
FMS	1.00	2.00	-0.16674	0.42907	0.920	-1.1761	0.8426
		3.00	-1.35203*	0.44137	0.007	-2.3904	-0.3137
	2.00	1.00	0.16674	0.42907	0.920	-0.8426	1.1761
		3.00	-1.18529*	0.41240	0.012	-2.1555	-0.2151
	3.00	1.00	1.35203*	0.44137	0.007	0.3137	2.3904
		2.00	1.18529*	0.41240	0.012	0.2151	2.1555

FRS	1.00	2.00	-0.19918	0.44376	0.895	-1.2431	0.8448
		3.00	-1.57192*	0.45648	0.002	-2.6458	-0.4981
	2.00	1.00	0.19918	0.44376	0.895	-0.8448	1.2431
		3.00	-1.37274*	0.42652	0.004	-2.3761	-0.3694
	3.00	1.00	1.57192*	0.45648	0.002	0.4981	2.6458
		2.00	1.37274*	0.42652	0.004	0.3694	2.3761
MPSS	1.00	2.00	-0.57282	1.06499	0.853	-3.0782	1.9326
		3.00	-3.97414*	1.09551	0.001	-6.5513	-1.3970
	2.00	1.00	0.57282	1.06499	0.853	-1.9326	3.0782
		3.00	-3.40132*	1.02362	0.003	-5.8094	-0.9933
	3.00	1.00	3.97414*	1.09551	0.001	1.3970	6.5513
		2.00	3.40132*	1.02362	0.003	0.9933	5.8094
Domai-1	1.00	2.00	-0.70236	0.31212	0.064	-1.4366	0.0319
		3.00	-2.27149*	0.32106	<0.001	-3.0268	-1.5162
	2.00	1.00	.70236	0.31212	0.064	-0.0319	1.4366
		3.00	-1.56913*	0.29999	<0.001	-2.2749	-0.8634
	3.00	1.00	2.27149*	0.32106	<0.001	1.5162	3.0268
		2.00	1.56913*	0.29999	<0.001	0.8634	2.2749
Domain-2	1.00	2.00	-0.28630	0.31012	0.626	-1.0159	0.4433
		3.00	-2.12880*	0.31901	<0.001	-2.8793	-1.3783
	2.00	1.00	.28630	0.31012	0.626	-0.4433	1.0159
		3.00	-1.84250*	0.29807	<0.001	-2.5437	-1.1413
	3.00	1.00	2.12880*	0.31901	<0.001	1.3783	2.8793
		2.00	1.84250*	0.29807	<0.001	1.1413	2.5437
Domain-3	1.00	2.00	-0.59551*	0.20067	0.009	-1.0676	-0.1234
		3.00	-1.11014*	0.20642	<0.001	-1.5957	-0.6245
	2.00	1.00	0.59551*	0.20067	0.009	0.1234	1.0676
		3.00	-0.51463*	.19287	0.022	-0.9684	-0.0609
	3.00	1.00	1.11014*	0.20642	<0.001	0.6245	1.5957
		2.00	0.51463*	0.19287	0.022	0.0609	0.9684
Domain-4	1.00	2.00	-0.72573	0.39057	0.152	-1.6445	0.1931
		3.00	-2.44519*	0.40176	<0.001	-3.3903	-1.5000
	2.00	1.00	0.72573	0.39057	0.152	-0.1931	1.6445
		3.00	-1.71946*	0.37540	<0.001	-2.6026	-0.8363
	3.00	1.00	2.44519*	0.40176	<0.001	1.5000	3.3903
		2.00	1.71946*	0.37540	<0.001	0.8363	2.6026
QLS	1.00	2.00	-2.339*	0.858	0.018	-4.36	-0.32
		3.00	-8.472*	0.882	<0.001	-10.55	-6.40
	2.00	1.00	2.339*	0.858	0.018	0.32	4.36
		3.00	-6.133*	0.824	<0.001	-8.07	-4.19
	3.00	1.00	8.472*	0.882	<0.001	6.40	10.55
		2.00	6.133*	0.824	<0.001	4.19	8.07

Note: $p < .001$, MS= Mean Square, 1= General Population, 2= Patients with Hepatitis-C, 3= Psychiatric Patients, PHQ-9= Patients Health Questionnaire-9, SOS= Significant Others Subscale, FMS= Family Subscale, FRS= Friend Subscales, MPSS= Multidimensional Perceived Social Support

DISCUSSION

This study compared depression levels in the general population, Hepatitis C patients, and people with a mental health condition. These groups would differ significantly in terms of depression, as evaluated by the Patient Health Questionnaire-9, according to the hypothesis. The hypothesis is supported by the findings of the one-way analysis of variance ($F = 14.505$, $p < 0.001$), which indicate a

substantial difference in the levels of depressive symptoms across the three groups. Compared to psychiatric patients, the general population ($M = 38.16$, $SD = 7.78$) and patients with Hepatitis C ($M = 37.72$, $SD = 7.01$) reported higher PHQ-9 scores. In particular, the general population reported a mean score of 38.16, with a standard deviation of 7.78. These findings are consistent with the

existing body of research, which provides evidence of the psychological impact that chronic illnesses and psychiatric problems have on individuals [14]. Furthermore, psychiatric patients face more direct psychological dysfunction, which may be the reason for the more severe depression symptoms that are reported in this group. This is in contrast to hepatitis C patients, who have physical sickness that might contribute to mental anguish [15]. Therefore, this may be a reflection of the influence that concomitant medical illnesses like hepatitis C have on psychological well-being, particularly when the condition is not treated or when persistent stresses, stigma, or a lack of access to mental health care accompany it. Additionally, extra context is revealed by examining relevant psychosocial variables, such as the degree to which one feels supported by society and the quality of one's life. Patients with psychiatric conditions and those with hepatitis C had lower scores on the Multidimensional Perceived Social Support (MPSS) scale when compared to the general population. This suggests that these patients have a lessened sense of support from their family, friends, and significant others [16]. In the second set of findings, it was found that the normal population reported much higher levels of felt social support in comparison to both patients with Hepatitis C and those with psychiatric problems. Based on the findings patients who suffer from psychiatric diseases reported the lowest levels of perceived social support. This is most likely due to the stigma that is associated with the condition, particularly when it is connected to activities such as injecting drugs [17]. The last hypothesis found significant group differences on the Quality-of-Life scale. In line with what was anticipated, the normal population reported the highest quality of life, followed by patients with hepatitis C, and finally, psychiatric patients scored the lowest. Existing research has shown that chronic physical illness and psychiatric illnesses hurt overall life satisfaction, physical functioning, and psychological well-being [18]. This tendency is consistent with the findings of those studies. In psychiatric patients, symptoms such as depression, anxiety, and cognitive abnormalities that have an impact on everyday functioning and interpersonal relationships may contribute to a lower quality of life [19, 20]. A study highlighted that cross-cutting symptoms, liver function, and perceived immune status predict quality of life in Hepatitis B and C patients, with social support and resilience acting as key mediators [20]. These symptoms may also make the quality of life even worse. In a similar vein, the negative effects of exhaustion, pain, and the psychological and social load of managing a chronic illness that is stigmatized can affect the quality of life of individuals who have Hepatitis C.

This study was cross-sectional in nature, limiting the ability to establish causal relationships between depression, social support, and quality of life. Additionally, reliance on

self-reported measures may introduce response bias and affect the accuracy of psychological assessments. Longitudinal studies incorporating clinical assessments are recommended to better understand causal pathways and temporal changes in psychological outcomes.

CONCLUSIONS

In this study, depression, perceived social support, and quality of life were found to significantly differ between the general population, Hepatitis C patients, and people with a mental health condition. While psychiatric patients displayed the greatest difficulties across all factors, the general population reported improved mental health, stronger social support, and a higher quality of life. These findings emphasize the necessity of psychological and social support interventions, particularly for clinical patients, to increase general well-being.

Authors' Contribution

Conceptualization: MS, ML

Methodology: ZHS, AAK, IJ, AP

Formal analysis: MS

Writing and Drafting: IR, AU

Review and Editing: MS, ML, ZHS, AAK, IJ, AP, IR, AU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparative Study between Ultrasound Guided Erector Spine Block versus Transversus Abdominis Plane Block for Post-Operative Analgesia in Laparoscopic Cholecystectomy

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ABSTRACT

Cholelithiasis is a common condition, and laparoscopic cholecystectomy (LC) is the preferred minimally invasive procedure for symptomatic gallstones. Postoperative pain management is crucial for enhancing recovery. Ultrasound-guided erector spinae plane block (US-ESP) and transversus abdominis plane block (TAP) are two regional anesthesia techniques used for postoperative analgesia. **Objective:** To compare the mean postoperative numeric rating scale (NRS) scores in patients undergoing LC with US-ESP and TAP blocks. **Methods:** This observational prospective study was approved by the Institutional Review Board (IRB) of RMI, Peshawar. This observational prospective study included 138 patients (69 in each group) who underwent LC at the Department of Anesthesia, RMI, Peshawar, from October 1, 2021, to April 1, 2023. Group A received US-ESP, and Group B received TAP. Postoperative NRS scores were recorded at 12 hours. All patients provided informed consent before participation. The study adhered to ethical guidelines and was approved by the Institutional Review Board (IRB) of Rehman Medical Institute. **Results:** The mean postoperative NRS score was significantly lower in Group A (1.521 ± 0.63) compared to Group B (2.304 ± 0.69) ($p=0.000$). Both groups had similar demographic and procedural characteristics. **Conclusions:** It was concluded that US-ESP is more effective than TAP in providing postoperative analgesia in LC patients, as evidenced by lower NRS scores.

INTRODUCTION

Cholelithiasis is a common comorbid in patients, but for symptomatic gallstone, the minimally invasive procedure used nowadays is laparoscopic cholecystectomy. During this procedure, 3 ports are inserted into the abdominal cavity. These breach points in the skin are painful post-op; op is responsible for the high intensity of post-operative

discomfort. Enhancing recovery after surgery is possible only with good pain control [1]. Postoperative nausea and vomiting (PONV) and respiratory depression are common side effects of the use of opioids for pain relief [2]. Various analgesic strategies have been suggested for the management of postoperative pain. Apart from using



opioids, the other options include intraperitoneal instillation with a local anesthetic, port-site infiltration and different nerve blocks (transversus abdominis, oblique subcostal transversus abdominis and paravertebral). These operations only address somatic pain, except for the paravertebral block, and in certain cases, they may not provide enough relief [3, 4]. Mounika et al., developed the subcostal technique of TAP block as a postoperative pain management treatment, particularly for upper abdominal procedures [5]. The effectiveness of ultrasound-guided oblique subcostal abdominis plane (US-OSTAP) blocks in reducing postoperative pain and narcotic use during the first 24 hours following laparoscopic surgery (LC) has been shown in several prior studies. The OSTAP block successfully reduces somatic discomfort and parietal pain in the anterior abdomen without affecting visceral nerves [6, 7]. The ventral and dorsal rami of the spinal nerves are targeted by ultrasound-guided erector spine plane block (US-ESP). Once the local anesthetic is injected, it spreads upwards and downwards along the spinal nerves, covering different dermatomes. Past case studies and clinical randomized controlled studies have demonstrated the efficacy of the US-ESP block in providing pain relief after various surgical operations, such as those involving the abdomen, chest, breasts, and spine [8, 9]. A study conducted by Tulgar and colleagues revealed that the average Numeric Rating Scale score after an ultrasound-guided erector spine block was 1.75 ± 0.99 . In contrast, the transversus abdominis plane block during laparoscopic cholecystectomy has a score of 2.2 ± 0.89 [10]. An example of peri-paravertebral plane block is erector spinae block. Although the exact mechanism of ultrasound-guided erector spine block is not completely understood, Sensation over a large area is blocked due to the spread of the local anesthetic to the ventral and dorsal rami of the spinal cord.

his study was carried out to compare the average postoperative numerical rating scale scores for transversus abdominis plane block with ultrasound-guided erector spinae block in laparoscopic cholecystectomy. This study aims to validate the impact of receiving an ultrasound-guided erector spine block on the decrease in I/V opioids used postoperatively, as no previous research has been conducted on this topic within our local population.

METHODS

This observational prospective study was conducted at the Department of Anesthesia, RMI, Peshawar, after obtaining permission from the ethical committee. The study duration was from 1st October 2021 to 1st April 2023. The study was approved by the Institutional Review Board (IRB) of RMI, Peshawar, with reference number (RMI/RMI-REC/Article Approval/131). The sample size was 138 (69 in each group).

Using power=80% and $\alpha=5\%$, the sample size was determined with a 95% confidence level. After a laparoscopic cholecystectomy, the mean postoperative score on the Numerical Rating Scale was 2.2 ± 0.89 , while the mean score with an ultrasound-guided erector spine block was 1.75 ± 0.99 . The sampling technique was non-probability consecutive sampling. The sample size was calculated based on a presumed effect size derived from a previous study by Tulgar et al., where the NRS difference between groups was approximately 0.45. Using an effect size of 0.5, a power of 80%, and α of 0.05, the minimum required sample size per group was determined to be 69. The sample size formula used was as follows: $n = (Z_{\alpha/2} + Z_{\beta})^2 * (SD1^2 + SD2^2) / (Mean1 - Mean2)^2$ [11]. Where: $Z_{\alpha/2} = 1.96$ (for a 95% confidence interval), $Z_{\beta} = 0.84$ (for 80% power). SD1 and SD2 = Standard deviations from the previous study (0.99 and 0.89, respectively). Mean1 and Mean2 = Mean NRS scores from previous research (1.75 and 2.2, respectively). The calculated sample size per group was 69, making a total of 138 participants. This calculation ensures adequate power to detect a clinically meaningful difference between groups while accounting for potential variability in pain perception and reporting. Inclusion Criteria: Age 18 to 50 years, both genders, undergoing laparoscopic cholecystectomy, ASA grade I and II (Annexure-II). Exclusion Criteria: Patients allergic to local anesthetic, patients with a history of bleeding disorders, patients on anticoagulant therapy, patients with severe liver/kidney diseases and patients with significant previous surgical history. Patients from the Department of Anesthesia, RMI, were included based on the established inclusion criteria. The procedure was explained to all patients, and consent was obtained. Demographic data (age and gender) were collected. Randomization was performed via block randomization, with 69 patients in each group. All patients received uniform induction protocols, and vital signs were monitored throughout the procedure. Patients in Group A were positioned in a left lateral decubitus position, longitudinal parasagittal orientation was chosen for the linear ultrasound probe with the patient's right side elevated, a 21-gauge, 10-centimeter needle was inserted using an approach that was not in line with the plane, precisely 2.5–3 cm to the side of the T9 spinous process, with the erector spinae muscles situated on the surface above the tip of the T9 transverse process. The tip of the needle was placed into the fascial plane on the erector spinae muscle's deep (anterior) side. The evident spread of fluid, which caused the erector spinae muscle to rise off the bone on ultrasonography, confirmed the positioning of the needle point. 10ml of 0.5% Inj Rupivacaine + 4mg Dexamethasone + diluted in 10ml normal saline combination were injected on each side. The identical

treatment was given to the other side. Group B employed the in-plane approach with a high-frequency linear transducer to complete blocks while supine. The transducer was positioned on the oblique plane below the costal margin. All three layers of abdominal muscles were recognized. A 21-gauge, 10-centimeter needle was placed utilizing a medial-to-lateral technique in-plane. The rectus abdominis muscle was the focus of a 10ml of 0.5% inj Rupivacaine + 4mg Dexamethasone + diluted in 10ml normal saline combination were injected which was injected just above the fascia. On both sides, the same method was used. The duration of the process was recorded for both groups. Postoperative pain assessment was conducted using the Numeric Rating Scale (NRS) at different time intervals: 20 minutes, 40 minutes, 1 hour, 3 hours, 6 hours, 9 hours, and 12 hours. Pain levels were measured both when the patient was at rest and when coughing. The final NRS score was recorded 12 hours after the surgery. The postoperative numeric rating scale score was observed and documented from both groups on a specifically constructed proforma (Annexure-I). Analysis was done with IBM-SPSS version 25.0. Frequencies and percentages were computed for qualitative variables (gender). Mean $\pm$ Standard deviation was used for quantitative variables (age, duration of procedure and postoperative numeric rating scale score). Both groups were compared for postoperative numeric rating scale scores. The differences in the mean postoperative numeric rating scale score of the two groups were statistically tested using the independent sample t-test. Postoperative numeric rating scale score was stratified by age, gender and duration of procedure. Post stratification using the independent sample t test for both groups, a statistically significant value of p was less than or equal to 0.05.

RESULTS

Age range: 18 to 50 years with a mean age of 32.811 ± 5.25 years, mean procedure duration 60.231 ± 5.17 minutes, and Group A's mean postoperative NRS score was 1.521 ± 0.63 . and mean age of 33.913 ± 6.60 years, mean procedure duration 61.087 ± 5.41 minutes and mean postoperative NRS score was 2.304 ± 0.69 in Group B. For gender, the frequency and percentage in both groups are shown in Table 1.

Table 1: Patients According to Age, Duration of Procedure, Postoperative NRS Score and Gender in Both Groups (n=138)

Demographics	Group A (n=69)	Group B (n=69)
	Mean $\pm$ SD	
Age (Years)	32.811 ± 5.25	33.913 ± 6.60
Duration of Procedure (Minutes)	60.231 ± 5.17	61.087 ± 5.41
Postoperative NRS Score	1.521 ± 0.63	2.304 ± 0.69
Gender		
Male	26 (37.7%)	37 (53.6%)

Female	43 (62.3%)	32 (46.4%)
Total	69 (100%)	69 (100%)

Group A's mean postoperative NRS score was 1.521 ± 0.63 , as compared to 2.304 ± 0.69 in group B ($p=0.000$), as shown in Table 2.

Table 2: Comparison of Mean Postoperative NRS Score in Both Groups (n=138)

Variables	Group A (n=69)	Group B (n=69)	t	p-value
Postoperative NRS score	1.521 ± 0.63	2.304 ± 0.69	-6.931	0.001

The p-value for male patients (0.962) suggests no meaningful difference, but the sample size imbalance between groups may have affected the results. Further analysis is needed to confirm the significance of these results when adjusting for potential confounders. Stratification of mean postoperative NRS score in both groups about age, gender and duration of procedure is shown in Table 3.

Table 3: Stratification of Mean Postoperative NRS Score Concerning Age, Gender and Duration of Procedure in Both Groups

Variables	Groups	Mean Postoperative NRS Score (Mean ± SD)	p-value
Age (Years)			
18-35	A (n=48)	1.479 ± 0.61	0.001
	B (n=43)	2.418 ± 0.62	
36-50	A (n=21)	1.619 ± 0.66	0.023
	B (n=26)	2.115 ± 0.76	
Gender			
Male	A (n=26)	1.653 ± 0.62	0.962
	B (n=37)	2.270 ± 0.65	
Female	A (n=43)	1.441 ± 0.62	0.001
	B (n=32)	2.343 ± 0.74	
Duration of Procedure (minutes)			
≤60	A (n=29)	1.344 ± 0.48	0.001
	B (n=25)	2.320 ± 0.69	
>60	A (n=40)	1.650 ± 0.69	0.001
	B (n=44)	2.295 ± 0.70	

DISCUSSION

Two main causes of postoperative pain in LC patients have been established: first is trauma of gallbladder resection causing visceral pain, CO₂ exposure to the peritoneum leading to stretching, and the second being the pain due to skin incision [11]. These two causes should be taken into account before starting any analgesic protocol after LC. According to our research, patients who underwent ultrasound-guided bilateral single-shot transversus abdominis plane block and bilateral single-shot erector spinae plane block (ESPB) used fewer analgesics within the first 24 hours and coughed and moved less. The control group's numerical rating scale was greater than the block group's during the first three hours. These were significant

reductions of visceral pain caused by Pneumoperitoneum and trauma to the gall bladder. While the difference in NRS scores between groups was statistically significant, both groups reported NRS scores under 4, indicating mild pain. This suggests that although ESPB demonstrates better numerical outcomes, the clinical difference may not be significant enough to impact routine postoperative protocols. A randomized controlled trial was done on the effect of ESPB in LC patients. The 9th thoracic vertebral level was chosen and injected with 20 ml of 0.375% concentration of bupivacaine as the local anesthetic agent; the NRS was significantly lowered in the first 3 hours, and less analgesia was used during the first 24 hours. ESPB was also performed postoperatively with a lower amount of local anesthetic, but the outcome was similar to preoperative blocks [12]. The exact amount of local anesthetic to be used in abdominal and thoracic procedures is not yet established [13]. Adequate reported amount in ESPB was 3.6 ml of local anesthetic per vertebral [14]. Local anesthetic distribution in the thoracic and lumbar region may differ, so the volume of local anesthetic should be determined according to the procedure/patient [15-17]. Three to seven vertebral levels in the cephalic as well as caudal region are covered when 20 ml of local anesthetic is applied at the T4 vertebral level [18]. Compared to our research, 10ml of 0.5% Ropivacaine with 4mg Dexamethasone diluted in 10ml normal saline provided better coverage and facial splitting and superior depth of analgesia postoperatively [19]. In a study reporting the distribution of the block and time taken for OSTAP to show its effect, it was reported that blockage of T7-T12 dermatomes blocks the sensory signals for the next 10 hours in the mid-abdomen and the lateral side of the abdomen [20]. Blocking of the anterior abdominal wall was done to provide analgesia for the incisions performed in LC. Like ESPB, which addresses both aspects, OSTAP causes the blockade of both somatic and visceral pain [21]. Results of this study have shown the superiority of ESPB over OSTAP, both have similar results in the long run. Procedure time plays an important role in the severity and time of visceral pain. To decide whether ESPB or OSTAP provide better analgesia will be better assessed through further studies involving longer procedures, such as laparoscopic bariatric procedures. Different studies regarding regional anesthetic procedures either use local anesthetic as it is or with N/Saline. Use of lidocaine in our anesthetic mixture so there's a low onset time at the end of the procedure. It was necessary to ensure that the block was in effect while the patient was being extubated and shifted to the PACU. In other articles regarding local anesthesia morphine is used for comparison, but in current study, we used tramadol instead of morphine as it has the same effect in postoperative LC patients [22].

This study is limited by its single-center design and

relatively small sample size, which may affect the external validity of the findings. Additionally, the short follow-up period restricted assessment to early postoperative outcomes only, without evaluating long-term analgesic efficacy or recovery parameters. Future multicenter randomized trials with larger sample sizes and longer follow-up are recommended to better compare ESPB and OSTAP, and to establish standardized dosing and technique protocols for laparoscopic procedures.

CONCLUSIONS

It was concluded that ultrasound-guided erector spine block (ESPB) is more effective than transversus abdominis plane (OSTAP) block in reducing postoperative pain. ESPB resulted in lower NRS scores across age groups, procedure durations, and genders. ESPB demonstrated superior analgesic depth and consistent pain relief in the first 12 hours after surgery.

Authors' Contribution

Conceptualization: SSA

Methodology: RA, DN, AT

Formal analysis: SK, SSS, AA, HM, MAAK

Writing and Drafting: SSA, MA, SK, SSS

Review and Editing: SSA, MA, RA, DN, AT, SK, SSS, AA, HM, MAAK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Association of Gestational Hypertension with Neonatal Cardiovascular Physiology

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ABSTRACT

Gestational hypertension (GH) is a common hypertensive disorder of pregnancy associated with increased maternal and neonatal risks. While its impact on maternal cardiovascular health is well-established, its effects on neonatal cardiovascular physiology remain insufficiently explored. **Objective:** To examine the association between GH severity and neonatal cardiovascular outcomes. **Methods:** A cross-sectional observational study was conducted at Health Net Hospital, Peshawar, including 150 mother-neonate pairs diagnosed with GH. Participants were categorized into mild, moderate, and severe GH groups per ACOG criteria. Neonatal cardiovascular parameters heart rate, blood pressure, pulmonary artery pressure, LVEF, and CHD, were assessed. One-way ANOVA and Chi-square tests analyzed group differences, while logistic regression identified independent predictors of NICU admission. **Results:** Of the 150 neonates, 34% required NICU admission, with all severe GH cases admitted ($p < 0.001$, Cramer's $V = 0.638$). One-way ANOVA showed no significant differences in heart rate, blood pressure, or LVEF across GH groups ($p > 0.05$), though LVEF showed a borderline trend ($p = 0.059$). Logistic regression confirmed GH severity as an independent predictor of NICU admission (OR: 0.181, 95% CI: 0.097–0.339, $p < 0.001$), while birth weight was non-significant ($p = 0.575$). **Conclusions:** It was concluded that the severity of gestational hypertension is significantly associated with adverse neonatal cardiovascular outcomes, particularly NICU admission. GH severity independently predicted NICU requirement, emphasizing the need for close monitoring and early intervention in pregnancies complicated by moderate to severe GH.

INTRODUCTION

Gestational hypertension (GH), defined as new-onset hypertension after 20 weeks of gestation without proteinuria, affects approximately 1% to 6% of pregnancies in Western countries [1]. GH poses notable risks to both maternal and fetal health, including preterm delivery, fetal growth restriction, and placental abruption [2, 3]. Although the long-term cardiovascular risks for women with GH chronic hypertension and cardiovascular disease (CVD) are well documented, the immediate cardiovascular effects on neonates remain underexplored. Most existing literature

has focused on preeclampsia, leaving the impact of GH itself, particularly across its severity spectrum, insufficiently studied [4, 5]. Given the rising incidence of hypertensive disorders in pregnancy, understanding how GH severity affects neonatal cardiovascular parameters is essential. While a few studies have touched on neonatal outcomes in hypertensive pregnancies [6], data specifically examining GH severity and its correlation with neonatal cardiovascular function, including parameters like heart rate, blood pressure (BP), left ventricular ejection



fraction (LVEF), and Neonatal Intensive Care Unit (NICU) admission, are scarce.

This study addresses the identified gap by evaluating the association between GH severity (mild, moderate, severe) and detailed neonatal cardiovascular outcomes. This study aims to determine whether increasing GH severity independently predicts adverse neonatal cardiac parameters and NICU admission, thereby contributing evidence to guide perinatal care and risk stratification.

METHODS

This cross-sectional observational study was conducted at Health Net Hospital, Peshawar, from October 2023 to October 2024, after obtaining ethical approval from the Ethics Review Committee (Approval Ref No: 3060/HNH/HR). The study aimed to assess the association between gestational hypertension (GH) and neonatal cardiovascular physiology. A total of 150 mother-neonate pairs were enrolled using non-probability consecutive sampling. The sample size was determined using Open Epi version 3.01. A total of 150 mother-neonate pairs was calculated based on a 95% confidence interval, 5% margin of error, and an expected NICU admission prevalence of 40% in gestational hypertension cases. The calculation used the standard formula for single population proportion: $n = [Z^2 \times P(1-P)] / d^2$, where $Z=1.96$, $p=0.40$, and $d=0.05$. This prevalence was derived from a prior study by Khan et al., (2022) [7], which highlighted neonatal complications associated with GH. This ensured sufficient statistical power and external validity for our analysis. This sampling method was chosen for its feasibility, although it may limit generalizability. Inclusion Criteria: pregnant women aged 18–45 years, Singleton pregnancies diagnosed with GH after 20 weeks of gestation, classified as mild, moderate, or severe per ACOG guidelines, Deliveries at ≥ 32 weeks of gestation, and Live-born neonates with complete cardiovascular assessment data. Exclusion criteria: chronic hypertension, preeclampsia, or eclampsia, Multiple gestations, Neonates with congenital anomalies or requiring immediate surgery, and Incomplete maternal or neonatal records. Data were collected using a structured proforma from patient records and direct assessments. Maternal variables included age, gravida, parity, BMI, mode of delivery, onset and severity of GH, antihypertensive use, proteinuria, and antenatal booking. Neonatal data included gender, birth weight, Apgar scores (1 min, 5 min), gestational age (term/preterm), NICU admission, and resuscitation status. Cardiovascular variables assessed were heart rate, systolic/diastolic BP, oxygen saturation, pulmonary artery pressure, LVEF, patent ductus arteriosus (PDA), interventricular septal thickness, right ventricular (RV) function, congenital heart disease (CHD), cardiomegaly, and inotrope requirement. Maternal BP was measured using a calibrated sphygmomanometer. GH was defined as BP $\geq 140/90$ mmHg

on two readings ≥ 4 hours apart. Neonatal cardiovascular evaluations were conducted by a Pediatric Cardiologist using Doppler echocardiography following standardized protocols. Resuscitation needs were assessed according to NRP guidelines. To ensure inter-observer reliability, a single cardiologist performed all echocardiographic evaluations. Maternal BP was measured thrice and averaged. Content validity of the proforma was ensured through expert review. Criterion validity was established by cross-checking echocardiographic findings with hospital records. Statistical validity was supported by Shapiro-Wilk and Levene's tests, and the Hosmer-Lemeshow test for logistic regression. Analysis was performed using SPSS version 23.0. A p -value < 0.05 was considered statistically significant. Continuous variables were reported as mean $\pm$ SD; categorical variables as frequencies and percentages. Shapiro-Wilk test, Q-Q plots, and skewness/kurtosis were used to test normality. One-way ANOVA compared cardiovascular outcomes (HR, BP, LVEF) across GH severity groups. Homogeneity of variance was assessed via Levene's test. Tukey's or Games-Howell post-hoc tests were used as appropriate. Chi-square tests analyzed categorical outcomes (NICU admission, CHD). Bonferroni correction and Cramer's V were applied for post-hoc significance and strength of association. Binary logistic regression was used to assess GH severity as a predictor of NICU admission. Variables included GH severity, gestational age, and birth weight. Adjusted odds ratios (OR) with 95% CI were reported. Model fit was assessed using the Omnibus test, Hosmer-Lemeshow test, classification accuracy, and Nagelkerke R^2 .

RESULTS

Most mothers were around 30 years old, and the majority delivered at term. Vaginal delivery was most common. Moderate and mild GH were more frequent than severe GH. Antihypertensive use and proteinuria were reported in nearly half and two-thirds of cases, respectively. Most mothers had booked antenatal care. Among neonates, mean birth weight and Apgar scores were within normal range. However, 34% required NICU admission and 42% were born preterm, indicating adverse neonatal effects despite generally stable maternal parameters (Table 1).

Table 1: Maternal and Neonatal Demographic and Clinical Characteristics (n=150)

Variables		Values
Maternal Characteristics		
Maternal Age (Years)	Range: 16.9–42.3	29.59 $\pm$ 4.71
Gravida	G1	45 (30.0%)
	G2	61 (40.7%)
	G3	31 (20.7%)
	G4	13 (8.7%)
Parity	P0	45 (30.0%)
	P1	61 (40.7%)

	P2	31(20.7%)
	P3	13(8.7%)
Gestational Age at Delivery (Weeks)	Range: 32.8–41.4	37.18 ± 1.78
Mode of Delivery	Normal Vaginal	90(60.0%)
	C-Section	51(34.0%)
	Assisted	9(6.0%)
Body Mass Index	Range: 17.2–38.3	28.02 ± 4.18
Pre-existing Conditions	Yes	53(35.3%)
	No	97(64.7%)
GH Onset	Early	43(28.7%)
	Late	107(71.3%)
GH Severity	Mild	61(40.7%)
	Moderate	63(42.0%)
	Severe	26(17.3%)
Antihypertensive Use	Yes	72(48.0%)
	No	78(52.0%)
Proteinuria	Present	94(62.7%)
	Absent	56(37.3%)
Antenatal Care	Booked	116(77.3%)
	Un-booked	34(22.7%)
Neonatal Characteristics		
Gender	Male	70(46.7%)
	Female	80(53.3%)
Birth Weight (Grams)	Range: 1651–3865	2802.39 ± 410.87
Apgar Score	1 min / 5 min	7.01 ± 1.34 / 7.50 ± 1.40
NICU Admission	Yes	51(34.0%)
	No	99(66.0%)
Resuscitation Needed	Yes	57(38.0%)
	No	93(62.0%)
Gestational Age at Birth	Preterm (<37 Weeks)	63(42.0%)
	Term (≥37 Weeks)	87(58.0%)

Neonatal vitals (heart rate, BP, oxygen saturation) were largely within normal limits. LVEF and RV function indicated good cardiac output in most cases. However, PDA was observed in 48%, and 15–18% of neonates had CHD, cardiomegaly, or required inotropes, suggesting subtle cardiovascular stress despite stable averages (Table 2).

Table 2: Neonatal Cardiovascular Physiology Parameters

Parameter	Unit	(Mean ± SD) / Frequency (%)
Heart Rate	bpm	140.76 ± 10.70
Systolic Blood Pressure	mmHg	65.68 ± 4.61
Diastolic Blood Pressure	mmHg	39.81 ± 5.20
Oxygen Saturation	%	96.27 ± 2.26
PDA	Present	72 (48.0%)
	Absent	78 (52.0%)
Pulmonary Artery Pressure	mmHg	30.32 ± 7.23
LVEF	%	59.96 ± 4.51
RV Function	Normal	133 (88.7%)
	Impaired	17 (11.3%)
Interventricular Septal Thickness	mm	3.96 ± 0.52
CHD	Yes	Yes: 15 (10.0%)
	No	135 (90.0%)
Cardiomegaly	Yes	27 (18.0%)
	No	123 (82.0%)
Inotropes Needed	Yes	22 (14.7%)
	No	128 (85.3%)

One-way ANOVA showed no significant differences in continuous variables across GH groups. LVEF had a borderline p-value (0.059) but was not significant after correction. Chi-square tests revealed a strong association between GH severity and NICU admission (p=0.000, Cramer's V=0.638). Other outcomes like PDA, CHD, and inotrope use showed no significant variation (Table 3).

Table 3: Association of GH Severity with Neonatal Cardiovascular Outcomes

Neonatal Variables	Mild GH	Moderate GH	Severe GH	p-value	Statistical Test	Interpretation
Heart Rate (bpm)	140.16 ± 11.68	140.70 ± 10.16	142.31 ± 9.78	0.695	One-Way ANOVA	No Significant Difference
Systolic BP (mmHg)	65.95 ± 4.65	65.84 ± 4.42	64.65 ± 5.03	0.458	One-Way ANOVA	No Significant Difference
Diastolic BP (mmHg)	39.72 ± 5.14	39.83 ± 4.95	39.96 ± 6.10	0.980	One-Way ANOVA	No Significant Difference
Pulmonary Artery Pressure (mmHg)	30.51 ± 6.86	29.53 ± 7.38	31.78 ± 7.71	0.398	One-Way ANOVA	No significant difference
LVEF (%)	58.91 ± 4.30	60.78 ± 4.89	60.44 ± 3.64	0.059	One-Way ANOVA	Trend (NS After Bonferroni Correction, p=0.198)
NICU Admission (Yes)	13 (21.3%)	12 (19.0%)	26 (100.0%)	<0.001	Chi-square	Significant (Cramer's V=0.638)
PDA (Present)	28 (45.9%)	29 (46.0%)	15 (57.7%)	0.553	Chi-square	No significant difference
CHD (Yes)	9 (14.8%)	4 (6.3%)	2 (7.7%)	0.270	Chi-square	No significant difference
Cardiomegaly (Yes)	9 (14.8%)	15 (23.8%)	3 (11.5%)	0.271	Chi-square	No significant difference
Inotropes Needed (Yes)	10 (16.4%)	11 (17.5%)	1 (3.8%)	0.226	Chi-square	No significant difference

Statistical tests: One-Way ANOVA for continuous variables, Chi-square test for categorical variables

Findings display the results of a logistic regression model analysing predictors of NICU admission. GH severity emerged as a strong and statistically significant predictor (OR: 0.181, 95% CI: 0.097–0.339, p<0.001). The odds ratio below 1 indicates that higher GH severity was associated with markedly increased odds of NICU admission. The narrow 95% confidence interval confirms the precision and robustness of this effect, directly addressing the journal comment regarding the importance of interpreting CIs for key outcomes. Gestational age at birth showed a borderline association (p=0.070), suggesting that preterm delivery may also contribute to NICU admissions, although not significantly in this model. Birth weight was not a

significant predictor ($p=0.575$), and its odds ratio was nearly 1 (1.000), indicating a negligible impact in the presence of other variables. The model's goodness-of-fit was acceptable, with a Nagelkerke R^2 value of 0.348, indicating that roughly 35% of the variability in NICU admission could be explained by the included predictors. These results emphasize GH severity as a clinically relevant and statistically validated independent predictor of adverse neonatal outcomes, particularly NICU requirement (Table 4).

Table 4: Binary Logistic Regression Predicting NICU Admission ($n=150$)

Predictors	B	SE	Wald	p-value	OR (Exp (B))	95% CI for OR
GH Severity	-1.710	0.321	28.43	<0.001	0.181	0.097-0.339
Gestational Age (Preterm)	0.746	0.411	3.29	0.070	2.108	0.942-4.720
Birth Weight (g)	0.000	0.001	0.315	0.575	1.000	0.999-1.001
Constant	1.954	1.607	1.479	0.224	7.059	—

The graph shows a direct relationship between gestational hypertension (GH) severity and NICU admission. In mild GH, 21.3% of neonates required NICU care, while 19% were admitted in moderate GH cases. However, all neonates (100%) born to mothers with severe GH required NICU admission. This trend highlights the impact of worsening maternal hypertension on neonatal outcomes, emphasizing the need for early intervention (Figure 1).

NICU Admission vs. GH Severity

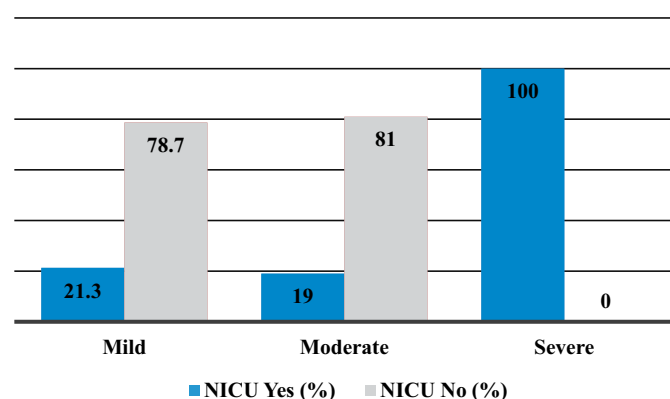


Figure 1: NICU Admission vs GH Severity

DISCUSSION

The findings of this study underscore a significant association between the severity of gestational hypertension (GH) and adverse neonatal cardiovascular outcomes. Notably, a marked increase in NICU admissions was observed among neonates born to mothers with severe GH, with all such cases requiring intensive care. This aligns with existing literature indicating that hypertensive disorders during pregnancy significantly elevate neonatal complications, including preterm birth and NICU admissions [4, 8]. Similar findings have been reported by Bromfield *et al.*, who demonstrated increased neonatal intensive care needs associated with severe hypertensive disorders in pregnancy [9]. Additionally, Li *et al.*, found comparable results, reinforcing the strong predictive relationship between hypertensive severity and neonatal outcomes [10]. The logistic regression analysis in this study identified GH severity as an independent predictor of NICU admission, even after adjusting for gestational age

and birth weight. Similar findings were documented by Lin *et al.*, and Rocha de Moura *et al.*, who reported severe GH as a critical determinant of adverse neonatal outcomes [11, 12]. Bond *et al.*, emphasized the necessity for stringent prenatal monitoring in severe GH cases to minimize neonatal morbidity [13]. Furthermore, the precision of our findings is reflected by the narrow confidence interval for GH severity (OR: 0.181, 95% CI: 0.097-0.339), reinforcing the robustness and reliability of this association. Interestingly, while severe GH was significantly associated with higher NICU admissions, other neonatal cardiovascular parameters, including heart rate, blood pressure, pulmonary artery pressure, and left ventricular ejection fraction (LVEF), did not differ significantly across GH severity categories. This finding aligns with recent studies by Miranda *et al.*, and Täufer *et al.*, who observed that maternal hypertensive disorders did not consistently impact specific cardiovascular parameters despite influencing overall neonatal morbidity [14, 15]. A potential explanation for this could be that neonatal compensatory mechanisms, such as improved cardiac resilience or rapid postpartum adaptation, might mitigate detectable differences across severity groups [16]. Although birth weight is widely recognized as a predictor of neonatal outcomes, it was non-significant in our logistic regression model ($p=0.575$). One possible explanation is multi-collinearity, as birth weight and gestational age may overlap in predicting neonatal outcomes. This is supported by findings from Phoswa *et al.*, and Baschat *et al.*, who identified gestational age as a more robust predictor of neonatal morbidity than birth weight alone, particularly in hypertensive pregnancies [17, 18]. It is also plausible that, in severe GH cases, preterm delivery rather than birth weight per se directly contributes to neonatal risk, a theory echoed by Kulkarni *et al.*, [19]. Future models should consider multi-collinearity assessments or interaction analyses to more accurately elucidate the independent effects of these variables. Our study also indicated a borderline significance in gestational age ($p=0.070$), suggesting a possible confounding role. Similar borderline effects have been previously reported by Tcheugui *et al.*, and Zbelo *et al.*, who stressed the importance of careful

interpretation of gestational age effects, especially in the context of maternal hypertension [20, 21]. In summary, this study emphasizes the critical need for early detection and effective management of GH to optimize neonatal outcomes. The demonstrated significant association between GH severity and NICU admission supports targeted prenatal care strategies.

The relatively small sample size and single-center design may limit the generalizability of the findings. Additionally, potential confounding factors such as maternal comorbidities and treatment variations were not fully controlled. Further research into underlying biological mechanisms and intervention strategies could substantially benefit clinical practice, enhancing neonatal health outcomes in pregnancies complicated by hypertension.

CONCLUSIONS

It was concluded that this study highlights a significant association between GH severity and neonatal cardiovascular outcomes, notably emphasizing GH severity as a critical predictor of NICU admission. Although other neonatal cardiovascular parameters were not significantly affected, the strong predictive value of GH severity underscores the need for early detection, close prenatal monitoring, and targeted clinical interventions. Implementing tailored management strategies for hypertensive pregnancies is crucial for enhancing neonatal health outcomes and reducing associated complications.

Authors' Contribution

Conceptualization: SA

Methodology: AM, SB, HG, KA

Formal analysis: SA, IK, AM

Writing and Drafting: SA, IK, AM, KA

Review and Editing: SA, IK, AM, SB, HG, KA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Preoperative Total Leukocyte Count: A Key Predictor for Better Optimization and Conversion Risk in Laparoscopic Cholecystectomy for Cholelithiasis

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ABSTRACT

Gallstone disease requires laparoscopic cholecystectomy (LC) as the standard of care. Sometimes, the surgeon decides to convert LC to open cholecystectomy (OC) for patient safety. Several factors help us predict preoperatively whether there is any chance of conversion of LC to OC. The role of elevated total leucocyte count (TLC) as a predictor for conversion is being proposed. This study investigates the association between pre-operative TLC levels and conversion rates from LC to OC. **Objective:** To determine the association between increased TLC and conversion from LC to OC. **Methods:** This study was conducted at Al-Tibri Medical College Hospital, Karachi, over eighteen months from 1st July 2023 to 31st December 2024. A total of 230 patients were included. We selected 115 patients with TLC above $11.0 \times 10^9/L$ and 115 patients with non-elevated TLC. All patients underwent LC, and conversions to OC were recorded. Data were analyzed using SPSS version 23.0. Mean and standard deviation were computed for numerical variables, and percentages for categorical variables. The chi-square test was applied to find the association between categorical variables. The relative risk (RR) was calculated to compare the risk of conversion of LC to OC among Elevated and Non-elevated TLC Groups. **Results:** The average age of patients was 31.82 ± 10.06 years. The conversion risk was 117% higher in the elevated TLC group compared to the non-elevated TLC group ($RR=2.17$, 95%CI: 1.32-3.56). **Conclusions:** It was concluded that elevated pre-operative TLC is significantly associated with a higher risk of conversion from LC to OC, indicating its potential as a predictive factor for surgical planning.

INTRODUCTION

Gallstone disease is a common condition requiring surgical intervention, with 6-8% of the global population affected by cholelithiasis [1, 2]. Laparoscopic cholecystectomy (LC) has become the gold standard due to its benefits in reducing hospital stay and promoting faster recovery [3, 4]. Despite its advantages, complications such as visceral injuries, hemorrhage, bile leaks, and strictures can necessitate conversion to open cholecystectomy (OC), increasing hospital stay, cost, and morbidity [4-6]. Conversion rates from LC to OC vary significantly, reported between 2% and 15% in various studies [7]. Factors

influencing conversion include patient anatomy, surgeon experience, and equipment quality [8, 9]. Identifying pre-operative predictive factors like TLC can aid in stratifying patients' risk for conversion [9, 10]. Several recent studies have explored the role of elevated pre-operative Total Leucocyte Count (TLC) in predicting conversion from laparoscopic to OC [9-11]. Elevated TLC is often considered a marker of systemic inflammation. Inflammation leads to increased tissue adhesions and distorted anatomy, which may complicate the laparoscopic procedure and necessitate conversion to open surgery. Amin et al.,



demonstrate that patients with elevated pre-operative TLC were significantly more likely to undergo conversion from LC to OC due to these complications [10]. A study by Dinçer *et al.*, also confirmed that elevated TLC is a significant predictor for conversion, suggesting that it could be integrated into pre-operative risk assessments [12]. However, conflicting evidence exists. While many studies have reported an association between elevated TLC and conversion rates, others have failed to establish a clear link [11]. This variability could be due to differences in patient populations, surgical expertise, and the degree of underlying inflammation. Some researchers argue that while TLC is useful in assessing the overall inflammatory status of the patient, it may not be a standalone factor in predicting conversion, and other factors such as patient anatomy and surgeon experience should also be considered [9-11]. This study aims to assess whether elevated pre-operative TLC is an independent risk factor for conversion from LC to OC. By identifying potential predictors such as TLC, surgical planning can be improved, and high-risk patients can be identified more accurately, thereby reducing the likelihood of complications and improving patient outcomes.

Although elevated pre-operative Total Leukocyte Count (TLC) has been proposed as a predictor for conversion from laparoscopic to open cholecystectomy, existing evidence remains inconsistent. Moreover, there is limited local data evaluating TLC as an independent predictor, highlighting the need for further investigation in this population. This study aims to determine the association between increased TLC and the conversion from laparoscopic cholecystectomy to open cholecystectomy.

METHODS

This analytical cross-sectional study was conducted at Al-Tibri Medical College Hospital, Karachi, after obtaining approval from the Institutional Ethical Review Committee (ref no. ATMC/IERC/13th/01-2023/04). It spanned over 18 months from 1st July 2023 to 31st December 2024. The sample size was calculated using the Open Epi online software for sample size calculation. Keeping the following values, with hypothesized frequency of cholelithiasis at 18.2 % as reported in a recent local study, the sample size was 230 at a 95% confidence level and a 5% margin of error. Therefore, 230 patients were included in the study [13]. Sample size $n = [DEFF * Np(1-p)] / [(d^2 / Z^2(1-\alpha/2 * (N-1) + p * (1-p))]$.

Table 1: Sample Size for Frequency in a Population

Variables	Sample Size
Total population size, considered in statistical tests (N)	1000000
The expected % frequency of the outcome factor found in the population (p)	18.2% +/-5
Assume 100 as the starting amount; confidence limits are then represented as a percentage (d)	5%

The design effect (DEFF) is important for cluster surveys	1
95%	229
80%	98
90%	162
97%	281
99%	395
99.9%	645
99.99%	901

Results from Open Epi, Version 3, open source calculator—SS-Propor. An equal number of participants diagnosed with symptomatic cholelithiasis were included in the present study, falling in two categories, TLC >11.0 X 10⁹ and TLC < 11.0 X 10⁹, comprising a total count of 230 patients. Patients with TLC >11.0 X 10⁹ were labelled as Elevated TLC Group, and those with TLC <11.0 X 10⁹ as Non-elevated TLC Group. The sampling technique employed was stratified random sampling. Patients included in the study were aged 18 to 60 years. Informed consent was obtained, and confidentiality was maintained. Patients were diagnosed with cholelithiasis based on history (right hypochondrial and epigastric pain may or may not radiating to back, pain and indigestion followed by intake of fatty food), detailed physical examination (Tenderness in right hypochondrium, Heart rate, presence /absence of jaundice), laboratory investigations including Complete blood count and Liver function tests and ultrasound reports (size and number of stones in gallbladder, gall bladder wall thickness of 3mm or less, presence/absence of pericholecystic fluid, common bile duct diameter 0.4cm or less.). All ultrasound examinations were performed by an experienced sonologist with a minimum of five years of experience. Confounding variables were controlled by excluding high-risk patients, including acute cholecystitis, empyema, gangrene, or gallbladder perforation; patients requiring common bile duct exploration or experiencing perioperative complications were not included. Patients with known comorbidities, pregnant women, children, and those unable to provide informed consent were also excluded from the study. Each patient underwent a standard four-port laparoscopic cholecystectomy performed by a consultant general surgeon with a minimum of five years of post-fellowship experience. The primary outcome measured was the rate of conversion from laparoscopic to open cholecystectomy in patients with elevated versus non-elevated TLC, which was recorded along with the reasons for conversion (difficult anatomy and presence of dense adhesions). Data were analyzed using SPSS version 23.0 Numerical variables were summarized using mean and standard deviation, while categorical variables were summarized by their frequencies and percentages. Researchers carried out the Chi-square test. A Chi-square test is used to check if there is a strong link between two sets of categorical variables. It

was used here to find out if people in the control group had different conversion rates than people in the test group. The data was found to be significant, since the p-value was below 0.05, and this led to rejecting the null hypothesis. The relative risk (RR) was calculated using data from a 95% confidence interval. Relative Risk (RR) is used to measure how likely it is for LC to turn into OC in the Elevated and Non-elevated TLC Groups.

RESULTS

The average age of patients in the Elevated TLC Group was 31.82 ± 10.06 years, compared to 28.8 ± 8.62 years in the Non-elevated TLC Group. There were 144 male and 86 female patients. The gender distribution showed a higher proportion of males in both the Elevated TLC Group (73%) and Non-elevated TLC Group (52.2%)(Figure 1).

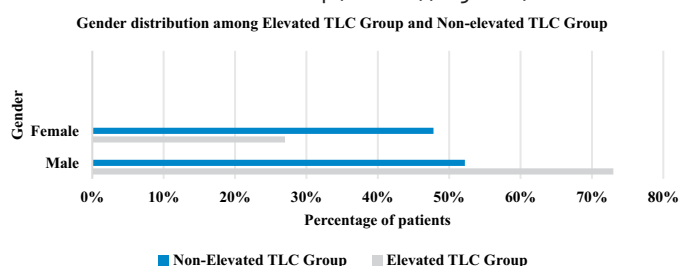


Figure 1: Gender Distribution of the Patients Concerning Groups

There is a statistically significant difference in age between the Elevated and Non-elevated TLC Groups. On average, the Elevated TLC Group is older by about 3 years, and this difference is significant ($p=0.027$)(Table 2).

Table 2: Demographic Characteristics of Patients in Each Group (n=115)

Variables	Elevated TLC Group (TLC $>11.0 \times 10^9/L$)	Non-elevated TLC Group (TLC $11.0 \times 10^9/L$)	p-Value
Number of Patients	115	115	*0.027
Age (mean $\pm$ SD)(Years)	31.82 ± 10.06	28.8 ± 8.62	

*Statistically Significant at $p\text{-value} < 0.050$

LC was converted to OC at a conversion rate of 24.8%. More patients in the Elevated TLC Group (33.9%) had their LC progress to OC, in comparison to the Non-elevated TLC Group (15.7%). It was found that LC may sometimes become OC. Subjects in the Elevated TLC Group were twice as likely ($RR=2.17$) to require surgery after an attempted laparoscopic procedure, compared to subjects in the Normal TLC Group who did not need surgery. The result shows that the association is statistically significant, with a small p-value of 0.001 and a confidence interval (CI) that prevents the estimate from being greater than 1. Our study indicates that there is very little chance that our result came about by chance (Table 3).

Table 3: Conversion Rates of Laparoscopic Cholecystectomy to Open Cholecystectomy in Elevated TLC Group and Non-Elevated TLC Groups

Conversion to Open Surgery	Elevated TLC Group (%)	Non-elevated TLC Group (%)	Total (%)	Relative Risk (RR)	95% CI	p-value
Yes	33.9%	15.7%	24.8%	2.17	1.32 - 3.56	*0.001
No	66%	84%	75.2%			

Statistical Significant at $p\text{-value} < 0.050$

It examines how likely certain groups are to switch from a condition called LC to one called OC, comparing those with total leucocyte count (Elevated TLC Group) to those with normal total leucocyte count (Non-Elevated TLC Group). Males categorized in the Elevated TLC Group underwent conversion to OC more than twice as often (38%) than males in the Non-elevated TLC Group (19.4%). They were twice as likely to require conversion, with a relative risk (RR) of 2.03. The difference between the groups was found to be statistically significant ($p=0.022$). Those with higher TLC levels were more likely to be converted to surgery as female patients (30%) compared to male patients (14.3%). For patients aged ≤ 40 , more people in the Elevated TLC Group (35%) converted to OC compared with the Non-elevated TLC Group (14.1%). It is shown by $RR=2.47$ that the risk of conversion is nearly doubled. According to the statistical results, the finding was highly significant ($p=0.001$). For patients over 40, the change in conversion rates between the groups did not reach a statistically significant difference. Younger individuals (aged less than 40) and male patients in the Elevated TLC Group had a much higher chance of converting OC from LC. The findings suggest that age and gender might affect conversion risk in people exposed to what was studied (Table 4).

Table 4: Conversion Rates from LC to OC Stratified by Gender and Age Group

Variables	Group	Elevated TLC Group (%)	Non-elevated TLC Group (%)	Relative Risk (RR)	95% CI	p-value
Gender	Male	38	(19.4)	2.03	1.09	*0.022
	Female	30	(14.3)			
Age	≤ 40	35	(14.1)	2.47	1.40	*0.001
	> 40	26.7	(21.7)			

DISCUSSION

On average, 24.8% of LC patients are converted to OC in our series, whereas studies from other countries show that usually between 2% and 15% of LC patients are switched to OC [4, 5]. A report from Pakistan reports that 3.7% of LC cases are diagnosed as OC [4], but another report cites a higher conversion rate of 7.78% [11]. Because we are studying how LC converts to OC in patients with increased TLC, and since the conversion rate of LC to OC in that group is high, standing at 33.8%. High TLC levels in patients before surgery are strongly linked to an increased risk of converting from LC to OC. Greater TLC in the blood points to silent cholecystitis or ongoing inflammation, which complicates surgery and leads to converting the procedure to open surgery. Oymaci *et al.*, reported that patients with higher TLC were more likely to undergo conversion because of stronger adhesions and difficulties during surgery, which is similar to what we observed [14]. Multiple studies agree that TLC can be used to forecast the chance of conversion in surgery. Dinçer *et al.*, found that a higher TLC is a major risk for developing PC [12], whereas Amin *et al.*, reported that elevated TLC before LC greatly increased the chances of a conversion operation [10]. We found that male patients were more often converted during surgery, which is in agreement with various other studies [15, 16]. This may be due to more severe disease at the time of presentation or more complex anatomy in males, which complicates laparoscopic dissection, however, few studies contradict these findings [17]. Additionally, younger patients (≤ 40 years) with elevated TLC had a significantly higher risk of conversion in our study, which contrasts with the general assumption that older age is a stronger predictor of conversion due to the presence of more fibrosis and more comorbidity [18]. Preoperative assessment of TLC can serve as an important tool in surgical planning. Patients with elevated TLC should be considered at higher risk for conversion, allowing for more informed surgical decisions and resource allocation. Furthermore, preoperative counselling can be tailored to better prepare patients for the possibility of conversion and the associated risks [19-21].

The study was limited by its single-center design and relatively small sample size, which may affect the generalizability of the findings. Additionally, potential confounding factors such as surgeon experience, intraoperative findings, and comorbid conditions were not fully adjusted for in the analysis. Future large-scale, multicenter studies incorporating comprehensive clinical and intraoperative variables are recommended to develop more accurate predictive models for conversion from LC to OC.

CONCLUSIONS

It was concluded that there was an association between raised total leucocyte counts (TLC) and the conversion from LC to OC because patients with raised TLC undergo conversion from LC to OC more frequently. This makes Increased TLC an important predictive marker for the risk of conversion from LC to OC. Preoperative identification of patients with elevated TLC will help the surgeon in better surgical planning, improving preoperative counseling and resource allocation, and potentially enhancing patient outcomes by reducing the incidence of complications associated with delayed conversion.

Authors' Contribution

Conceptualization: HWA

Methodology: HWA, RK, TMG

Formal analysis: RK, TMG, SK, JB

Writing and Drafting: RN

Review and Editing: HWA, RK, TMG, SK, RN, JB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article



Evaluation of Variability in Macular Thickness in Primary Open Angle Glaucoma: A Spectral Domain Optical Coherence Tomography-Based Study

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ABSTRACT

Globally, glaucoma, especially primary open-angle glaucoma (POAG), is one of the leading causes of blindness. This disease is connected to damage of the optic nerve head, death of retinal ganglion cells and visual field abnormalities. **Objectives:** To check the macular thickness and total macular volume using spectral-domain optical coherence tomography (SD-OCT) among patients of POAG and subjects without glaucoma. **Methods:** The observational case-control study, where 40 participants had POAG and 40 participants the same age did not. Only the right eye or only the left eye from each subject was examined in the study. All subjects had a thorough check of their eyes which included history, eye chart testing, slit-lamp examination, dilated fundus inspection, gonioscopy and measuring intraocular pressure (IOP). Visual fields were assessed using the Humphrey Field Analyzer. Macular thickness (MT) was analyzed with SD-OCT using OCT Spectralis. Parameters evaluated were macular inner thickness (MIT), macular outer thickness (MOT), macular central thickness (MCT) and macular total volume (MTV). **Results:** Patients with POAG exhibited markedly reduced MTV, MIT and MOT in comparison to healthy controls, with the greatest decline observed in the temporal as well as the inferior quadrants. These observations confirm that structural differences in the macular parameters are correlated with glaucoma and can aid in early diagnosis and monitoring progression. **Conclusion:** This study emphasizes the diagnostic utility of SD-OCT in determining macular thickness variability in individuals with POAG. Our findings show that macular thickness is much lower in glaucomatous eyes than in healthy controls, with distinct patterns of regional thinning indicating retinal ganglion cell vulnerability.

INTRODUCTION

When a person has glaucoma, the retinal ganglion cells (RGCs) and their axons are damaged, which results in damage to the optic nerve and certain kinds of visual field problems [1, 2]. It is well-known around the globe as one of the main causes of permanent vision problems [3]. To manage the disease and save vision, it's very important to identify it early and watch it closely [2, 4]. Glaucoma is clinically recognized by checking for damage to the optic nerve head and measuring visual field defects. Using standard perimetry, abnormalities in the visual field are found only after much of the retinal nerve fiber layer (RNFL) is affected [5]. Appropriate diagnosis of glaucomatous

damage in the early stages helps save sight. Because of this, testing the retinal nerve fiber layer and the retinal ganglion cell layer helps find glaucoma at an early stage [6]. Examining the macula is interesting because it contains a big group of retinal ganglion cells, many of which are affected in the early stages of glaucoma. The macular area has 4-6 layers containing ganglion cells, which make up about 30-35% of its total thickness. For this reason, damage to macular ganglion cells causes the retinal nerve fiber layer to become much thinner [7]. There is a strong connection between RNFL thinning, reduced vision fields, changes in macular thickness and reduced ganglion cell



density, which means looking at the macula can provide important information about the early stages of glaucoma [8, 9]. SD-OCT is now used regularly to capture detailed cross-sectional images of the retina. By using SD-OCT, you can identify inner retinal and macular thickening, which makes it valuable for diagnosing the early effects of glaucoma, especially when there is little to no thinning around the optic nerve [10]. POAG causing changes in the macular area has attracted more attention because studies suggest that early glaucomatous change may take place in the macula and lead to problems with central vision. At the moment, it is not understood why there can be significant differences in macular thickness within glaucomatous eyes. This variability is necessary for us to detect health problems, observe changes in the condition and decide what care should include. Based on what we saw in the reviewed research, we proposed that SD-OCT values for macular thickness are the same in eyes with primary open-angle glaucoma as in those of similarly-aged healthy people. These metrics measured with SD-OCT can play a big role in detecting early changes in the macula of glaucoma patients and may be used for diagnosis and tracking of POAG.

Although SD-OCT is widely used for glaucoma assessment, variability in macular thickness parameters in POAG and their diagnostic significance remain unclear. Moreover, there is limited local evidence comparing region-specific macular measurements between POAG patients and healthy individuals. This study aims to evaluate region-specific macular thinning in POAG eyes compared to healthy individuals. Macular central thickness (MCT), macular inner thickness (MIT), macular outer thickness (MOT), and macular total volume (MTV) in POAG patients are compared to healthy individuals.

METHODS

This observational case-control study was carried out at the Al-Shifa Trust Eye Hospital (ASTEH), Rawalpindi, Pakistan, from May 15th, 2024, to December 30th, 2024, using non-probability consecutive sampling. It included 80 participants segregated into two categories: Group 1 consisted of 40 individuals diagnosed with POAG, while Group 2 comprised 40 healthy control subjects. Ethical approval was obtained from the institute's Ethical Review Committee on May 3, 2024 (approval number: ERC-17/AST-24). Before enrollment, all participants provided informed consent following detailed counselling about the study. The study adhered to the principles of the Declaration of Helsinki. Patients included in the study were referred to the Glaucoma Department from the General OPD (Outpatient Department). The diagnosis of POAG in Group-1 was made on intraocular pressure (IOP) measurements of more than 21mm of Hg on Goldman applanation tonometer on at least 3 occasions, presence of glaucomatous optic nerve head

changes (a cup-disc ratio (CDR) exceeding 0.4 or an inter-eye CDR disparity greater than 0.2), and detection of characteristic visual field defects using the Humphrey Visual Field Analyzer (Carl Zeiss). Each patient exhibited loss of visual fields (mean deviation >6dB) in at least two successive automated perimetric examinations. Gonioscopy was done utilizing Posner 4-mirror gonioscopes which verified open anterior chamber angles (Shaffer grades 3 or 4) and the exclusion of secondary glaucoma or non-glaucomatous optic neuropathy. In contrast, participants in Group 2, which included the healthy participants, displayed no signs or symptoms of glaucoma, had no relevant ocular history, and had no retinal diseases. Their IOP measurements on the Goldman applanation tonometer were all below 21 mmHg on more than 2 occasions, and no abnormalities were observed in their optic nerve heads or visual fields. Exclusion criteria included subjects with a history of ocular surgery or trauma, lenticular opacities, diabetic retinopathy, macular dystrophy or degeneration, epiretinal membrane, macular edema, retinal detachment, non-glaucomatous optic nerve diseases, or spherical equivalent refractive error larger than ± 6 diopters. Open-Source Epidemiologic Statistics for Public Health, Version 3.01 [11] was used to calculate how many cases in each group should be included to allow statistical comparison. The reference study by Sharma et al., [10] shows, using a statistical power of 95%, significance of 0.05 and a 95% confidence interval, that the sample size required for the mean outer macular thickness was determined as 15 participants for each group. As a way to get a better estimate with some discrepancy in data accounted for, the groups were set at 40, giving a total of 80 participating individuals. All the participants were examined which involved taking down their history, confirming eyesight using the Snellen visual acuity chart, checking the eye on a slit lamp and seeing the back of the eye with a fundoscope. More assessment steps were performed with the 4-mirror gonioscopes for gonioscopy, and pressured IOP was measured using Goldmann Applanation Tonometry. To perform the dilated fundus examination, a +90-diopter lens was used, and perimetry was completed with the Humphrey Visual Field Analyzer (Carl Zeiss, USA). The thickness of the macula was evaluated in all patients with SD-OCT, using the OCT Spectralis (Heidelberg Engineering, Inc., Germany), by only one trained person. Macular inner thickness (MIT) was measured within the innermost 3 mm of the retina, outer macular thickness (MOT) in the region between 3 mm and 6 mm and total macular volume (MTV) was also measured. IBM SPSS Statistics version 26.0 on Windows was chosen for data analysis. To make sure continuous variables are normally distributed, the Shapiro-Wilk test was applied ahead of parametric tests. The independent t-test method was chosen to check if the given mean differences can be seen for normally distributed data. Mean plus or minus SD was

used to show quantitative data. A p-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

Muscular thickness map is shown in Figure 1.

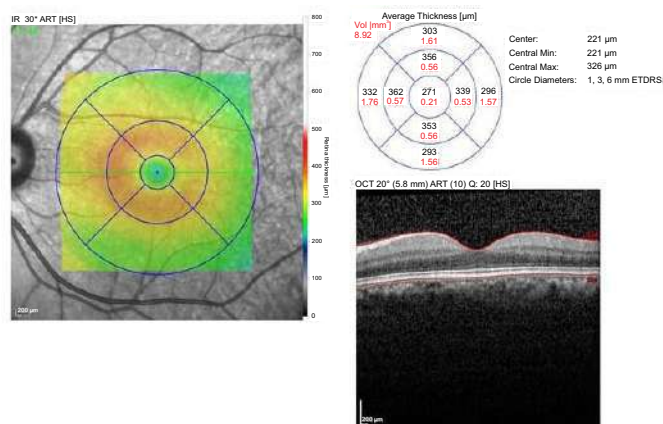


Figure 1: Macular Thickness Map

In total, 80 subjects were inducted in the study, with 40 individuals identified as POAG forming Group-1 and 40 disease-free individuals comprising Group-2. There was no remarkable age disparity between the two groups ($p=0.019$); nevertheless, the male-to-female ratio differed slightly, with Group-1 showing a nearly equal distribution (21:20) compared to Group-2 (19:22). The mean intraocular

pressure (IOP) was notably elevated in Group-1 (17.98 mmHg) compared to Group-2 (14.37 mmHg, $p<0.001$). Additionally, the cup-to-disc (CD) ratio was markedly increased in Group 1 (0.6) as compared to subjects in Group 2 (0.2, $p<0.001$), emphasizing the structural differences associated with glaucoma (Table 1).

Table 1: Baseline Demographic and Clinical Features of the Subjects

Demographic Features	Group 1 (n=40)	Group 2 (n=40)	p-Value
Age (Years)	54.83	50.28	0.019
Male: Female Patient Ratio	20:20	19:21	0.5
Cup Disc Ratio	0.62	0.26	<0.001
Mean IOP (mmHg)	17.98	14.45	<0.001

Analysis of the OCT macular thickness map demonstrated a significant decline in both inner and outer thickness of the macula across all quadrants in patients with diagnosed POAG compared to healthy controls. For macular inner thickness (MIT), Group-1 exhibited significantly lower values in the temporal ($309.76 \pm 21.05 \mu\text{m}$ vs. $319.56 \pm 16.76 \mu\text{m}$, $p=0.022$, Cohen's $d=0.52$), superior ($319.37 \pm 25.59 \mu\text{m}$ vs. $332.32 \pm 18.76 \mu\text{m}$, $p=0.011$, Cohen's $d=0.58$), nasal ($321.27 \pm 26.88 \mu\text{m}$ vs. $333.59 \pm 18.34 \mu\text{m}$, $p=0.018$, Cohen's $d=0.54$), and inferior quadrants ($315.1 \pm 24.39 \mu\text{m}$ vs. $330.2 \pm 17.33 \mu\text{m}$, $p=0.002$, Cohen's $d=0.73$) (Table 2).

Table 2: Macular Inner Thickness (MIT) Across All Quadrants

Variables	Group 1, POAG (n=40)	Group 2, Controls (n=40)	p-value	Mean Difference	95%CI Lower Limit	95%CI Upper Limit	Effect Size Cohen's d
	Mean (μm) ± SD (μm)						
Temporal	309.30 ± 21.10	319.43 ± 16.95	0.020	-10.12	-18.64	-1.60	0.52
Superior	318.90 ± 25.74	332.20 ± 18.90	0.010	-13-30	-23.35	-3.24	0.58
Nasal	320.90 ± 27.12	333.53 ± 18.57	0.017	-12-62	-22.97	-2.27	0.54
Inferior	314.53 ± 24.42	330.20 ± 17.55	0.001	-15.67	-25.14	-6.20	0.73

A similar pattern was observed for macular outer thickness (MOT), where POAG patients showed significantly thinner measurements in the temporal ($265.37 \pm 17.78 \mu\text{m}$ vs. $277.67 \pm 15.79 \mu\text{m}$, $p=0.001$, Cohen's $d=0.74$), superior ($280.32 \pm 19.60 \mu\text{m}$ vs. $290.34 \pm 14.70 \mu\text{m}$, $p=0.011$, Cohen's $d=0.61$), nasal ($294.73 \pm 23.32 \mu\text{m}$ vs. $307.27 \pm 15.83 \mu\text{m}$, $p=0.004$, Cohen's $d=0.67$), and inferior quadrants ($265.61 \pm 19.57 \mu\text{m}$ vs. $279.00 \pm 13.54 \mu\text{m}$, $p=0.001$, Cohen's $d=0.84$) (Table 3).

Table 3: Macular Outer Thickness (MOT) Across All Quadrants

Variables	Group 1, POAG (n=40)	Group 2, Controls (n=40)	p-value	Mean Difference	95%CI Lower Limit	95%CI Upper Limit	Effect Size Cohen's d
	Mean (μm) ± SD (μm)						
Temporal	265.03 ±17.87	277.63 ± 15.99	0.001	-12.60	-20.15	-5.04	0.74
Superior	279.75 ± 19.50	290.43 ± 14.87	0.007	-10.67	-18.39	-2.95	0.61
Nasal	294.18 ± 22.32	307.33 ± 16.02	0.003	-13.15	-21.80	-4.50	0.67
Inferior	264.98 ± 19.39	279.10 ± 13.70	<0.001	-14.12	-21.60	-6.65	0.84

Macular central thickness (MCT) was also found to be lower in the POAG group ($255.02 \pm 20.882 \mu\text{m}$) as compared to the control group ($260.12 \pm 18.021 \mu\text{m}$), but these results were not statistically significant ($p=0.240$, Cohen's $d=0.26$). Macular total volume (MTV) was seen to be lower in the POAG group ($8.01 \pm 0.628 \text{ mm}^3$) as compared to the healthy group ($8.39 \pm 0.391 \text{ mm}^3$, $p=0.001$, Cohen's $d=0.76$) (Table 4).

Table 4: Comparison of Macular Central Thickness (MCT) and Macular Total Volume Between Groups

Group 1, POAG (n=40)	Group 2, Controls (n=40)	p-value	Mean Difference	95%CI Lower Limit	95%CI Upper Limit	Effect Size Cohen's d
Mean (mm ³) ± SD (mm ³)						
Macular Central Thickness						
255.02 ± 20.88	260.12 ± 18.02	0.240	-5.09	-13.67	3.47	0.26
Macular Total Volume						
7.99 ± 0.62	8.39 ± 0.39	0.001	-0.39	-0.63	-0.16	0.76

These findings highlight the substantial structural alterations in macular parameters associated with glaucoma, reinforcing their diagnostic significance in differentiating glaucomatous eyes from healthy eyes. Such reductions in macular thickness and volume underline the importance of these metrics as potential biomarkers for the identification of early glaucomatous damage and monitoring of POAG.

DISCUSSION

POAG leads to a gradual loss of retinal ganglion cells and their axons, which causes optic neuropathy and typical problems with a person's field of vision [1, 12]. Glaucoma leads to vision problems mainly because many retinal ganglion cell (RGC) axons and somas atrophy, stopping visual information from reaching the brain. It is believed that injury to the retinal ganglion cells and their axons happens in the optic nerve head. Because the macula has a high number of RGCs, it is now seen as a key area for checking changes in glaucoma. Even though RGCs cannot be counted directly in the living eye, retinal thickness measurements can be taken using different methods. Since retinal thickness decreases as RGCs and retinal nerve fibers are lost, measuring thickness can show the same damage. A person may have structural damage in the RNFL and optic nerve head before any obvious sight loss [5, 12]. The researchers in this study noted a strong link between thinner macular thickness and people who are Glaucoma suspects [13]. The study backs up the results by revealing a reduction in macular thickness in POAG patients, which suggests a reduction of RGCs in the macular area. Antwi-Boasiako *et al.*, showed in their research that changes in the density of RGCs in the macula observed with OCT were linked to difficulties with vision in non-human primates [14]. Similarly, Mohammadzadeh *et al.*, argued that OCT thickness of the macula is closely linked to different visual field results, so macular OCT scans should play a role in diagnosis and treatment planning for glaucoma [15]. Yadav *et al.*, performed studies that show a strong connection between thinning of the macula and the retinal nerve layer in eyes experiencing glaucomatous damage [16]. Mehta *et al.*, agreed with the study results and reported that joining GCIP and RNFL parameters helps improve both the sensitivity and specificity for spotting the early stages of glaucoma [17]. In the study by Pedro *et al.*, using macular thickness instead of peripapillary RNFL in glaucoma screening and detecting progression offered more benefits to patients who had trouble with visual field studies [18]. We observed, as other noted, that POAG patients showed lower macular thickness inside and outside the region compared to those in the control group.

The thickness of the inner macula in POAG patients is 315.90 µm, compared to 328.84 µm in people with no disease. In the same way, POAG patients had an outer macular thickness of 275.98 µm, compared to 288.62 µm in healthy people. This pattern is strongly supported by statistics and matches what the published literature has found which confirms that macular factors are beneficial for detecting glaucoma. Doctors may use the volume of the macula as a possible marker to catch glaucoma early. The study of Nowroozzadeh *et al.*, pointed out that macular sublayer volume relates strongly to glaucoma, making it a worthy biomarker [19]. Mohammadzadeh *et al.*, proved that optical coherence tomography (OCT) volume scans can help separate patients with perimetric glaucoma from healthy individuals [20]. People with POAG showed a significantly lower mean macular volume (7.99 ± 0.62 mm³) than healthy individuals (8.39 ± 0.39 mm³) which again highlights its usefulness in diagnosis. It follows on from the previous studies and brings new findings, confirming a meaningful relationship between glaucomatous damage and the thickness and volume of the macula. It can assist in watching glaucoma as it progresses in both the early and more advanced phases. Research with more people and over time is required to check our conclusions and make sure the macular changes are good diagnostic and prognostic tools. The main problems making it difficult to notice developments in the macula are that there is no defined external standard and a lot of variation between repeat tests in patients. Moreover, examining the right-angle view change in the macula shown by SD-OCT and changes in visual evoked potentials and visual field tests might give a better understanding of glaucoma-related diagnosis and progression.

This study is limited by its cross-sectional design, which restricts the ability to assess longitudinal progression of macular changes in glaucoma. Additionally, variability in OCT measurements and lack of a standardized reference for macular parameters may affect the consistency and reproducibility of findings. Future longitudinal studies with larger sample sizes and standardized OCT protocols are recommended to validate macular thickness and volume as

reliable diagnostic and prognostic markers in glaucoma.

CONCLUSIONS

This study underlines the diagnostic value of SD-OCT in assessing macular thickness variations in patients with POAG. Our findings reveal that glaucomatous eyes have much lower macular thickness than healthy controls, with different patterns of regional thinning indicating retinal ganglion cell susceptibility. These results affirm that SD-OCT provides reliable, non-invasive, and reproducible measurements that can detect early glaucomatous changes, monitor progression, and potentially guide therapeutic interventions.

Authors' Contribution

Conceptualization: TT

Methodology: TT, FA, AA, FK

Formal analysis: TT

Writing and Drafting: MA, US

Review and Editing: TT, MA, FA, US, AA, FK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Hematological Ratios versus Disease Characteristics versus Surgeons' Experience and Expertise: What Stands Out as Predictor of Conversion to Open Cholecystectomy?

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ABSTRACT

Conversion of laparoscopic to open cholecystectomy is often a surprise for the surgeon.

Objective: To evaluate predictors like inflammatory ratios, gallbladder wall thickness and surgeons' experience to see what predicts conversion best. **Methods:** Retrospective cohort study was done on adult patients diagnosed with acute cholecystitis (Tokyo guidelines) at Surayya Azeem Hospital from 2021 to 2024. Data collected included demographics, CBC findings, surgeons' experience, operation details and ultrasound findings. Patients with chronic cholecystitis, comorbidities and other gallbladder pathologies were excluded. Ratios like NLR, MLR, PLR, SIRI, SII, NLPR and d-NLR were calculated. Chi square, Mann Whitney U, binary logistic regression and ROC analysis were used as per requirement. P-value of less than 0.05 was considered significant. **Results:** 80% of 475 patients were females. 22 (4.8%) patients underwent conversion. Old age and male gender were associated with adverse outcome. WBC count, NLR, d-NLR, SIRI, SII and NLPR were higher in conversion group. Platelet count, PLR and MLR had no associations. Higher hemoglobin (>12.3 g/dL) and ALC (> 1.8x10⁹/L) were predictive of successful laparoscopic procedure. Highest predictive value for conversion was found for NLR and d-NLR (AUC=0.84) followed SIRI (AUC=0.78) with cut-offs of 4.97, 3.76, and 1.69 respectively. Gallbladder wall thickness of >7mm (AUC=0.64) and inexperienced surgeons (AUC=0.69) also increase the probability of conversion. **Conclusion:** Systemic inflammatory indices predict conversion better than ultrasound findings and surgeons' experience. Experienced laparoscopic surgeons should operate on patients with thick gallbladder wall and high inflammatory ratios to minimize the risk of conversion.

INTRODUCTION

Laparoscopic cholecystectomy is gold standard procedure for gall bladder diseases [1]. It has replaced open cholecystectomy for most operations [2]. The reasons include early mobility of the patients, shorter hospital stay, less pain and cosmetic advantages. However, difficult cholecystectomy is commonly encountered by surgeons

that necessitates conversion to open cholecystectomy [3]. Difficult cholecystectomy has been defined by a number of parameters that include Visual Analogue scale (VAS) for pain of 8 and above, surgery spanning more than 75 minutes and/or conversion to open cholecystectomy [4]. Many factors have been associated with increased risk of



conversion. Male gender and obesity (BMI > 30 kg/m²) have higher conversion rates as compared to females and non-obese patients. Past history of acute inflammatory pathologies involving gallbladder (acute cholecystitis) and in the vicinity of gallbladder or bile duct (acute pancreatitis), as well as acute inflammation at the time of surgery have higher rate of conversion [5, 6]. Multiple long pain attacks (more than five pain attacks that last longer than four hours) predict difficult laparoscopy and subsequent conversion with high sensitivity [7]. Among comorbidities, diabetes mellitus and its association with severity of infectious diseases has a positive predictive value for conversion [5]. Past history of abdominal surgery also demands extra vigilance from the surgeon and predicts higher possibility of conversion [6]. Preoperative ultrasonographic findings are also used for predicting the course of cholecystectomy [7]. These include increased thickness of gallbladder wall, fibrosis and presence of multiple large calculi [3-7]. Therefore, preoperative ultrasound has shown great utility in predicting the fate of cholecystectomy. Intraoperative findings and difficulties play the final part in difficult decision making. Anatomical factors like abnormal Callot's triangle anatomy and intrahepatic gallbladder are difficult to operate upon [3]. Finally, the single most important finding that alerts the surgeon towards possible unsuccessful laparoscopic procedure is the presence of extensive adhesions at the time of surgery [8]. Neutrophil to lymphocyte ratio (NLR), Platelet to lymphocyte count (PLR), monocyte to lymphocyte ratio (MLR), Systemic Inflammatory Response Index (SIRI), Systemic Immune Inflammation Index (SII), Neutrophil to platelet x lymphocyte ratio (NLPR) and derived neutrophil to lymphocyte ratio (d-NLR) are ratios derived from complete blood count through calculations. These, along with ESR, are hematological markers of inflammation [9]. Like other acute inflammatory conditions, they are raised in case of acute cholecystitis and correlate with the severity of disease [10, 11]. In daily practice, it has been observed that ultrasound findings sometimes do not correlate well with disease severity. In this study, the patients were addressed without any comorbidities and extensive previous abdominal surgeries. Since gallbladder wall thickness and comorbidities have been linked to increased probability of conversion and there is divided opinion about surgeons' expertise in this regard in the literature, it was aimed to find predictive value of CBC parameters and ratios like NLR, PLR, MLR, SIRI, SII, NLPR and d-NLR for conversion of laparoscopic cholecystectomy to open procedure. CBC is readily available and cost-effective investigation with reasonable turn-around time in the context of emergency setting. Predictors derived through this test will be both easily and timely available. The predictive value will be compared with gallbladder wall thickness and surgeons'

expertise to establish which of these has highest predictive value. This, along with other adjuncts of diagnosis, will help the surgeon in anticipating clear picture of the severity of the disease, making more confident preoperative decisions and conveying clear information to the patients regarding the course of their operation. Precious time can be saved and difficulties as a result of unexpected intraoperative findings can be minimized if preoperative prediction can be strong enough to guide treatment decisions.

Although ultrasound findings and clinical factors are used to predict difficult laparoscopic cholecystectomy, their accuracy is often inconsistent. There is limited local evidence evaluating CBC-derived inflammatory markers as predictors of conversion to open cholecystectomy, highlighting a gap this study aims to address. The study aimed to determine cut-off values for these pre-operative CBC parameters along with gallbladder wall thickness on ultrasound that can guide surgeons to anticipate operative difficulty and decide what level of expertise of operating surgeon might be needed for the surgery.

METHODS

This retrospective cohort study was conducted at Surayya Azeem Hospital after obtaining ethical approval (Ref. No. 1316/25/MS/SATH). Data was collected over one week from hospital records of 457 adult patients who presented with acute cholecystitis between 2021 and 2024. Informed consent was not obtained as the study used retrospective data. Inclusion criteria were adult patients diagnosed with acute cholecystitis (Tokyo criteria) who underwent early laparoscopic cholecystectomy. Exclusion criteria included chronic cholecystitis, comorbidities, other gallbladder pathologies, and interval cholecystectomy. Data collected included demographics, clinical history, examination findings (e.g., Murphy's sign), ultrasound reports (e.g., gallbladder wall thickness), CBC (analyzed using Sysmex XN-1000), and surgeon expertise. Systemic inflammatory indices such as NLR, PLR, MLR, SIRI, SII, NLPR, and d-NLR were calculated and validated in SPSS version 27. Gallbladder wall thickness was stratified into four groups, and operative outcomes were categorized as successful laparoscopic or converted to open cholecystectomy. Well-experienced surgeons were defined as those with >200 laparoscopic cholecystectomies in the past 5 years. Statistical analysis included Chi-square for categorical variables, Kolmogorov-Smirnov for normality testing, Mann-Whitney U for comparing indices, and logistic regression for univariate and multivariate analysis. ROC analysis was performed for significant predictors, with AUC ≥0.7 considered acceptable. Findings were presented in tables and figures.

RESULTS

A total of 457 patients were included in the study. The study cohort had 90 (19.7%) male patients and 367 (80.3%) females. Male to female ratio was 1:5. Age distribution in the study population as shown in Figure 1.

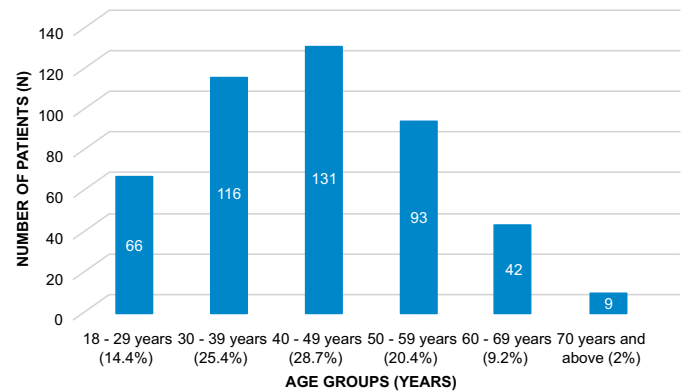


Figure 1: Patient Distribution According to Age Groups

The CBC characteristics, calculated and derived parameters are listed along with their statistics in table 1.

Table 1: CBC Parameters, Calculated and Derived Parameters

Variables	Median	Inter-Quartile Range	Minimum	Maximum	Mean $\pm$ SD
Hemoglobin (g/dL)	12.2	11.2 – 13.1	7.0	16.8	12.2 $\pm$ 1.63
WBC count (x10 ⁹ /L)	8.6	7.1 – 10.9	3.0	28	9.27 $\pm$ 3.33
Platelet count (x10 ⁹ /L)	285.0	224 – 349	33	835	297.14 $\pm$ 103.95
Absolute neutrophil count (x10 ⁹ /L)	5.39	4.21 – 7.30	1.65	25.48	6.24 $\pm$ 3.24
Absolute lymphocyte count (x10 ⁹ /L)	2.41	1.80 – 2.93	0.34	4.93	2.42 $\pm$ 0.85
Absolute monocyte count (x10 ⁹ /L)	0.34	0.24 – 0.48	0.05	6.44	0.41 $\pm$ 0.40
Neutrophil to lymphocyte ratio (NLR)	2.17	1.61 – 3.36	0.75	35.39	3.24 $\pm$ 3.35
Monocyte to lymphocyte ratio (MLR)	0.14	0.10 – 0.23	0.02	7.83	0.21 $\pm$ 0.40
Platelet to lymphocyte ratio (PLR)	120.90	88.98 – 163.83	10.55	1117.24	143.15 $\pm$ 97.72
Systemic immune inflammatory index (SIRI)	0.76	0.43 – 1.44	0.08	45.39	1.55 $\pm$ 3.29
Systemic inflammatory index (SII)	633.6	411.15 – 1012.50	58.24	11664.00	1001.81 $\pm$ 1286.47
Neutrophil to lymphocyte x platelet ratio (NLPR)	0.0081	0.0055 – 0.0124	0.0018	0.1883	0.0122 $\pm$ 0.0154
Derived neutrophil to lymphocyte ratio (d-NLR)	1.78	1.32 – 2.57	0.47	10.11	2.35 $\pm$ 1.75

The patterns of sonographic wall thickness were shown in figure 2.

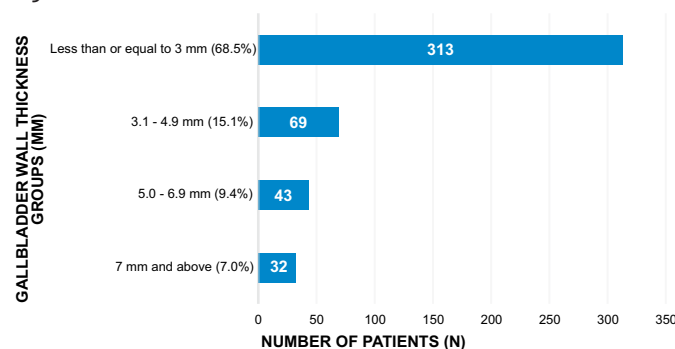


Figure 2: Gallbladder wall thickness distribution in the study population

Comparison of demographic details, CBC parameters and ratios, disease characteristics and operation details are summarized in table 2.

Table 2: Comparison of Successful Versus Converted Group

Variables	Successful Laparoscopic Cholecystectomy Frequency (%)	Conversion to Open Cholecystectomy Frequency (%)
Total patients (n=457)	435 (95.2%)	22 (4.8%)
Age (Years)		
18 – 29 Years	65 (14.9%)	1 (4.5%)
30 – 39 Years	114 (26.2%)	2 (9.1%)
40 – 49 Years	129 (29.7%)	2 (9.1%)
50 – 59 Years	81 (18.6%)	12 (54.5%)
60 – 69 Years	38 (8.7%)	4 (18.2%)
>70 Years	8 (1.8%)	1 (4.5%)
Gender		
Male	82 (18.9%)	8 (36.4%)
Female	353 (81.1%)	14 (63.6%)
CBC Parameters And Ratios (Median Values)		
Hemoglobin (g/dL)	12.3	11.6
Platelet count (x10 ⁹ /L)	285	284.5
WBC count (x10 ⁹ /L)	8.5	13.5
Absolute neutrophil count (x10 ⁹ /L)	5.31	11.8
Absolute lymphocyte count (x10 ⁹ /L)	2.46	1.47

Absolute monocyte count (x10 ⁹ /L)	0.35	0.31
Neutrophil to lymphocyte ratio (NLR)	2.17	8.45
Monocyte to lymphocyte ratio (MLR)	0.14	0.27
Platelet to lymphocyte ratio (PLR)	118.17	210.56
Systemic Immune Inflammation Index (SII)	619.84	2357.70
Systemic Inflammatory Response Index (SIRI)	0.72	3.11
Neutrophil to Platelet x lymphocyte ratio (NLPR)	0.0077	0.0216
Derived neutrophil to lymphocyte ratio (d-NLR)	1.70	5.27
Operation Characteristics (Operating Surgeon)		
Senior Consultant (n=238) (52.1%)	234 (98.3%)	4 (1.7%)
Junior Consultant (n=219) (47.9%)	201 (91.8%)	18 (8.2%)
Disease Characteristics (Gallbladder Wall Thickness)		
< 3 mm (n=313)	302 (96.5%)	11 (3.5%)
3.1 – 4.9 mm (n=69)	67 (97.1%)	2 (2.9%)
5.0 – 6.9 mm (n=43)	40 (93.0%)	3 (7.0%)
>7 mm (n=32)	26 (81.2%)	6 (18.8%)

Chi Square test was used to see if there is statistically significant association between conversion and categorical variables. Mann-Whitney U test was used to compare median values for continuous variables between the two groups.

Table 3: Statistical Significance of Difference of Variables between the Study Groups

Variables	Chi-Square~ And Mann Whitney-U Test~~ Results (p-Value)
Age (Years)	
18 – 29 Years	<0.001*
30 – 39 Years	

40 – 49 Years		
50 – 59 Years		
60 – 69 Years		
> 70 Years		
Gender	0.040*	
Hemoglobin (g/dL)	0.030*	
Platelet count (x10 ⁹ /L)	0.350	
WBC count (x10 ⁹ /L)	<0.001*	
Absolute neutrophil count (x10 ⁹ /L)	<0.001*	
Absolute lymphocyte count (x10 ⁹ /L)	<0.001*	
Absolute monocyte count (x10 ⁹ /L)	0.610	
Neutrophil to lymphocyte ratio (NLR)	<0.001*	
Monocyte to lymphocyte ratio (MLR)	<0.001*	
Platelet to lymphocyte ratio (PLR)	<0.001*	
Systemic Immune Inflammation Index (SII)	<0.001*	
Systemic Inflammatory Response Index (SIRI)	<0.001*	
Neutrophil to Platelet x lymphocyte ratio (NLPR)	<0.001*	
Derived neutrophil to lymphocyte ratio (d-NLR)	<0.001*	
Operating surgeon	0.001*	
Gallbladder Wall Thickness	< 3mm	0.001*
	3.1 – 4.9 mm	
	5.1 – 6.9 mm	
	> 7 mm	

~ Chi-square test was used for categorical variables. ~~ Mann-Whitney U test was used for continuous variables

Univariate and multivariate analyses were done through logistic regression are given in table 4.

Table 4: Univariate Analysis and Multivariate Analysis for Conversion to Open Cholecystectomy Summary

Variables		Univariate Analysis [~]			
		p-Value	Odds Ratio (OR)	Confidence Intervals	
				Lower Limit	Upper Limit
18 – 29 Years	18 – 29 Years	0.005* (combined)	Reference ^{~~}		
	30 – 39 Years	0.910	1.14	0.10	12.82
	40 – 49 Years	0.990	1.008	0.09	11.32
	50 – 59 Years	0.030*	9.63	1.22	76.00
	60 – 69 Years	0.090	6.84	0.74	63.47
	>70 Years	0.150	8.10	0.46	142.93
Gender		Reference ^{~~} – Male			
		0.050	0.41	0.16	1.00
Hemoglobin (g/dL)		0.030*	0.75	0.58	0.96
Platelet count (x10 ⁹ /L)		0.090	1.00	0.99	1.01
WBC count (x10 ⁹ /L)		<0.001*	1.30	1.18	1.44
Absolute neutrophil count (x10 ⁹ /L)		<0.001*	1.35	1.22	1.49
Absolute lymphocyte count (x10 ⁹ /L)		< 0.001*	0.20	0.10	0.40
Absolute monocyte count (x10 ⁹ /L)		0.390	1.34	0.69	2.61

Neutrophil to lymphocyte ratio (NLR)		< 0.001*	1.26	1.15	1.38
Monocyte to lymphocyte ratio (MLR)		0.160	1.43	0.86	2.38
Platelet to lymphocyte ratio (PLR)		0.001*	1.004	1.002	1.007
Systemic Immune Inflammation Index (SII)		<0.001*	1.00	1.000	1.001
Systemic Inflammatory Response Index (SIRI)		0.002*	1.15	1.05	1.25
Neutrophil to Platelet x lymphocyte ratio (NLPR)		<0.001*	2.49 x 10 ¹⁵	2.64 x 10 ⁻⁷	2.34 x 10 ²³
Derived neutrophil to lymphocyte ratio (d-NLR)		<0.001*	1.73	1.47	2.01
Operating surgeon's experience		Reference [~] - experienced surgeons			
		0.003*	5.24	1.74	15.73
Gallbladder wall thickness	<3mm	0.006* (combined)	Reference [~]		
	3.1 – 4.9 mm	0.790	0.82	0.18	3.78
	5.1 – 6.9 mm	0.280	2.06	0.55	7.70
	>7 mm	<0.001*	6.34	2.17	18.51
Variables		Multivariate Analysis [~]			
		p-Value	Odds Ratio (OR)	Confidence Intervals	
Age (Years)	18 – 29 Years	0.006* (combined)	Reference [~]	Lower Limit	Upper Limit
	30 – 39 Years	0.790	1.40	0.11	17.51
	40 – 49 Years	0.970	0.96	0.07	12.29
	50 – 59 Years	0.020	11.61	1.31	102.66
	60 – 69 Years	0.050	10.11	0.96	106.82
	> 70 Years	0.120	12.90	0.53	313.76
Gender		Reference [~] - Males			
		0.070	0.35	0.11	1.11
Hemoglobin (g/dL)		0.004*	0.61	0.44	0.85
Platelet count (x10 ⁹ /L)		0.830	1.00	0.99	1.00
WBC count (x10 ⁹ /L)		<0.001*	1.35	1.13	1.61
Absolute neutrophil count (x10 ⁹ /L)		<0.001*	1.52	1.24	1.85
Absolute lymphocyte count (x10 ⁹ /L)		<0.001*	0.19	0.07	0.49
Absolute monocyte count (x10 ⁹ /L)		0.330	1.66	0.60	4.58
Neutrophil to lymphocyte ratio (NLR)		<0.001*	1.31	1.14	1.50
Monocyte to lymphocyte ratio (MLR)		0.080	1.18	0.92	3.52
Platelet to lymphocyte ratio (PLR)		0.060	1.004	1.000	1.009
Systemic Immune Inflammation Index (SII)		<0.001*	1.001	1.000	1.001
Systemic Inflammatory Response Index (SIRI)		0.003*	1.15	1.04	1.26
Neutrophil to Platelet x lymphocyte ratio (NLPR)		<0.001*	>1.05 x 10 ²¹	1.51 x 10 ⁻⁸	7.29 x 10 ³³
Derived neutrophil to lymphocyte ratio (d-NLR)		<0.001*	2.18	1.56	3.04
Operating surgeon's experience		Reference [~] - experienced surgeons			
		<0.001*	9.695	2.55	36.92
Gallbladder wall thickness	<3mm	0.04* (combined)	Reference [~]		
	3.1 – 4.9 mm	0.520	0.58	0.11	3.00
	5.1 – 6.9 mm	0.390	2.01	0.41	9.81
	>7 mm	0.010*	5.77	1.52	21.88

[~] Univariate analysis and Multivariate analysis was done using logistic regression

[~] Reference categories are mentioned for categorical variables only

ROC curves were made for the variables found to be significant in logistic regression. ROC curves are given in Figure 3 – 7 and results are summarized in table 5.

Table 5: ROC Analysis for Factors Analyzed

Variables	Area Under Curve (AUC)	Sensitivity (%)	Specificity (%)	Cut-off value (equal and above)
Variables and Cut Offs Predictive of Conversion				
WBC count (x10 ⁹ /L)	0.75	68.0%	83.5%	11.65
ANC (x10 ⁹ /L)	0.79	68.2%	89.9%	9.79
NLR	0.84	72.7%	89%	4.97

SIRI	0.78	72.7%	82.1%	1.69
SII	0.83	64%	93%	1913.08
NLPR	0.81	81.8%	79%	0.013
d-NLR	0.84	72.7%	89.9%	3.76
Wall thickness (mm)	0.64	40.9%	84.8%	5.0
Variables and Cut Offs Predictive Of Successful Laparoscopic Procedure				
Hemoglobin (g/dL)	0.64	47.6%	77.3%	12.3
ALC ($\times 10^9/L$)	0.83	78.4%	86.4%	1.8

Figure 3 illustrated the ROC (Receiver Operating Characteristic) curves for CBC parameters in predicting conversion to open cholecystectomy.

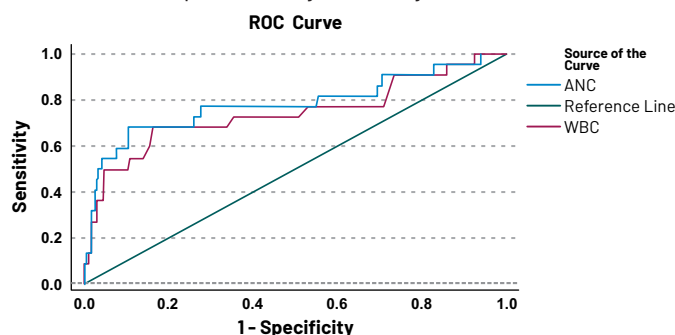


Figure 3: ROC curves for CBC parameters that predict conversion. AUC for ANC = 0.79. AUC for WBC count = 0.75

Figure 4 displayed ROC (Receiver Operating Characteristic) curves for various CBC-derived inflammatory ratios predicting the probability of conversion to open cholecystectomy.

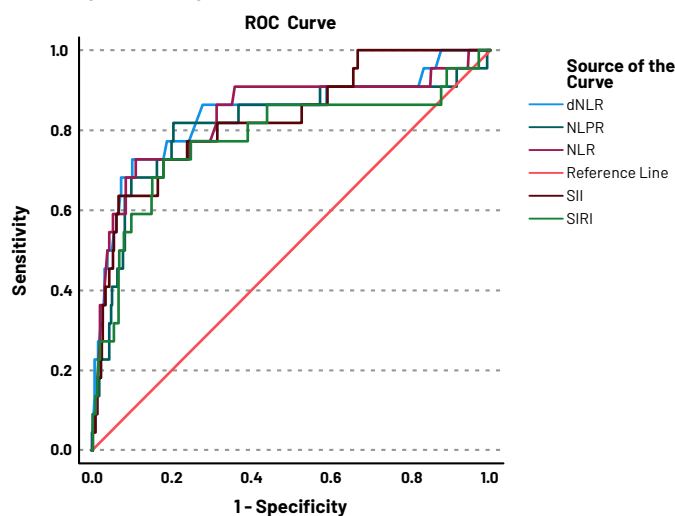


Figure 4: ROC curves for ratios derived from CBC that predict probability of conversion. AUC for NLR = 0.84. AUC for SIRI = 0.78. AUC for SII = 0.83. AUC for NLPR = 0.81. AUC for d-NLR = 0.84

Figure 5 showed the ROC (Receiver Operating Characteristic) curve for gallbladder wall thickness as a predictor of conversion to open cholecystectomy. The area under the curve (AUC) is 0.64, indicating a modest discriminatory ability.

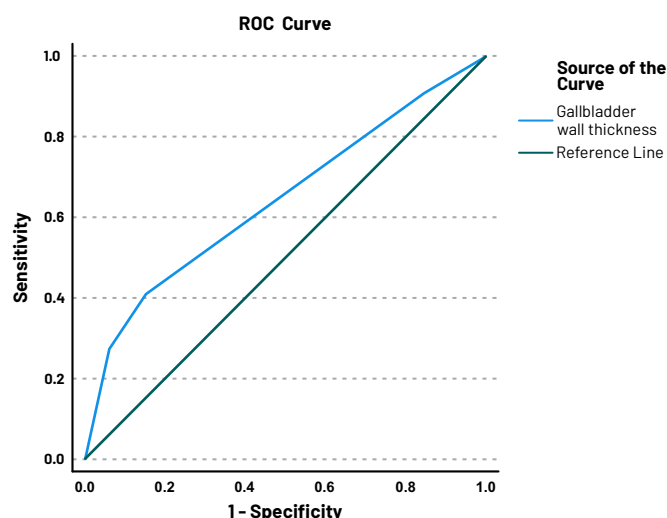


Figure 5: ROC curve for gallbladder wall thickness. AUC = 0.64.

Figure 6 illustrated the ROC (Receiver Operating Characteristic) curve evaluating surgeons' experience as a predictor for conversion to open cholecystectomy. The area under the curve (AUC) is 0.69, suggesting a fair predictive value, indicating that lower surgical experience may modestly increase the risk of conversion.

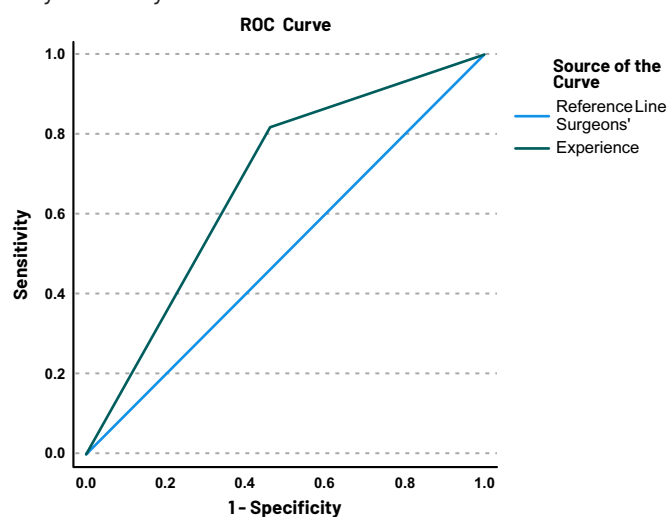


Figure 6: ROC curve for surgeons' experience as predictor for conversion. AUC = 0.69.

Figure 7 presented the ROC (Receiver Operating Characteristic) curves for parameters associated with successful laparoscopic cholecystectomy. The area under the curve (AUC) for absolute lymphocyte count (ALC) is 0.83, indicating good predictive accuracy. Hemoglobin

shows a lower AUC of 0.64, suggesting modest discriminatory ability.

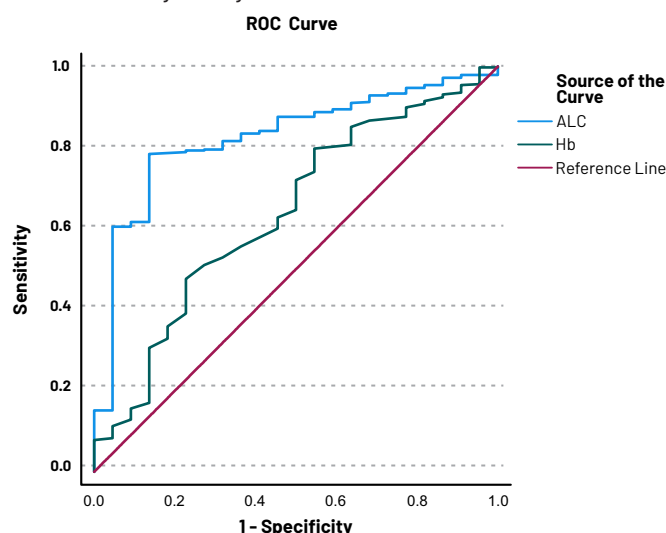


Figure 7: ROC curves for Parameters Associated with Successful Laparoscopic Cholecystectomy. AUC for ALC = 0.83. AUC for Hemoglobin=0.64.

DISCUSSION

NLR and PLR have been widely studied in relation to complications in laparoscopic cholecystectomy. Serban et al., found NLR > 4.19 predictive of advanced inflammation and conversion risk, with 85.5% sensitivity and 66.9% specificity. They concluded NLR was also superior to PLR and SII in predicting postoperative complications [12]. A Turkish study found a positive association between NLR and conversion in emergency cholecystectomy, but not in elective cases, and no independent predictive value in multivariate analysis [13]. Kartal M also found no predictive power for NLR or PLR in surgical complications [14]. In contrast, Moloney B.M et al., proposed an NLR cut-off of 3.5 as predictive of conversion [15]. SIRI and SII, known inflammatory markers, were also evaluated. Efgan et al., showed SII > 4631.293 to be 100% sensitive and 86% specific for systemic inflammation post-cholecystectomy. SIRI > 5.924 was 61.75% sensitive and 65.71% specific for gallstones in acute cholecystitis [16]. MLR has limited literature in this context, though Durak D et al., reported a cut-off of 0.2693 for predicting procedural difficulty [17]. Ultrasound findings such as gallbladder wall thickness, pericholecystic fluid, fibrosed gallbladder, and sonographic Murphy's sign are helpful in assessing disease severity. Morales-Maza et al., found wall thickness ≥ 4 mm associated with higher conversion rates and another study reported a 5.75 mm cut-off [18, 19]. In this study, most patients with acute cholecystitis were females (around three-fourths of the population), with highest numbers in the 40–49 age group, followed by 30–39. These demographics match existing literature [20]. Over half of

the converted cases were in the 50–59 age group, a statistically significant finding in both univariate ($p = 0.04$) and multivariate analysis ($p = 0.006$). Conversion risk increased >10-fold above age 50 and >12-fold above 70. Due to a small number of patients above 70, conclusions in this age bracket are limited. Some studies associate age > 60 with increased conversion risk [21]. Patients with comorbidities were excluded, so the effect of chronic illnesses like diabetes could not be analyzed. More than 80% of successful cases were females, who showed 65% lower conversion risk, though this was not statistically significant. Some studies report worse outcomes in males, but no such association was found here [5, 6, 18]. Surgeons with fewer than 200 laparoscopic cholecystectomies were considered inexperienced. The senior to junior consultant ratio was 1.1:1. Conversion rate was 4.8%, with 82% of conversions performed by junior consultants—a statistically significant result. These findings align with studies reporting higher complication rates among less experienced surgeons, though not all evaluate conversion as a complication [22, 23]. Surgeon expertise was an independent predictor of conversion, with junior surgeons showing a 9-fold increased risk. Gallbladder wall thickness on ultrasound was categorized: ≤ 3 mm (about two-thirds), 3.1–4.9 mm (15%), 5.1–6.9 mm (9.2%), and ≥ 7 mm (6%). Normal wall thickness in acute cholecystitis contrasts with some literature though others state thickening isn't exclusive to the condition [24, 25]. Thickened, inflamed gallbladder was noted intraoperatively. Wall thickness was significant in both univariate and multivariate analysis. Conversion rates were lower in patients with normal or minimally thickened walls, with no significant difference between these two groups. Wall thickness ≥ 5 mm carried 2-fold increased risk; ≥ 7 mm carried >5-fold increased risk. ROC analysis showed >5 mm as the cut-off for predicting conversion. Logistic regression confirmed the 7 mm group had significant p-values and confidence intervals. CBC trends showed significantly higher hemoglobin in successful cases. Platelet count was comparable. WBC was significantly higher in converted cases, consistent with prior research [19]. Median ANC, NLR, MLR, PLR, SIRI, SII, NLPR, and d-NLR were higher in converted cases. ALC and AMC were lower in successful laparoscopies. Univariate and multivariate analyses were used to assess independent predictors. Hemoglobin >12.3 g/dL reduced conversion risk by 47% ($p = 0.004$). Platelet count was not significant. Each unit increase in WBC and ANC was associated with 35% and 52% increased risk of conversion, respectively ($p < 0.001$). Higher ALC was protective, with 81% lower risk per unit rise. AMC showed 66% increased risk but was not statistically significant ($p = 0.44$). NLR cut-off was 4.97, with 31% increased conversion risk per unit rise.

MLR and PLR were not significant in multivariate analysis, with 18% and 0.4% increased risk per unit, respectively. PLR was significant in univariate analysis but lost significance after adjusting for confounders. MLR was not significant in univariate analysis. SIRI was significant with a cut-off of 1.69 and a 15% risk increase per unit. SII was also an independent predictor with a cut-off of 1913.08 and 0.1% risk increase per unit. d-NLR had a cut-off of 3.76, with a 2-fold increased conversion risk per unit rise. NLPR showed an exponential odds ratio (1.15×10^8 to 7.29×10^{23}), suggesting high risk, though the wide confidence interval calls for caution. These wide intervals may stem from the low conversion rate in the sample (457 patients), not small sample size itself. Multivariate analysis found the best predictors were NLR and d-NLR, followed by SIRI. Though SII and NLPR had significant p-values, they were excluded due to insignificant or excessively wide confidence intervals. These were followed by surgeon experience and gallbladder wall thickness. Given the shift toward minimally invasive surgery, the study recommends targeted training in laparoscopic techniques. In resource-constrained settings, rotations or collaborative workshops with well-equipped centers should be arranged. Most patients had normal gallbladder wall thickness, raising questions about ultrasound's role in acute cholecystitis diagnosis. Previous studies have shown diabetes and past abdominal surgeries increase conversion risk, but these factors could not be assessed here due to patient exclusion. Only two patients had past surgeries. Wider confidence intervals in some variables suggest that larger cohort studies are needed to better define effect sizes and improve predictive accuracy. This study excluded patients with comorbidities such as diabetes and prior abdominal surgeries, limiting the ability to assess their impact on conversion risk. Additionally, the relatively low conversion rate resulted in wide confidence intervals for some variables, affecting the precision of risk estimates. Future large-scale prospective studies including diverse patient populations are recommended to validate inflammatory markers and improve predictive models for conversion in laparoscopic cholecystectomy.

CONCLUSIONS

Among the factors compared, systemic inflammatory indices specially NLR, d-NLR and SII were found to have highest predictive value for conversion followed by surgeons' experience with laparoscopic cholecystectomy and gallbladder wall thickness. However, interpretation of these indices should be cautious and in conjunction with clinical context. Therefore, it was concluded that patients with acute cholecystitis who have high systemic inflammatory indices at presentation and thickened gallbladder wall should be operated upon by experienced laparoscopic surgeons to minimize chances of conversion.

Caution should also be exercised in old aged patients and in those with low hemoglobin.

Authors' Contribution

Conceptualization: MA¹

Methodology: SA, MA¹

Formal analysis: MA¹

Writing and Drafting: MA¹, MUHF, SA, MA²

Review and Editing: MA¹, MUHF, SA, MA²

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



The Effects of Aerobic Training and *Moringa oleifera* on High-Density Lipoprotein and Cardiac Endurance among Males

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ABSTRACT

Aerobic training is a form of physical workout in which heart and lungs work efficiently to supply oxygen to the muscles for improving athletic performance. **Objective:** To investigate the effect of moderate aerobic training and *Moringa oleifera* leaf powder (MOLP) on high-density lipoprotein (HDL) and cardiac endurance among males. **Methods:** One hundred (100) male volunteers of age group 38.9 ± 6.7 years were randomly and divided into four groups i.e. the control group (T_0), the moringa group (T_1), the aerobic group (T_2), and the Combined Group (T_3). *Moringa oleifera* leaf powder (3 gm) was given to the T_1 and T_3 daily for five days a week for 12 weeks, while the T_0 continued a normal diet routine. **Results:** Results indicate an increase in HDL posttest mean values of three interventional groups T_1 (41.80 ± 4.81 mg/dl), T_2 (42.08 ± 1.28 mg/dl) and T_3 (43.40 ± 1.77 mg/dl) as compared to control group T_0 (36.28 ± 1.86 mg/dl). Beep tests mean values of the post-test of interventional groups T_1 (10.1 ± 1.24), T_2 (10.2 ± 1.25) and T_3 (12.0 ± 1.18) and control group T_0 ($7.3 \pm .67$) were recorded. **Conclusions:** It was concluded that moderate aerobic training and MOLP have a positive effect on HDL and cardiac endurance among the interventional groups (T_1 , T_2 , and T_3), with more significant improvement in T_3 and no improvement in the control group.

INTRODUCTION

Aerobic training is a form of physical exercise in which the heart and lungs work efficiently to supply oxygen to the muscles, improving cardiovascular function and endurance. Regular aerobic exercise lowers resting heart rate, increases blood volume, and enhances overall health by improving body weight, energy levels, sleep patterns, and athletic performance [1]. Importantly, it reduces the risk of chronic diseases such as heart disease, diabetes, and cancer. Insufficiency aerobic activity influences approximately 17% of heart disease, 12% of diabetes, and 10% of breast cancer cases globally [2]. Health professionals recommend engaging in aerobic activities like running, cycling, swimming, and rowing for 20-30

minutes, three to five times per week, to improve physical fitness and cardiac endurance [3]. Several studies concluded that *Moringa* leaves provide several health advantages, including anti-diabetic, antibacterial, anti-cancer, and anti-inflammatory properties. *Moringa* has been extensively used as a health-promoting food against various diseases and health issues [4]. The estimates from the World Health Organization (WHO) say that 80% of nations with limited resources and 60% of people worldwide acquire their primary medical assistance from herbal medicine [5]. *Moringa* is a highly nutritious plant that can help with many health issues, improve mineral deficiency and prevent malnutrition [6]. The combination



of herbal supplements with regular aerobic exercise can improve physical performance and reduce the harmful effects of synthetic medicines [7]. Research shows that regular exercise and herbal supplements (*Moringa*) can dramatically increase HDL levels and cardiac endurance, when physical treatment is used along with herbal supplements [8, 9]. A lack of physical activity is a big concern by 2030, nearly 40% of adults in the U.S. could develop heart disease because of a sedentary lifestyle [10]. It was investigated the impact of aerobic training on hemoglobin and cardiovascular efficiency and discovered that hemoglobin levels and heart function significantly increased [11, 12]. Herbal products are abundant in nutrients and phytochemicals that have positive health effects and *Moringa* supplements are frequently used to treat malnutrition and boost nursing mothers' milk production [13, 14]. Recent studies have highlighted the synergistic benefits of aerobic exercise and *Moringa oleifera* supplementation on cardiovascular performance and metabolic health. Gbedinhessi et al., demonstrated that supplementation with *Moringa oleifera* leaf powder significantly enhanced cardiorespiratory performance and endurance in trained individuals during a 20 km cycling time-trial, suggesting improved aerobic capacity and oxygen utilization [15]. Similarly, Muhammed et al., conducted a randomized controlled trial in patients with type 2 diabetes and found that combining aerobic exercise with *Moringa oleifera* supplementation led to notable improvements in glycemic control and metabolic health markers, indicating a cardioprotective effect [16]. Emerging evidence supports the role of *Moringa oleifera* in enhancing physical endurance through metabolic and antioxidant pathways. Bian et al., investigated the effects of a flavonoid-rich concentrate derived from *Moringa oleifera* leaves and found that it significantly prolonged exhaustive swimming time in mice by boosting energy metabolism and enhancing antioxidant capacity [17]. The ability of the heart and lungs to make sure that muscles get enough oxygen during extended physical activity is known as cardiac endurance and a sedentary lifestyle raises the risk of coronary heart diseases. It is estimated that physical inactivity accounts for over 23 million deaths globally, making it the fourth leading cause of death. A sedentary lifestyle raises the risk of coronary heart diseases [18]. According to scientific research, *Moringa oleifera* is a rich source of macro, micro- nutrients and bioactive compounds that can help prevent several chronic illnesses and health problems [19]. This research could be helpful in examining the pharmacological potential of *Moringa oleifera* and increasing the possibility of developing effective drugs that will enhance human health [20]. Cholesterol is transported throughout the body by lipoproteins and is necessary for cell proliferation,

hormone manufacturing, and food digestion. HDL, the "good" cholesterol, dramatically lowers the risk of coronary heart disease by clearing cholesterol from the arteries [21]. The current study aims to ascertain if moderate aerobic exercise or *Moringa oleifera*, either separately or in combination, affects cardiac endurance and high-density lipoprotein (HDL) levels. A Randomized Control Trial (RCT) was set up to evaluate the following hypotheses that were created for the investigation. The study hypothesized that moderate aerobic training and *Moringa oleifera* has a positive impact on endurance in male adults.

METHODS

This study followed a Randomized Controlled Trial (RCT) design and was conducted at the Directorate of Sports, Quaid-i-Azam University (QAU), Islamabad, Pakistan. The study utilized the university's playground for moderate aerobic training, the Plant Sciences Laboratory for the analysis of *Moringa oleifera* leaf, and the Armed Forces Institute of Cardiology (AFIC) Pathological Laboratory for blood sample testing. The ethical approval from the Institutional Review Board (IRB) of the University of Lahore and the Bio-Ethics Committee (BEC-FBS-QAU2023-535) of Quaid-i-Azam University, Islamabad, Pakistan. The clinical trial registered under Clinical Trials.gov ID NCT04164771. The study was conducted over a period of 3 months from September to November, 2022. Sample size was determined using G*Power software with a one-way ANOVA analysis comparing four groups: control, aerobic training, *Moringa oleifera*, and their combination. Using medium effect size ($f=0.25$), alpha of 0.05 and power of 0.80, a sample of 100 (25 per group) was estimated. After accounting for 10% dropout, the final estimate retained 100 (25 in each group). A total of 100 male volunteers aged 38.9 ± 6.7 years were recruited following predefined inclusion and exclusion criteria. Participants were screened based on their lipid profile and cardiovascular endurance, ensuring homogeneity in baseline health conditions. The inclusion criteria for participants were as follows: low-density lipoprotein (LDL) levels ranging from 160 to 189 mg/dL, high-density lipoprotein (HDL) levels below 40 mg/dL, triglyceride levels between 200 and 499 mg/dL, and total cholesterol levels exceeding 200 mg/dL. Additionally, participants were required to have a beep test score of less than 7.9 or a VO_2 max of less than 40%. Individuals with pre-existing cardiovascular diseases, metabolic disorders, or those on lipid-lowering medications were excluded from the study. Prior to participation, all volunteers were fully informed about the study procedure, including pre-testing, aerobic training protocols, and post-testing after the intervention period. Written informed consent was obtained from each participant. The sampling strategy was based on convenient sampling techniques, and data were collected from a census of 100 participants regularly visiting the study settings. Based on participants'

characteristics and inclusion criteria of the study, 100 participants were found eligible, which were divided into 4 equal groups. Participants who met the inclusion criteria were randomly assigned into four groups ($n = 25$ per group) using a computer-generated randomization protocol to reduce selection bias. The groups were as follows: T₀ (control group), which received no intervention and continued their usual diet; T₁ (*Moringa* group), which received 3 g/day of *Moringa oleifera* leaf powder; T₂ (aerobic group), which engaged in moderate aerobic exercise at 45–60% intensity for 30 minutes per day, five days per week; and T₃ (combined group), which received both *Moringa* supplementation (3 g/day) and aerobic training as outlined in the T₁ and T₂ protocols. Several recent studies reinforce the beneficial role of *Moringa oleifera* in enhancing lipid metabolism, physical endurance, and muscular function. Khan et al., reported that *Moringa oleifera* leaf powder significantly improved lipid profiles in male rabbits by lowering total cholesterol and triglycerides while increasing HDL levels, suggesting strong potential for cardiovascular risk reduction [22]. Similarly, Ray et al., highlighted the broader application of *Moringa oleifera* in improving human physical performance, attributing its effects to its rich nutritional and adaptogenic profile [23]. From a muscular perspective, Nayak et al., found that *Moringa oleifera* extract counteracted exercise- and dexamethasone-induced skeletal muscle impairment, implying protective effects on muscle function under stress conditions [24]. Moreover, Tsuk et al., in a pilot study, observed improved physical fitness outcomes in young adults consuming a commercial *Moringa* supplement, adding early clinical support for its ergogenic use [26]. Collectively, these studies highlight *Moringa oleifera*'s multifaceted benefits in enhancing HDL, preserving muscle integrity, and improving endurance, making it a promising natural adjunct in athletic and cardiovascular health interventions for males. The randomization ensured equal distribution of participants across groups, reducing potential confounding variables. The study followed a parallel-group design, with interventions applied independently to assess their isolated and combined effects on lipid profile and cardiovascular endurance. Qualified technical officials conducted the beep test to assess cardiac endurance. Blood samples were collected by trained paramedical staff under sterile conditions at AFIC, Rawalpindi. A 5 ml venous blood sample was drawn from the antecubital vein of each participant after an overnight fast of 10–12 hours. The collected samples were immediately stored in EDTA tubes and transported in a temperature-controlled container to the laboratory for lipid profiling. Data analysis was conducted using SPSS (Version 23.0) and Minitab (Version 16). Appropriate statistical methods were employed to ensure a rigorous evaluation of the intervention effects. The Shapiro-Wilk test was used to assess the normality of pre- and post-intervention data. Within-group differences were

evaluated using paired samples t-tests. One-way ANOVA was performed to compare mean differences across the four groups, contingent on the assumption of normality. Post-hoc analysis was carried out using Tukey's pairwise comparisons to identify significant inter-group differences. Additionally, scatter plots were generated to visualize data trends and relationships. The randomization, strict inclusion criteria, and statistical approach ensured internal validity and minimized bias, allowing for an accurate assessment of the effects of *Moringa oleifera* supplementation and aerobic training on lipid profiles and cardiovascular endurance.

RESULTS

The study was conducted on 100 male adult participants. Due to non-normal distribution, the Shapiro-Wilk test was applied to report pre-and-intervention data of HDL and Beep test of all experimental groups and control groups, and the results are given in table 1.

Table 1: Group Comparison of HDL and Beep Pre-Test

Variables	Group	Statistic	df	Significance (p-Value)	CI
HDL Pre-Test	Control group T ₀	0.998	25	>0.073	0.996-1.00
	Moringa group T ₁	0.995	25	>0.069	0.992-0.998
	Aerobic group T ₂	0.997	25	>0.091	0.994-1.00
	Combined group T ₃	0.997	25	>0.085	0.994-1.00
Beep Pre-Test	Control group T ₀	0.975	25	>0.080	0.965-0.985
	Moringa group T ₁	0.953	25	>0.068	0.940-0.966
	Aerobic group T ₂	0.987	25	>0.063	0.978-0.996
	Combined group T ₃	0.963	25	>0.079	0.950-0.976

The result indicated that the significance values in all cases were greater than the selected significance value (0.05), drawing the inference that the data was symmetrical and represented a normal distribution. The data were thus amenable to parametric analysis and application of relevant statistical tests which were applied. Box plots were drawn for explanatory data analysis, as depicted in figure 1.

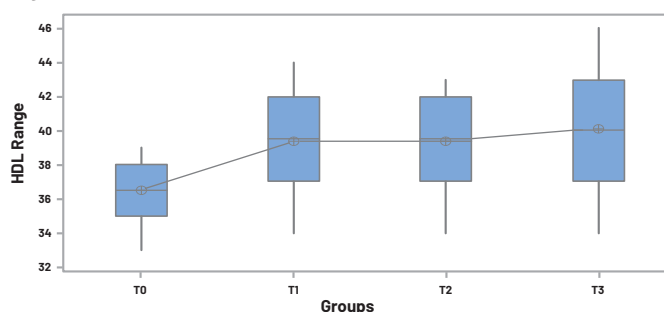


Figure 1: Box Plot of HDL data of all groups (T₀, T₁, T₂, and T₃)

Box plots of four groups showed that the data of HDL values in all groups (T₀, T₁, T₂, and T₃) were normally distributed, with no outliers. The interventional groups (T₁, T₂, and T₃) had a higher spread compared to the control group (T₀). Scattered plots were drawn for the Beep test for all groups (T₀, T₁, T₂, and T₃), with the results depicted in figure 2.

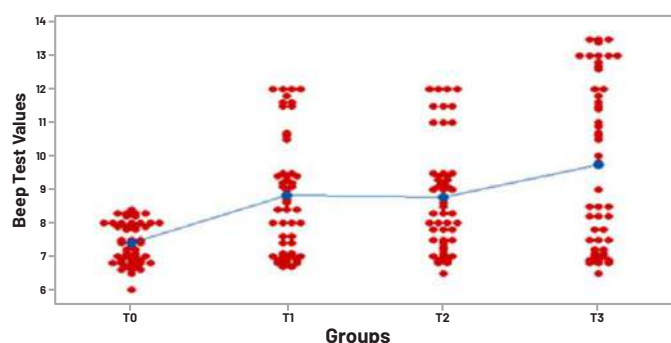


Figure 2: Scatter Plots of the Beep Test for all Groups

The Scatter plots showed that a strong positive relationship existed in the Beep test values in all four groups (T_0 , T_1 , T_2 , and T_3), with higher values in the interventional groups compared to the control group and the highest one in the combined group (T_3). As such, the interventions had a positive effect on cardiac endurance, with more prominence in the combined intervention. A paired samples t-test was used to compare the mean values of pre-tests and post-tests of both variables in the combined group (T_3), results tabulated in table 2.

Table 2: Paired Samples T-Test for HDL and Cardiac Endurance (N=25)

Variables	Group	Mean $\pm$ SD	Diff	p-Value
HDL	Pre-Test	36.96 $\pm$ 1.48 mg/dl	6.44	<0.001
	Post-Test	43.40 $\pm$ 1.78 mg/dl		
Cardiac Endurance	Pre-Test	7.49 $\pm$ 0.69 (VO2 max 38.1%)	4.53	<0.001
	Post-Test	12.03 $\pm$ 1.17 (VO2 max 54.6%)		

The findings showed that the p-values for HDL and cardiac endurance in the combined group (T_3) were both less than 0.001, which is well below the 0.050 threshold. This means there was a significant (<0.001) improvement from the pre-test to the post-test. As a result, the null hypothesis was rejected, confirming that moderate aerobic training and *Moringa oleifera* had a meaningful positive impact on HDL levels and cardiac endurance. Analysis of Variance (ANOVA) was conducted for comparison of Beep tests for the four groups (T_0 , T_1 , T_2 , and T_3), to evaluate the effect on cardiac endurance, at a significance level (<0.050), with the results tabulated in table 3.

Table 3: Comparison within Group of Beep Comparison Test

Source	DF	Adj SS	Adj MS	F-Value	p-Value
Beep	3	141.7	47.250	15.31	<0.001
Error	196	605.1	3.087		
Total	199	746.8			

The one-way ANOVA revealed that there was a statistically significant difference in mean Beep test scores between at least two groups ($F(3, 196) = [15.31]$, $p = 0.001$). Given the result of the ANOVA, Tukey's HSD test was conducted to ascertain the Pre and Post-test comparison for the four groups, and pairwise comparisons for the six groups (T_1-T_2 ,

T_1-T_3 , T_1-T_0 , T_2-T_3 , T_2-T_0 , T_3-T_0), at significance level (<0.050) (Confidence Interval (CI)=95%). The results are compiled in table 4. Tukey's HSD test helps in determining differences of values within group.

Table 4: Tukey's Grouping Information on Pre and Post Beep Test Scores

Group Comparison	Mean Difference (I-J)	Significance	95% CI	Effect Size (Cohen's d)
$T_0 - T_1$	3.016*	<0.001	3.6355, 2.3965	2.01
$T_0 - T_2$	2.844*	<0.001	3.4635, 2.2245	1.90
$T_0 - T_3$	4.776*	<0.001	5.3955, 4.1565	3.18
$T_1 - T_2$	1.760 B	<0.001	2.3795, 1.1405	1.17
$T_2 - T_3$	1.932*	<0.001	2.5515, 1.3125	1.29

As reflected in table 4, the groups T_1 and T_2 having a shared alphabet "B" in means, had no significant difference, while groups T_0 and T_3 , not having a shared alphabet with any other group, had a significant difference. The results demonstrate that both *Moringa* supplementation and aerobic exercise are individually effective, but their combination produces a substantially greater effect, as evidenced by the large and statistically significant interaction. This supports the conclusion that the combined intervention (T_3 group) has a synergistic benefit, reinforcing the value of integrating both strategies for maximum effect (Table 5).

Table 5: Two-Way ANOVA Summary for Effects of *Moringa* Supplementation and Aerobic Exercise on Post-Intervention Outcome

Source	Type III Sum of Squares	df	Mean Square	F	p-Value	Partial η^2
Corrected Model	293.491	3	97.830	80.808	<0.001	0.716
Intercept	3923.185	1	3923.185	3240.541	<0.001	0.971
<i>Moringa</i> (main effect)	123.393	1	123.393	101.922	<0.001	0.515
Aerobic (main effect)	89.719	1	89.719	74.107	<0.001	0.436
<i>Moringa</i> $\times$ Aerobic (interaction)	285.127	1	285.127	235.514	<0.001	0.710
Error	116.223	96	1.211	-	-	-
Total	10272.190	100	-	-	-	-

Tukey's simultaneous pairwise comparison indicated that the pair T_2-T_1 , the two interventions, containing a zero in its confidence interval had no significant difference, whereas pairs T_3-T_1 , and T_3-T_2 , close to zero but not included, had significant differences, though by a small degree. In other words, the two interventions had individual effects on the Beep score of the same magnitude, but their joint effect was significantly different from their individual effects. The pairs T_1-T_0 , T_2-T_0 , and T_3-T_0 , having confidence intervals distant from zero, were significantly different. The overall position had been that the three interventional groups' pre- and post-Beep test scores were significantly different from the control group, while inter se, the effects of the two inventions individually were alike but significantly different

from their joint effect, the latter being more pronounced.

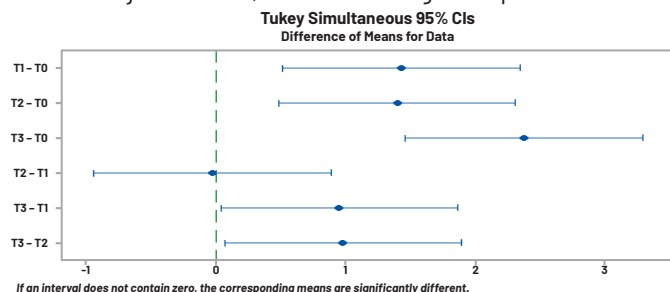


Figure 3: Tukey's Simultaneous Pairwise Comparison

DISCUSSION

The growing interest in natural supplements for enhancing physical fitness and cardiovascular health has led to increased investigation into the potential of *Moringa oleifera* [26]. Another research study was implemented to check the effect of *Moringa oleifera* supplement on physical fitness of young adults and discovered the results that there was no impact on physical activity performance but encouraging signs that the *Moringa oleifera* has beneficial impacts on physiological processes [26]. This study contradicts the current study results in some way because this study carried out with two interventions aerobic training and *Moringa oleifera* as a supplement and elaborated that aerobic training and Moringa leaf powder have significant effects on High density lipoprotein and cardiac endurance. The results of the current study showed that moderate aerobic training and administering *Moringa oleifera* to male adult persons for 12 weeks had a significant positive effect on HDL and Cardiac Endurance. The Beep test used to guess cardiac endurance, analysis showed improvements in the two interventional groups (T1 and T2) but in combined group (T3) showing the most significant improvement. On the other hand, lipid profile was carried out to check the HDL level and paired samples t-test were used to evaluate the HDL of all interventional groups. However, when *Moringa oleifera* leaf powder and moderate aerobic training were provided to combined group (T3), cardiac endurance and HDL increased significantly as compared to other two treatment groups. According to Tukey's pairwise comparisons, and the ANOVA analysis confirmed that the Beep test scores of the groups differed significantly (i.e., <0.05). These findings support other studies showing that regular aerobic exercise improves cardiovascular efficiency [26]. The results of this study are also in line with the larger body of research on the advantages of moderate aerobic exercise and the use of herbal remedies to support cardiovascular health. The present investigation verified that *Moringa oleifera* and moderate aerobic exercise raise cardiac endurance and HDL levels.

The study relied on indirect measures such as the Beep test for cardiac endurance, which may not fully reflect true

cardiopulmonary capacity. Additionally, absence of blinding and placebo control may introduce performance and expectation bias. Future research should incorporate randomized controlled designs with objective cardiopulmonary assessments (e.g., VO_2 max) to strengthen the validity of findings.

CONCLUSIONS

According to the current study's findings, HDL and cardiac endurance are significantly improved by participating in 12 weeks of aerobic exercise and taking a supplement of *Moringa oleifera* leaf powder among adult males.

Authors' Contribution

Conceptualization: MSA

Methodology: MSA

Formal analysis: NA

Writing and Drafting: MSA, NA, MKM

Review and Editing: MSA, NA, MKM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Urological Complications in Patients Undergoing Hemodialysis and Peritoneal Dialysis

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ABSTRACT

Urological complications (UCs) remain a significant concern following kidney transplantation (KT), contributing to both morbidity and mortality. **Objectives:** To determine the prevalence of urological complications and associated factors in patients receiving hemodialysis (HD) and peritoneal dialysis (PD). **Methods:** A comparative cross-sectional study was conducted in the Department of Urology at Bacha Khan Medical College and Mardan Medical Complex, Mardan. A tertiary hospital, involving 310 dialysis patients. Data on demographics, comorbidities, and urological complications were collected. Urological complications assessed included urinary tract infections (UTI), bladder dysfunction, nephrolithiasis, hematuria, and urethral stricture. Laboratory tests were used to evaluate renal function parameters. T-tests discover differences between groups, and chi-squares are used for identifying differences in categorical data. If the p-value was less than 0.050, the result regarded as statistically significant. **Results:** The mean age of participants was 58.7 ± 12.3 years, and the majority were male (58.1%). Diabetes and hypertension were prevalent in 45.8% and 71.0% of patients, respectively. The prevalence of urological complications included UTIs (27.4%), bladder dysfunction (19.4%), LUTS (29.7%), hematuria (15.5%), and nephrolithiasis (11.3%). HD patients had a significantly lower residual urine output compared to PD patients (80 mL/day vs. 200 mL/day, $p < 0.001$). UTI and bladder dysfunction were significantly more common in diabetic patients ($p = 0.030$ and $p = 0.020$, respectively). Patients who received dialysis for longer duration had more LUTS ($p = 0.030$). There was a significant difference in albumin levels between HD patients and PD patients ($p = 0.040$). **Conclusions:** Urological complications are common in dialysis patients, with significant associations observed with dialysis modality, diabetes, and residual urine output.

INTRODUCTION

Urological complications (UCs) remain a significant concern following kidney transplantation (KT), contributing to both morbidity and mortality [1, 2]. Among the most common UCs observed in KT recipients are urine leakage, ureteral stricture, and vesicoureteral reflux (VUR) [3]. Fortunately, the overall incidence of UCs has recently decreased to less than 10%, mainly due to advancements in surgical techniques and perioperative care [4]. Routine prophylactic ureteral stenting during ureteroneocystostomy has reduced the incidence of major urological complications to nearly 2%-5% [5]. There has also been substantial advancement from the standard Lead better-Politano techniques to the extra-vesical Lich-Gregoir technique regarding surgical trauma and

anastomotic success rates [6]. Improvements in microsurgical instruments, hemostasis, and overall intraoperative visualization have also helped contribute to their gradual decrease. Using better surgical techniques with subsequent improvements in immunosuppressive strategies and infection control are collectively responsible for the decreasing incidence of UCs reported by transplant centers worldwide [7]. In Japan, people with advanced kidney disease remain on dialysis treatment (DT) for a long time due to the critical shortage of available organ donors. In this context, hemodialysis (HD) is the dominant form of therapy over peritoneal dialysis (PD) [8]. In long-term HD patients, who are typically anuric or oliguric, it is common for the bladder to be used



infrequently. Bladder atrophy leads to loss of bladder capacity, loss of bladder compliance, and loss of detrusor activity [9]. The structural changes associated with bladder atrophy include the development of fibrosis, loss of urothelial thickness, and increased collagen deposition that results in stiffening and, ultimately, loss of bladder function [10]. These changes pose significant surgical challenges during ureteral reimplants for KT, particularly for patients with a severely atrophic bladder. Treatment and rehabilitation of bladder atrophy in long-term dialysis patients entails a complex approach including both pre- and post-operative focus [9]. Patients with bladder atrophy can use bladder cycling, or coaxing the bladder to function with sterile saline instillations before transplant, as a way to help improve bladder function and capacity [11]. Urodynamic studies are useful to determine the degree of bladder dysfunction and guide future surgical procedures [12]. Intra-operatively, surgeons can employ alternative surgical strategies such as ureteroureterostomy, the use of ureteral stents, or augmentation cystoplasty (using bowel segments) where the bladder has significant fibrosis or is contracted [12]. There are over 2 million people globally on dialysis therapies, and this is a small fraction of those who could potentially benefit from renal replacement therapy [13]. In America, at least 7 million people have chronic kidney disease (CKD), and most of those people will ultimately progress to end-stage renal disease (ESRD) [14]. At this point, a renal transplant or dialysis is required to live. HD is still the most common type of dialysis. The long-term effects of HD can lead to physical complications that impact individuals, impact physical activity, and lead to restrictions on diet and medications [15]. Continuous ambulatory peritoneal dialysis (CAPD) provides a better home option with flexibility and is the preferred form of dialysis in many countries (Mexico, Canada, the United Kingdom, and Hong Kong, to name a few) [16]. CAPD conserves vascular access and allows more independence [17]. CAPD is still heavy with potential pitfalls, including infections from the insertion of the catheter and infections from contamination [18]. The overall mortality rate with CAPD may be lower, and the ease of usage and being at home for patients is invaluable. Significant improvements to PD in the last 25 years have resulted in improved outcomes, including enhanced catheter design, improved connector systems, and perhaps more biocompatible dialysis solutions [16]. While major advancements have been made in dialysis and transplantation management, there are several risk factors, such as bladder atrophy as a result of prolonged DT, which continue to increase the risk of post-KT UCs. That said, there is limited literature that examines bladder capacity specifically about UCs.

The existing literature often involves small sample sizes

and varying and unidentified methods, making it difficult to make solid clinical recommendations. Further research is also warranted to better understand this relationship and establish evidence-based management for at-risk patients. This study aims to determine the prevalence of urological complications and associated factors in patients receiving hemodialysis HD and PD.

METHODS

The comparative cross-sectional study was conducted in the Urology Department of Bacha Khan Medical College (Mardan) from March to September 2023. The analysis sought to discover differences in urological complications (UCs) between patients receiving HD and patients receiving PD. The study was allowed to proceed after it received ethical clearance from the Institutional Review Board of Bacha Khan Medical College (Ethical Approval No. 298/BKMC). The participants were given pertinent information and assured that their data would be kept private (confidential) and that they could decide not to take part in the study. It was carried out while respecting rules about patient rights and the privacy of participants. Only adult patients with ESRD undergoing dialysis for at least a month were considered for this research. There were 186 patients in the HD group and 124 in the PD group for the study. Further division of patients was made based on whether they had diabetes (Diabetes: 142, No Diabetes: 168) and the length of dialysis (≤ 2 years: 102, 2-5 years: 109, >5 years: 99). The study didn't include people who were set to have urological surgery or had problems with their mental state. Open Epi software (Version 3.01) was used to set the sample size according to the main outcome of interest, which was urological complications in dialysis patients. A previous study by Abushamma et al., reported that 20% of HD patients and 10% of PD patients experienced lower urinary tract symptoms (LUTS) [19]. The proportions were taken into account when the answer was found. Setting the significance level (α) as 0.050 and the power ($1-\beta$) to 80%, we determined that 310 patients had to be included in the study: 186 went on HD and 124 went on PD; $n = [(Z_{\alpha/2} + Z_{\beta})^2 \times (P_1(1-P_1) + p_2(1-p_2))] / (p_1 - p_2)^2$. P_1 stands for the proportion seen in the HD group and p_2 is for the PD group. The study included adults (aged 18 or older) who had been living with HD or PD for a month and had given their informed consent to take part. Those excluded were people who had had previous urological surgery or showed cognitive impairments. A structured questionnaire was utilized to gather demographic information, which included: age, gender, duration of dialysis, and co-morbidities. Urological complications such as lower urinary tract symptoms (LUTS), hematuria, and prostatomegaly were noted within the structured questionnaire, and other clinical and laboratory investigations were performed if needed. Urological

complications were categorized based on patient-reported symptoms. Data collection was accomplished through clinical and laboratory assessment. Every patient had a comprehensive urological assessment, including assessment of urological symptoms: urgency, frequency, dysuria, nocturia, and retention. Patient-reported symptoms were categorized as mild, moderate, and severe. Clinically relevant blood and urine samples were analyzed to assess renal function and verify any hematuria. Urine cultures were performed when UTIs were suspected. Imaging studies, including ultrasound and CT with contrast as needed, were performed to detect nephrolithiasis. Digital rectal examination was performed to assess for prostatomegaly in male patients, which was also viewed with imaging and/or transrectal ultrasound, if required. The primary outcome variable was the presence of urological complications; specifically, LUTS, hematuria, and prostatomegaly. The secondary outcome variables also included nephrolithiasis, bladder dysfunction, and UTIs. Urological complications were classified based on symptoms. Hematuria was defined as the presence of blood in urine, while prostatomegaly was assessed through physical examination and imaging in male patients. Qualitative variables included dialysis type (HD or PD), urological complication (presence/absence), type of urological complication (urinary tract infection, bladder dysfunction, hematuria, or obstructive uropathy), sex of patient, diabetes status, and hypertension status. Quantitative variables included patient age, months in dialysis, residual urine output (in mL/day), serum creatinine, serum albumin, and hemoglobin. SPSS version 26 was used for the entry and analysis of all data. The data were stratified according to important results such as the presence of diabetes, duration of dialysis, and residual urine for comparison of subgroups. The statistical analysis performed consisted of descriptive and inferential statistics to evaluate both the prevalence of urological complications among individuals receiving HD and PD, and the associated factors. For categorical variables, the data was shown as the number of cases and as percentages, while the data for continuous variables was presented as the mean $\pm$ SD. HD patients were compared to PD patients, patients with and without urological problems and to those with and without diabetes. The Chi-square test (or, if possible, Fisher's exact test) was applied to compare the frequencies of different categories. The independent samples t-test analysis method was applied to see if there were differences in continuous variables. All the statistical tests were considered statistically significant when the p-value was below 0.050.

RESULTS

The demographic and clinical attributes of the study cohort (n=310) were predominantly similar between HD and PD patients. The average age of the entire population was 58.7 ± 12.3 years, with no significant difference between the HD (59.2 ± 12.5 years) and PD (57.9 ± 12.0 years) groups ($p=0.420$). The PD group comprised a greater percentage of male (60.5%) than the HD group (56.5%); however, this discrepancy was not statistically significant ($p=0.480$). The incidence of diabetes mellitus (45.8%) and hypertension (71.0%) was comparable between the groups, with p-values of 0.520 and 0.430, respectively. The average duration of dialysis was 4.8 ± 3.2 years, with no significant difference observed between the groups ($p=0.210$). A notable disparity was noted in residual urine production, with PD patients exhibiting a much greater median output (200 (100–500) mL/day) in contrast to HD patients (80 (30–300) mL/day, $p<0.001$). The Body Mass Index (BMI) was comparable among groups (27.5 ± 4.6 kg/m² in the whole population, 27.8 ± 4.7 in HD, and 27.1 ± 4.5 in PD, $p=0.35$), and a minor percentage of patients (11.3%) had a history of urological surgery, with no significant disparity between the dialysis modalities ($p=0.720$) (Table 1).

Table 1: Demographic Characteristics among Respondents

Characteristics	Total (310)	HD (186, 60%)	PD (124, 40%)	p-Value
Age (Years, mean $\pm$ SD)	58.7 ± 12.3	59.2 ± 12.5	57.9 ± 12.0	0.420
Sex (Male)	180 (58.1%)	105 (56.5%)	75 (60.5%)	0.480
Diabetes Mellitus	142 (45.8%)	88 (47.3%)	54 (43.5%)	0.520
Hypertension	220 (71.0%)	135 (72.6%)	85 (68.5%)	0.430
Dialysis Duration (Years, mean $\pm$ SD)	4.8 ± 3.2	5.1 ± 3.4	4.5 ± 3.0	0.210
Residual Urine Output (mL/day, median [IQR])	120 (50–400)	80 (30–300)	200 (100–500)	<0.001*
BMI (kg/m ² , mean $\pm$ SD)	27.5 ± 4.6	27.8 ± 4.7	27.1 ± 4.5	0.350
History of Urological Surgery	35 (11.3%)	22 (11.8%)	13 (10.5%)	0.720

Statistical Test Used: Independent t-test for continuous variables and chi-square test for categorical variables. Asterisk (*) indicates a statistically significant difference ($p\text{-value}<0.050$)

The incidence of urological problems was greater in diabetic patients than in non-diabetic individuals, with notable disparities noted for urinary tract infections (UTIs) and bladder dysfunction. Specifically, 31.7% of diabetic patients reported UTIs, in contrast to 23.8% of non-diabetic patients ($p=0.030$), while 25.4% of diabetic patients exhibited bladder dysfunction, compared to 14.3% of non-diabetic patients ($p=0.020$). More diabetes patients had nephrolithiasis, with a rate of 14.8%, compared to 8.3% in non-diabetic patients, but it was not considered significant by statistical analysis ($p=0.120$). Diabetics were more likely to present with lower urinary tract symptoms (LUTS) and hematuria, but these increased risks were not proven through statistics ($p=0.070$ and $p=0.060$,

respectively). The study found that 21.1% of diabetic men were more likely to have increased prostate size (prostatomegaly), though this difference did not achieve statistical significance ($p=0.080$). There was not much difference in urethral stricture between the two groups ($p=0.380$). Serum creatinine, levels of blood urea nitrogen (BUN) and glomerular filtration rate (GFR) were mostly equal between HD and PD patients. Unlike in HD patients, whose albumin levels were usually low, PD patients generally showed higher albumin levels (3.8 ± 0.6 g/dL) ($p=0.040$). No significant difference was found in haemoglobin between the HD and PD groups (10.2 ± 1.3 g/dL versus 10.6 ± 1.4 g/dL, respectively) (Table 2).

Table 2: Prevalence of Urological Complications by Diabetes Status and Impact of Dialysis Modality on Renal Function Parameters

Complications	Diabetes (n=142, 45.8%)	No Diabetes (n=168, 54.2%)	p-Value
Urological Complications by Diabetes Status			
Urinary Tract Infection	45 (31.7%)	40 (23.8%)	0.030*
Bladder Dysfunction	36 (25.4%)	24 (14.3%)	0.020*
Nephrolithiasis (Kidney Stones)	21 (14.8%)	14 (8.3%)	0.120
LUTS	50 (35.2%)	42 (25.0%)	0.070
Hematuria	28 (19.7%)	20 (11.9%)	0.060
Prostatomegaly (Male, n=180)	30 (21.1%)	10 (11.9%)	0.080
Urethral Stricture	10 (7.0%)	8 (4.8%)	0.380
Renal Function			
Parameters	(HD) (n=186, 60%)	(PD) (n=124, 40%)	-
Serum Creatinine	6.2 ± 2.1	5.8 ± 1.9	0.120
BUN	45.3 ± 18.2	42.1 ± 16.4	0.160
GFR (mL/min/1.73m ²)	13.5 ± 5.1	14.8 ± 5.7	0.090
Albumin	3.5 ± 0.7	3.8 ± 0.6	0.040*
Hemoglobin	10.2 ± 1.3	10.6 ± 1.4	0.230

The frequency of urological problems was examined in three categories, defined by the length of time on dialysis: ≤ 2 years, 2-5 years, and > 5 years. The incidence of urethral stricture, hematuria, urinary tract infections (UTIs), and nephrolithiasis (kidney stones) were not significantly different across the groups ($p=0.470$, $p=0.910$, and $p=0.240$, respectively). Statistically significant ($p=0.060$), the prevalence of bladder dysfunction was higher in patients whose dialysis treatments lasted longer; specifically, 25.3% of patients whose dialysis treatments lasted more than 5 years compared to 14.7% in patients whose treatments lasted 2 years or less and 18.3% in patients whose treatments lasted 2-5 years. Lower urinary tract symptoms (LUTS) were shown to be more common in patients with longer dialysis duration. Specifically, 34.3% of patients with dialysis for more than 5 years, 32.1% of patients with 2-5 years, and 22.5% of patients with ≤ 2 years reported LUTS ($p=0.030$). Although the tendency towards a higher prevalence of prostatomegaly was not statistically significant ($p=0.130$), it did occur in patients whose dialysis

treatments lasted longer (Table 3).

Table 3: Association of Dialysis Duration with Urological Complications

Complications	Dialysis Duration ≤ 2 Years (n=102, 32.9%)	Dialysis Duration 2-5 Years (n=109, 35.2%)	Dialysis Duration > 5 Years (n=99, 31.9%)	p-Value
UTI	24 (23.5%)	32 (29.4%)	29 (29.3%)	0.470
Bladder Dysfunction	15 (14.7%)	20 (18.3%)	25 (25.3%)	0.060
Nephrolithiasis (Kidney Stones)	11 (10.8%)	12 (11.0%)	12 (12.1%)	0.910
LUTS	23 (22.5%)	35 (32.1%)	34 (34.3%)	0.030*
Hematuria	12 (11.8%)	16 (14.7%)	20 (20.2%)	0.240
Prostatomegaly (Male Only, n=180)	9 (7.6%)	14 (12.6%)	17 (16.5%)	0.130
Urethral Stricture	5 (4.9%)	7 (6.4%)	6 (6.1%)	0.720

Statistical Test Used: Chi-square test. Asterisk (*) indicates a statistically significant difference ($p\text{-value} < 0.050$)

The frequency of urological problems was evaluated in three categories, according to residual urine output: less than or equal to 100 mL/day, 101-300 mL/day, and more than 300 mL/day. The incidence of urinary tract infections (UTIs) varied significantly among the groups. Specifically, 34.7% of patients with residual urine output of 100 mL or less per day had UTIs, compared to 26.9% in the 101-300 mL/day group and 17.6% in the > 300 mL/day group ($p=0.020$). Bladder dysfunction, nephrolithiasis (kidney stones), hematuria, prostatomegaly, and urethral stricture were not significantly different in prevalence. There was no significant difference in the prevalence of bladder dysfunction between the groups, with 24.0% of individuals with 100 mL/day or less experiencing it, 15.4% with 101-300 mL/day, and 17.6% with > 300 mL/day. The p-value calculated was 0.130. There was not a significant difference in the frequency of kidney stones or enlarged prostate between groups ($p=0.210$ for each). Urethral stricture, hematuria or LUTS did not show significant differences in any of the groups ($p=0.560$, $p=0.910$ and 0.560, respectively) (Table 4).

Table 4: Correlation Between Urological Complications and Residual Urine Output

Complications	≤ 100 mL/day (n=121, 39.0%)	101-300 mL/day (n=104, 33.5%)	> 300 mL/day (n=85, 27.4%)	p-Value
UTI	42 (34.7%)	28 (26.9%)	15 (17.6%)	0.020*
Bladder Dysfunction	29 (24.0%)	16 (15.4%)	15 (17.6%)	0.130
Nephrolithiasis (Kidney Stones)	18 (14.9%)	9 (8.7%)	8 (9.4%)	0.210
LUTS	32 (26.4%)	36 (34.6%)	24 (28.2%)	0.170
Hematuria	18 (14.9%)	16 (15.4%)	14 (16.5%)	0.910
Prostatomegaly (Male Only, n=180)	18 (15.1%)	9 (8.7%)	8 (9.4%)	0.210
Urethral Stricture	8 (6.6%)	6 (5.8%)	4 (4.7%)	0.560

Statistical Test Used: Chi-square test. Asterisk (*) indicates a statistically significant difference ($p\text{-value} < 0.050$)

The multivariate logistic regression analysis indicated that Hemodialysis (HD) had a statistically significant increased risk of urological complications compared with Peritoneal Dialysis (PD) (OR=1.46, 95% CI: 1.11-1.93, $p=0.021$). Diabetes was also a significant risk factor, diabetic patients had more than double the odds of complications (OR=2.06, 95% CI: 1.56-2.73, $p=0.001$). The hydration status and residual renal function indicators were significant as dehydrated patients (OR=1.82, 95% CI: 1.33-2.48, $p=0.001$) and patients with abnormal renal function (OR=1.62, 95% CI: 1.21-2.14, $p=0.002$) in the week preceding urological assessment were at greater odds of complications. However, the duration of dialysis showed no significant association with urological complications ($p=0.316$ (Table 5)).

Table 5: Multivariate Logistic Regression Analysis for the Association Between Dialysis Type and Urological Complications, Adjusted for Potential Confounders

Complications	Odds Ratio (OR)	95% Confidence Interval (CI)	p-Value
Dialysis Type (HD vs. PD)	1.46	1.11 - 1.93	0.021
Diabetes (Yes vs. No)	2.06	1.56 - 2.73	0.001
Dialysis Duration (≤ 2 Years)	1.22	0.86 - 1.68	0.316
Hydration Status (Normal vs. Dehydrated)	1.82	1.33 - 2.48	0.001
Residual Renal Function (Normal vs. Abnormal)	1.62	1.21 - 2.14	0.002

DISCUSSION

The current study aims to determine the frequency of urological problems in dialysis patients and to find out if they differ in HD patients, PD patients and patients with diabetes, with additional factors such as dialysis time and residual kidney function considered. This can help us understand the urological health of these patients and the importance of understanding, managing, and monitoring any complications. We found a much higher prevalence of urinary tract infection (UTI) and bladder dysfunction published by our comparison. 31.7% of diabetic patients reported a UTI vs. 23.8% of non-diabetic patients, and 25.4% reported bladder dysfunction vs. 14.3% of non-diabetic patients. This is consistent with previous studies by Xin *et al.*, from China and Defeudis *et al.*, from Italy, who both suggested that diabetes may increase the risk of urological complications, considering immune function, nerve damage, and poor mechanisms of bladder control [20, 21]. Our findings also suggest that diabetes may lead to greater nephrolithiasis incidence, although not statistically significant, but an incidence of 14.8% in a diabetic population versus 8.3% in a non-diabetic population agrees with the study by Ejaz *et al.*, from Greece who have demonstrated a greater incidence of kidney stones in diabetic patients [22]. Patients of PD had statistically higher albumin levels compared to HD patients (3.8 ± 0.6 g/dL vs. 3.5 ± 0.7 , $p=0.040$), which may suggest that PD patients exhibited better nutritional status or lower

protein loss than HD, as suggested by literature such as Huang *et al.*, [23]. Our study found a higher association of lower urinary tract symptoms (LUTS) with longer dialysis durations (<0.030). Our patients who were on dialysis for greater than 5 years were more likely to have LUTS than patients on shorter durations of dialysis. These results are similar to those observed by Scherberich *et al.*, who found that long duration of dialysis increases the risks of LUTS due to chronic uremia, altered bladder activity, and reduced residual renal function [24]. Concerning the residual urine output, we found that patients with less urinary volume had a higher prevalence of UTIs. 34.7% of patients with residual urine output ≤ 100 mL/day had UTIs, compared to 17.6% in patients with residual urine output >300 mL/day. This is consistent with a study by Scherberich *et al.*, which demonstrated that patients with low residual urine output are at increased risk for UTI, at least in the dialysis population [24]. The multivariate logistic regression analysis identified several statistically significant predictors of complications involving the urinary tract. Patients receiving hemodialysis (HD) were at a 46% higher risk of complications of the urinary tract compared to peritoneal dialysis (PD) (OR=1.46, $p=0.021$), consistent with earlier findings by Bello *et al.*, [25]. Diabetic patients were also a significant risk factor, as they had over twice the odds of urological complications (OR=2.06, $p=0.001$). This reflects the well-established association between diabetes and urological complications in patients requiring dialysis [26]. This study highlights the necessity of judicious surveillance for urologic complications in dialysis facilities as a function of the patient demographics, namely in patients with diabetes, or with less residual renal function, or abnormal hydration status. This also emphasizes personalized approaches to care strategies, such as glycemic control and regular screening. The cross-sectional design limits causal inference, and the single-center setting may restrict generalizability to broader populations. Additionally, reliance on patient-reported symptoms and residual urine estimates may introduce reporting bias. Future multicenter longitudinal studies incorporating objective urodynamic assessments are recommended to better establish causal relationships and refine risk stratification in dialysis patients.

CONCLUSIONS

How dialysis is delivered, diabetes presence, ongoing dialysis, amount of normal kidney function remains and urological conditions are linked. Our study shows that diabetes and dehydration are major dangers associated with urological complications which is in line with previous research. HD patients had higher rates of urological problems than PD patients, but dialysis modality did not greatly impact most renal function markers. Proper care of diabetes, water levels and dialysis method may lower the risk of urological problems in this group.

Authors' Contribution

Conceptualization: RK

Methodology: RK

Formal analysis: ZAK

Writing and Drafting: ZAK

Review and Editing: RK, ZAK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Forensic Evaluation of Injury Pattern in Pedestrian Road Traffic Accidents in Karachi

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ABSTRACT

Pedestrian-related injuries are among the top of all road traffic-related injuries in Pakistan.

Objectives: To determine the pattern of injuries and responsible factors for pedestrian fatality due to road traffic accidents in Karachi. **Methods:** This retrospective study was carried out at the Department of Forensic Medicine, Karachi Institute of Medical Sciences. Victims involved in pedestrian road traffic accident fatalities, belonging to either gender of any age from three major hospitals in Karachi, were evaluated. Information was recorded in a semi-structured written questionnaire. The multivariate logistic regression analysis was performed for multiple variables simultaneously and reports adjusted odds ratios to determine the independent contribution of each factor to pedestrian mortality. A p-value less than 0.050 was considered statistically significant. **Results:** A total of 681 deceased pedestrians were examined and evaluated for the patterns and factors. The majority of the deceased were male (81.0%) with a mean age of 34.7 ± 2.9 years. The highest proportion (39.2%) of fatalities due to RTA was reported in the 18-30 years' age group. Over two-thirds (74.6%) of accidents took place on the main roads of the city. Common injuries that resulted in death included fatal injuries to the brain and associated vessels (64.4%) and thoracic injuries (14.7%). **Conclusion:** The findings highlight a significant prevalence of male victims, particularly in the 18-30 age group, with brain injuries being the leading cause of death. The analysis also emphasizes the critical role of accident timing, with peak fatalities occurring between 12:00 pm and 4:00 pm, and on main roads.

INTRODUCTION

The spatial mobility provided by automobiles on the local, regional, and global scale has an enormous effect on everyday travel and the flow of commodities globally [1]. Among all types of transport-related mishaps, road traffic accidents (RTAs) have arisen as an essential counter-product of increased motorization and a fast-paced lifestyle, and RTAs are regarded as a modern-day plague [2]. Pedestrian road traffic injuries pose a major global public health challenge, accounting for an estimated 270,000 fatalities annually according to the World Health Organization (WHO) [3]. Pedestrians face

disproportionately higher risks of death and serious injury compared to occupants of motor vehicles, with fatality rates per distance travelled being over four times greater. This vulnerability is attributed to their unprotected state upon collision impact and the biomechanical forces involved, which are influenced by factors such as vehicle type, speed, and impact zone [4]. Road fatalities are predicted to rise in the next two decades in most developing countries, like Pakistan, if appropriate strategies and planning are not taken [3, 5]. The high burden of road traffic injuries in most of these developing



countries is due to the growing number of motor vehicles, disregard for traffic regulations, defective roads, poor health infrastructure, and meager ambulance service [5]. The W.H.O. has estimated that in Pakistan, over 30,000 people die due to traffic accidents per year. While over 75% of road crash fatalities and injuries involved the age groups (15 - 64 years). Moreover, the male-to-female fatality ratio with the 15-49-year age group, who are most vulnerable to fatalities in Pakistan [6, 7]. Forensic pathologists play an important role in investigating pedestrian road traffic fatalities through post-mortem examination and determination of cause and manner of death [8]. Autopsy findings provide objective evidence to characterize injury patterns sustained, which can provide insights into crash dynamics and impact mechanisms. Detailed documentation of trauma patterns, including location, severity and associations between injuries, aids reconstruction of the collision event. Such data assists law enforcement investigations and helps establish whether impairment, reckless or dangerous driving may have contributed to the incident [7, 9]. Some studies have examined injury patterns in a specific group of road users involved in fatal RTCs, but comparisons between different road user groups are limited. Head injuries appear to be more prevalent among pedestrians and cyclists compared to motor vehicle occupants [10]. The severity and type of pedestrian injuries are influenced by multiple factors, including the height of the pedestrian, the design of the striking vehicle, and road conditions at the time of the accident [11]. Forensic studies have also highlighted the importance of toxicological analysis in pedestrian RTAs. Alcohol and drug consumption among pedestrians has been identified as a contributing factor in a significant number of fatal accidents [12]. Blood alcohol concentration (BAC) levels and toxicology screenings are routinely performed in forensic evaluations to determine impairment, which can influence legal responsibility in traffic accidents. Additionally, forensic entomology and post-mortem interval (PMI) assessments can be useful in cases where there is a delay in discovering the victim, aiding in estimating the time of death and accident occurrence [13]. From a road safety perspective, analysis of pedestrian fatality autopsy results can help identify high-risk scenarios and vulnerable groups. Injury profiles correlated with variables such as age, gender, road environment and vehicle types involved may guide the targeting of effective countermeasures [14, 15]. Comparison of findings across jurisdictions enhances understanding of international trends and evaluation of existing intervention strategies. However, standardized protocols for thorough documentation of autopsy results are needed to optimize such analyses [16]. Pedestrian road traffic accidents (RTAs) are a significant public health and

forensic concern, particularly in densely populated urban centers like Karachi, where high traffic volume, inadequate pedestrian infrastructure, and non-compliance with traffic laws contribute to fatal injuries.

Understanding the injury patterns in these accidents is crucial for improving forensic investigations, guiding clinical management, and informing policy decisions aimed at enhancing pedestrian safety. However, existing literature lacks region-specific data correlating injury severity with demographic, environmental, and toxicological factors, limiting its applicability to Karachi's unique traffic and urban landscape. This study aims to analyze and classify injury patterns in pedestrian RTAs, correlate autopsy findings with clinical records, toxicology results, and environmental factors, and compare the findings with global and historical data to identify previously unreported trends.

METHODS

This Retrospective study was carried out from 1st February 2024 to 31st January 2025 by the Department of Forensic Medicine, Karachi Institute of Medical Sciences (KIMS), Karachi, in collaboration with Forensic experts of Shaheed Mohtarma Benazir Bhutto Medical College (SMBMC), Lyari and Liaquat National Hospital and Medical College (LNHMC), Karachi. The data were collected from the medico-legal examiner's office of three different mortuaries of public hospitals, including Lyari General Hospital, Civil Hospital Karachi and Abbas Hospital, which are responsible for investigating all sudden, unexpected, violent or suspicious deaths within their jurisdictions. Furthermore, these hospitals also encompass the urban, suburban and rural road networks of Karachi. Ethical approval was received by the Institutional Review board of KIMS as an exempt retrospective study using de-identified data (Reference No.14(a)/24/IRB/KIMS). While permission to collect data from all the hospitals was also collected. All applicable ethical guidelines for using the data records were followed. Cases were included based on the cause of death that was attributable to injuries sustained from a motor vehicle collision while the decedent was a pedestrian. Deceased cases with other causes of death and those who were riders or occupants, alcohol or drug users were excluded. A semi-structured data collection form was used to collect information about the deceased victims. Questionnaire including the demographic details (age, sex, and residential area), Collision details (location, date/time, vehicle types involved, etc.), Injury characteristics (descriptions, locations, severity, cause and manner of death were evaluated. The Abbreviated Injury Scale (AIS) is commonly used to classify the severity of injuries. This system categorizes injuries based on their severity in various body regions (e.g., brain, chest, abdomen), helping to assess the impact of each injury on

the victim's survival and treatment needs [17]. To ensure accuracy, a second data collector was involved who independently extracted data from 10% of reports, with discrepancies resolved by consensus. Data privacy was ensured as only the investigator has the access to the collected information. Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. The descriptive statistics characterized demographic profiles and frequencies of variables were presented as frequencies and percentages in tables and figures. The dependent variable is pedestrian mortality, and the independent variables include gender, age group, accident time, and accident location, as these factors were evaluated for their association with pedestrian fatalities and injuries. The multivariate logistic regression analysis was performed for multiple variables simultaneously and reports adjusted odds ratios (ORs) to determine the independent contribution of each factor to pedestrian mortality. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 681 deceased pedestrians were examined and evaluated for patterns and factors during the study duration. The demographic details, accident timings, time of injury to death and number of cases are presented. The study findings revealed that the majority of pedestrians were male compared to their counterparts, with the male: female autopsy ratio being 5.8:1. The Highest number of fatalities due to RTA were reported in the 18-30 years' age group while the age group of >60 years reported the lowest number of deaths. The most common time of accidents was 12:00 am – 4:00 pm. Over half of the victims died within seconds to minutes of arrival at the facility. Moreover, the maximum number of incidents was reported in the year 2023 (Table 1).

Table 1: Demographic Characteristics of Pedestrian RTA Fatalities(n=681)

Study variables	n (%)
Sex	
Male	552 (81.0%)
Female	129 (19.0%)
Age	
<18 years	96 (14.1%)
18-30 years	267 (39.2%)
31-45 years	195 (28.6%)
46-60 years	85 (12.5%)
>60 years	38 (5.6%)
Reported Time of Collision	
6:00 am-11:59 am	265 (39.0%)
12:00 pm-4:00 pm	301 (44.2%)
6:00 pm-11:59 pm	97 (14.2%)
12:00 am-5:59 am	18 (2.6%)

Reported Time of Death on Arrival at Facility	
Within seconds to minutes	398 (58.4%)
1-3 hours	226 (33.2%)
Within 24 hours	37 (5.4%)
>24 hours	20 (3.0%)
Year Wise Deaths	
2019	126 (18.6%)
2020	105 (15.4%)
2021	143 (21.0%)
2022	148 (21.7%)
2023	159 (23.3%)

A significant number, 269 (39.5%) of RTAs involved four-wheelers (cars), followed by trucks/loaders 199 (29.2%), buses/pickups 153 (22.5%) and motorbikes/ rickshaw 60 (8.8%). Among the victims, the majority, 390 (57.3%) were had one site of injury, followed by 171 (25.1%) of the victims had more than 2 sites, and 120 (17.6%) had more than two sites of injury. Whereas, among the pedestrian victim injuries, 488 had head and neck injuries, 165 had abdominal and pelvic region injuries, 145 reported with thoracic region injuries, while 103 suffered from injuries to their lower extremities, and 58 had upper extremities injuries. Among the type of injuries, majority 520 (76.5%), of victims were with lacerations, 406 (59.6%), 307 (45.1%) were with contusions whereas, and 161 (23.6%) had fractures. Whereas, on assessing the site of fractures, it was observed that the skull was the most common site for the fracture, 87 (54.1%), followed by fractures to ribs and sternal bone, 29 (18.0%). The fractures to the upper extremity, lower limb, pelvis and neck were observed in 17 (10.6%), 14 (8.7%), 10 (6.2%) and 04 (2.4%) of the cases, respectively. The graphical presentation of month-wise fatalities due to RTA. The highest number of fatalities was reported in January, November, and December. When the yearly distribution of the cases was studied, a significant rise in several RTA-related fatalities was observed from 2019 to 2023. The number of deaths recorded between March and July 2020 compared to the rest of the studied years. This sharp decline was presumably a result of the implementation of stringent measures and lockdowns to contain the COVID-19 pandemic at that time (Figure 1).

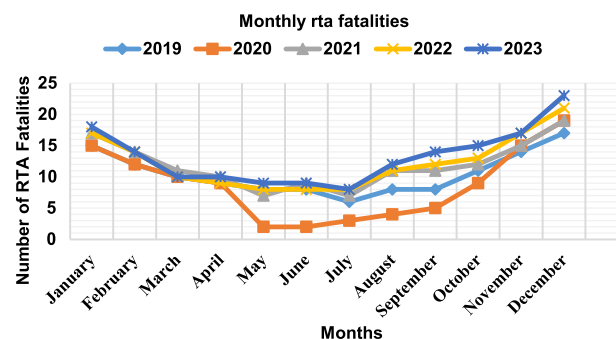


Figure 1: Month-Wise Fatalities Due to RTA in the Last 5 Years (n=681)

The study demonstrated that most 508 (74.6%) accidents took place on the main roads of the city, followed by link roads 106 (15.6%), around about 59 (8.6%) and house streets 8 (1.2%). The victims were examined for the cause of death, it was observed that most of the deaths resulted from fatal injuries to the brain and associated vessels of the victims (Table 2).

Table 2: Distribution of Cause of Death According to the Site of Injury (n=681)

Cause of Deaths	n (%)
Brain And Associated Vessels Injuries	438 (64.4%)
Thoracic /Abdominal Aorta or Both Injury	59 (8.7%)
Thoracic Visceral Injury	41 (6.0%)
Abdominal Visceral Injury	15 (2.2%)
Femoral Vessels Injury	76 (11.1%)
Brachial / Radial Vessel Injury	19 (2.8%)
Pelvic Region Injury	33 (4.8%)

Results show the higher relative risks for pedestrian mortality in different groups. Men were more than five times more likely than women to die from RTAs ($p<0.050$), underscoring their high susceptibility to accidents. The risk of brain injury death was 1.5 times higher in the 18–30 age group, indicating that this population needs priority interventions. Enforcing traffic laws during peak hours may help prevent brain injuries, as accidents that occur in the afternoon have a 1.7-fold increased risk of brain damage. The multivariate analysis of independent risk factors of pedestrian mortality after adjusting the confounders demonstrated that, compared to the remaining age groups, pedestrian victims aged 18–30 years had 2.1 times higher adjusted risks of mortality due to RTA whereas, comparing females, males have a 3.4 times higher probability of dying in pedestrian RTAs. Moreover, there was 1.9 times higher probability of (adjusted mortality risk) associated with afternoon time RTAs (12–4 pm) considered as a high-risk period, and main highways were found to be associated with 1.6 times higher odds of pedestrian mortality (Table 3).

Table 3: Risk Assessment and Multivariate Logistic Regression Analysis of Different Factors for Pedestrian Mortality

Risk Assessment			
Outcome	Exposure	RR (95% CI)	p-Value
Death	Males	5.8 (4.8–7.0)	0.000*
Brain Injury Death	Age Group (18–30 Years)	1.5 (1.2–1.9)	0.037*
Brain Injuries	Accident Time (12–4 pm)	1.7 (1.4–2.1)	0.001*
Head Injuries	Main Roads	2.3 (1.8–2.9)	<0.001*
Multivariate Logistic Regression Analysis			
Study Variables	Adjusted OR	95% CI	P-Value
Male Gender	3.4	2.5–4.6	<0.001*
Age Group (18–30 Years)	2.1	1.5–3.0	<0.001*
Accident Time (12–4 pm)	1.9	1.3–2.7	0.001*

Main Road (Location)	1.6	1.2–2.1	0.034*

*Statistically significant $p<0.050$

DISCUSSION

Pedestrians are among the most vulnerable road users, with fatality risks disproportionately higher compared to motor vehicle occupants. Determining causes and manners of pedestrian RTA deaths through post-mortem examination is very important in forensic investigations [18]. The findings of medico-legal autopsies are legitimate proof in a court of law and are carried out by the laws of all countries. An extensive epidemiological profile can be created based on autopsy findings that could assist in the future implementation of suitable preventive measures [19, 20]. The present study was designed to determine the pattern of injuries and responsible factors for pedestrian fatality due to road traffic accidents in Karachi, Sindh. This study demonstrated the different injury patterns, site of injuries, timings and months of fatalities in pedestrian victims of different age groups through a prospective analysis of data. Based on the findings, a high proportion (39.2%) of fatalities were observed in the age group between 18–30 years. Our findings are consistent with those reported by Uddin et al., Khurshid et al., and Chaturvedi et al., [21–23]. Whereas, Hb et al., reported that RTA fatalities were common among those aged 40 years and above, which is higher than our findings [24]. Concerning gender, the findings of our study revealed that there were over two-thirds of the victims were males (81.0%) compared to female (19.0%). Hb et al., Yadav et al., and Talpur et al., also reported identical findings like the present study, with a higher proportion of male victims compared to their counterparts [24–26]. This may be due to the societal expectations and a greater inclination towards outdoor activities, as men are more vulnerable to RTAs than women. Moreover, in comparison to adolescents and elderly people, young people are presumably more engaged, and their activities presumably require them to travel more frequently. The study's findings about the involvement of the younger age group in RTAs may be explained by the fact that this is not only the generation with the greatest potential for society, but also the most energetic period of life in terms of both physical and social activity. Therefore, it may be considered a significant loss when such economically productive people pass away. A significant number (39.6%) of RTAs involved four-wheelers (cars), followed by trucks/loaders (29.4%), buses/pickups (22.2%) and motorbikes/ rickshaw (9.8%). Our findings are in line with research by Talpur et al., [26]. With the greater increase in number of vehicles The cars on crowded and open city roads, whereas trucks and loaders on main highways, district highways, or even city roads are typically involved in accidents because of careless over-speeding, driving while intoxicated, frequent lane changes without

signaling, and poorer vehicle stability as well as decline in following road traffic regulations resulting in increasing number of accidents. The majority of accidents in this study (44.2%) occurred between the hours of 12:00 pm and 4:00 pm, with early morning hours (6:00 am to 11:59 am) accounting for 39.0% of all accidents. These findings are in line with Talpur et al., however, some national and international studies reported that the majority of accidents occurred during night timings [26]. Since automobiles travel at a faster speed on main roads, RTIs primarily happen on these routes, followed by residential streets and connection roads. This aligns with the findings of research conducted in Pakistan and India [22, 27]. The findings of the present study also showed that RTIs were common on the main roads of the city. Over two-thirds of victims suffered fatal head and neck region injuries, followed by injuries to the abdomen, pelvis and thoracic region. Among the type of injuries, majority 520 (76.5%) of victims were with lacerations, 406 (59.6%), 307 (45.1%) were with contusions whereas, and 161 (23.6%) had fractures of which skull was the most common site for the fracture 87(54.1%), followed by fracture to ribs and sternal bone 29(18.0%). Fatal brain injuries and associated vessels of victims in the present study we found at peak, as most (64.4%) of the deaths resulted from these injuries. Our study findings are consistent with the findings reported by different national and international studies found that the leading cause of fatalities or deaths in their studies was acute head trauma, which resulted in the ultimate cause of death, cardio-respiratory failure [26, 28]. The alarming findings of our study are that over 5 years, the majority of RTA victims (58.4%) died within seconds to minutes before they arrived at the emergency unit; they may have died at the scene of the accident or while being transported. Other studies from LMICs also reported this observation [25, 29]. This raises serious concerns over the absence of pre-hospital management services, a referral mechanism, and delayed emergency services. Other potential causes could be the absence of an adequate emergency management service in the nearby the site of accidents. Moreover, the increasing number of mortalities among younger people in the last five-year period is raising a serious concern. The study is limited by its single-center design and reliance on medico-legal autopsy records, which may not capture pre-hospital factors and behavioral variables influencing RTAs. Additionally, lack of detailed information on environmental conditions and emergency response times may have affected comprehensive risk assessment. Future multicenter studies incorporating pre-hospital care data, road safety factors, and emergency response systems are recommended to develop targeted interventions for reducing pedestrian fatalities.

CONCLUSIONS

The findings highlight a significant prevalence of male victims, particularly in the 18-30 age group, with brain injuries being the leading cause of death. The analysis also emphasizes the critical role of accident timing, with peak fatalities occurring between 12:00 pm and 4:00 pm, and on main roads. These findings underscore the need for targeted interventions, such as improved road safety measures, enforcement of traffic laws during peak hours, and public education to reduce pedestrian fatalities.

Authors' Contribution

Conceptualization: AW

Methodology: AW, SAQ, HR, MN

Formal analysis: AW, IAK, SAQ

Writing and Drafting: AW, IAK, FAK, SAQ

Review and Editing: AW, IAK, FAK, SAQ, HR, MN

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Factors Affecting Non Compliance to Medication in Epileptic Patients

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ABSTRACT

Non-compliance with antiepileptic medications is a significant concern, leading to poor seizure control, increased hospitalization, and higher healthcare costs. **Objective:** To identify factors contributing to non-compliance among epileptic patients. **Methods:** A cross-sectional study was conducted at Akhtar Saeed Trust Hospital, Lahore, from July 2023 to March 2024, including 200 epileptic patients aged 18-60 years identified as non-compliant using the Morisky Medication Adherence Scale (MMAS-4). Patients with psychiatric illnesses, hearing problems, or those pregnant/lactating were excluded. Data on demographics and contributing factors (e.g., high costs, forgetfulness, unemployment) were collected via structured proformas. Statistical analysis using SPSS version 25.0 included descriptive statistics and stratified analyses to explore relationships between factors and demographics, with significance at $p < 0.05$. **Results:** Of 200 patients, 67.5% were male. High cost (57.5%) was the leading factor, followed by forgetfulness (55.0%), prolonged treatment duration (32.5%), unemployment (29.5%), and medication complexity (16.5%). Monthly household income significantly influenced these factors; high costs and prolonged treatment duration were predominant in low-income groups ($p < 0.001$). Forgetfulness was uniformly reported across socio-economic strata ($p = 0.094$). **Conclusions:** High medication costs and forgetfulness are primary contributors to non-compliance among epileptic patients. Strategies like cost reduction, simplified regimens, and reminder interventions are essential to enhance adherence and improve clinical outcomes.

INTRODUCTION

Epilepsy, a chronic neurological disorder characterized by recurrent, unprovoked seizures, affects over 65 million individuals worldwide. Epilepsy affects approximately 50 million individuals globally, with a prevalence of 9.99 per 1,000 people in Pakistan, translating to about 2 million individuals nationwide. [1, 2]. Antiepileptic drugs (AEDs) are the mainstay of epilepsy treatment, offering the potential for seizure freedom in nearly two-thirds of patients when

adhered to correctly [3]. However, non-compliance with medication regimens among epileptic patients is a critical issue that continues to undermine effective treatment outcomes. [4]. The World Health Organization (WHO) classifies medication non-compliance as a major public health concern, particularly in chronic conditions like epilepsy [5]. Understanding the multifaceted factors that affect adherence is therefore crucial in improving



outcomes for patients suffering from epilepsy [6]. Adherence to AEDs remains suboptimal due to patient-related and socioeconomic factors, highlighting the need to identify underlying causes and design targeted interventions [7]. Medication non-compliance in epileptic patients arises from patient-related, treatment-related, socioeconomic, and healthcare system factors. [8]. Cognitive impairments and forgetfulness also contribute significantly, particularly among elderly patients who may be managing multiple comorbidities and medications simultaneously [9]. Treatment-related factors also play an essential role in adherence. The complexity of the prescribed regimen like polypharmacy, the frequency of dosing, and the occurrence of adverse effects are critical determinants of compliance [10]. Many AEDs are associated with side effects, ranging from mild drowsiness to severe mood and cognitive changes, significantly impact adherence; with an Ethiopian study showing patients experiencing adverse effects were 13.68 times more likely to be non-compliant (aOR: 13.68; 95% CI: 3.27–56.97) [11]. Socioeconomic factors like financial constraints, low health literacy, and limited healthcare access hinder AED adherence, with a Bangladeshi study showing a strong positive correlation between AED costs and adherence levels [12]. Cultural beliefs and stigma in societies like India hinder epilepsy treatment adherence, as fear of ostracization deters care. Despite 87% awareness and 83.7% identifying it as neurological stigma remains a barrier [13]. A study conducted in Pakistan showed that 44.4% exhibited non-compliance to AED and was more prevalent among patients with longer illness duration and those on polypharmacy [10]. Another study suggested that the primary reasons for non-compliance among epilepsy patients were the high cost of treatment (54%) in self-paying patients, while uncontrolled seizures (33.3%) and misleading by local quacks (25%) were major factors among those receiving free treatment [14]. According to Awan *et al.*, among epilepsy patients 26.7% were non-compliant with AED treatment, with forgetfulness being the most common reason (72.5%), followed by affordability issues (12.5%) and symptom relief (7.5%) [15]. Non-adherence was significantly associated with poor seizure control (77.5% vs. 49.1%, $p = 0.001$) and a higher frequency of convulsive seizures in the past year ($p = 0.006$), highlighting the critical impact of adherence on treatment outcomes [9].

Despite the availability of effective antiepileptic drugs, medication non-compliance remains a significant barrier to optimal seizure control, particularly in low- and middle-income countries like Pakistan. While various factors influencing adherence have been identified globally, there is limited context-specific data quantifying the relative contribution of these factors in local populations. This gap

hinders the development of targeted interventions to improve adherence and treatment outcomes. The study aimed to determine the frequency of contributing factors leading to non-compliance with antiepileptic medications in patients diagnosed with epilepsy.

METHODS

A cross sectional study was conducted at Akhtar Saeed Trust Hospital, Department of Medicine and Allied, Lahore. The study was approved by the Ethical Review Committee of Akhtar Saeed Trust Hospital, in accordance with the ethical principles for medical research involving human subjects outlined in the Declaration of Helsinki (IRB no.2023/ASTH/687). The study was conducted from July 15, 2023 to March, 2024 (for 8 months). Patients were required to have been taking antiepileptic drugs (AEDs) for more than three months and were identified as non-compliant using the Morisky Medication Adherence Scale (MMAS-4) the scale was translated in local language as well [15, 16]. The MMAS-4 was employed to assess medication adherence among epileptic patients in this study [17]. Sample size of 200 was calculated at 95% confidence level and 5% margin of error and taking an expected percentage of noncompliance as 44.4% [10]. A non-probability convenience sampling method was used for patient selection. Patients with Epilepsy who were taking AED for more than three months and were non-compliant to medication were enrolled from the Outpatient Department after taking informed consent. A patient answering YES to ≤ 2 questions on the Morisky Medication Adherence Scale (MMAS-4) was deemed non-compliant i.e., (a) Patient has ever forgotten to take medication; (b) Patient has ever had problems remembering to take medication; (c) Patient has stopped medication due to worsening symptoms; (d) Patient has stopped medication due to alleviating symptoms. Patient's self-reports were cross checked with prescription records to validate adherence to reduce recall bias. Bio data was entered in a pre-designed structured proforma. Various contributing factors determining compliance like unemployment, income per month in PKR high cost, forgetfulness, complexity of medicine, prolonged duration of treatment were noted [17, 18]. All information was kept confidential and all patients were managed as per hospital protocol. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 25.0. Chi-square test was used for categorical variable comparisons. Qualitative data like gender and contributing factors were presented as frequencies and percentages. Quantitative data i.e., age was presented as means and standard deviations. Data were stratified for age, gender, socio-economic status and educational status and a p-value of less than 0.05 was considered statistically significant. Specifically employing the chi-square test to analyze relationships between categorical variables such as household income, educational levels, and medication adherence outcomes. This method was

selected due to its appropriateness for categorical data, which does not require normality tests that are necessary for continuous data analyses like t-tests or ANOVA. Additionally, we checked that the sample size was adequate to provide expected frequencies in the contingency tables, requiring that each cell have a minimum expected count of five to uphold the chi-square test's accuracy; where this criterion was not met, Fisher's exact test was utilized, suitable for smaller sample sizes.

RESULTS

A total of 200 patients with diagnosis of Epilepsy were included. Age range in this study was from 18 to 60 years with a mean age of 39.5 ± 12.5 years. Most of the patients 73 (36.5%) were in 46-60 years of age group, while 57 (28.5%) and 70 (35.0%) were in 18-30 years and 31-45 years of age groups respectively (Table 1). According to household income 74 (37.0%) had monthly income <25,000 per month, while 66 (33.0%) and 60 (30.0%) had monthly income 25,000-50,000 and >50,000 per month respectively (Table 1). According to educational status, 44 (22.0%) were illiterate, while 80 (40.0%) and 76 (38.0%) did middle and matriculation or higher respectively. According to contributing factors of non-compliance to medications in epileptic patients, high cost 115 (57.5%) was the most common factor followed by forgetfulness in 110 (55.0%), prolonged duration of treatment in 65 (32.5%), unemployment in 59 (29.5%) and complexity of medicine in 33 (16.5%). Table 1 illustrated the socio-demographic characteristics of a study population totaling 200 individuals, categorized by gender, age groups, and socio-economic status. Gender-wise, males were predominant, constituting 67.5% (n=135) of the participants, while females accounted for 32.5% (n=65). The age distribution showed a spread across three defined groups: 18-30 years (n=57, 28.5%), 31-45 years (n=70, 35.0%), and 46-60 years

(n=73, 36.5%). In terms of monthly income, participants were divided into (<25,000; 37.0%, n=74) (26,000-50,000; 33.0%, n=66), and (>51,000; 30.0%, n=60) income brackets.

Table 1: Socio-Demographic Profile of study participants

Variables	Frequency (%)
Gender	
Male	135 (67.5)
Female	65 (32.5)
Age Groups	
18-30 Years	57 (28.5)
31-45 Years	70 (35.0)
46-60 Years	73 (36.5)
Household Income per Month (PKR)	
<25,000	74 (37.0)
26-50,000	66 (33.0)
>51,000	60 (30.0)
Total	200 (100.0)

Table 2 shows that high cost was the most frequently occurred issue, reported by 115 participants (57.5%),

Table 2: Frequency of Contributing Factors

Factors	Frequency (%)
Complexity of Medicine	33/200 (16.5)
Unemployment	59/200 (29.5)
High Cost	115/200 (57.5)
Forgetfulness	110/200 (55.0)
Prolonged Duration of Treatment	65/200 (32.5)

The table 3 reveals significant differences based on monthly household income: complexity of medicine and unemployment exhibited notable decreases in frequency as monthly income increased, with p-values of 0.004 and 0.001, respectively, indicating strong statistical significance.

Table 3: Stratification of Contributing Factors with Respect to Socio-Economic Status

Contributing Factors	Socio-Economic Status			p-Value
	<25,000 Frequency (%)	26-50,000 Frequency (%)	>51,000 Frequency (%)	
Complexity of Medicine	16 (21.6)	15 (22.7)	2 (3.3)	0.004
Unemployment	29 (39.2)	28 (42.4)	2 (3.3)	0.001
High Cost	68 (91.9)	39 (59.1)	8 (13.3)	0.001
Forgetfulness	44 (59.5)	40 (60.6)	26 (43.3)	0.094
Prolonged Duration of Treatment	32 (43.2)	29 (43.9)	4 (6.7)	0.001

The findings in table 4 suggest that the complexity of medicine, which increased across the age groups (from 10.5% in 18-30 years to 21.9% in 46-60 years), did not reach statistical significance (p-value of 0.216). Unemployment and high cost showed slight variations in percentages across the age groups but remained statistically non-significant with p-values of 0.416 and 0.956, respectively. Forgetfulness and prolonged duration of treatment also exhibited minor percentage differences across age groups but without statistical significance (p-values of 0.812 and 0.434, respectively).

Table 4: Stratification of Contributing Factors with Respect to Age

Contributing Factors	18-30 Years Frequency (%)	31-45 Years Frequency (%)	46-60 Years Frequency (%)	p-Value
Complexity of Medicine	6 (10.5)	11 (15.7)	16 (21.9)	0.216
Unemployment	13 (22.8)	22 (31.4)	24 (32.9)	0.416
High Cost	33 (57.9)	41 (58.6)	41 (56.2)	0.956

Forgetfulness	32 (56.1)	40 (57.1)	38 (52.1)	0.812
Prolonged Duration of Treatment	15 (26.3)	23 (32.9)	27 (37.0)	0.434

DISCUSSION

Poor medication compliance is a widespread issue, even among patients with epilepsy who understand the risks of seizures and death. Indicators of non-compliance in epilepsy include inconsistent requests for repeat prescriptions of antiepileptic drugs (AEDs), lack of improvement with appropriate treatment, and increased seizure frequency. However, identifying all non-compliant patients remains challenging [18, 19]. According to the current study among 200 patients, 135 (67.5%) were males and 65 (32.5%) were females showing bias in healthcare access or a higher frequency of diagnosed epilepsy in males. Literature often shows mixed results regarding gender differences. Some studies find no significant disparity, while others, like Hauser WA and Hesdorffer DC observed a slight male predominance, possibly due to higher exposure to risk factors such as head injuries and strokes in adulthood [20]. In this study, the age group of older adults (46-60 years) emerged as the most prominent, suggesting a possible higher occurrence of epilepsy or enhanced diagnostic rates within this demographic. A demographic study by Lezaic indicated that while epilepsy can begin at any age, there was a notable incidence peak in the population over 60 years. This reflects an increased risk due to age-associated conditions like stroke and Alzheimer's disease [21]. The current results revealed that among the epilepsy patients studied, 37.0% of the sample belonged to the category, with a monthly income of less than 25,000 PKR. Mandorf S *et al.*, found that in their study, 24% of patients couldn't consistently afford medications, 49% had medical insurance, and 78% of low-income patients sought free drugs or financial aid, contributing to non-adherence to AEDs [8]. The study highlighted the primary reasons for non-compliance with medication among epileptic patients, identifying high medication costs as the most significant factor, affecting 115 out of 200 patients (57.5%). This is contrasting with findings by Govil *et al.*, who reported that only 8.2% of their cohort cited economic constraints as a major barrier to epilepsy treatment, patients were unable to afford to purchase medicines [22]. Despite both studies being conducted in low-income settings, it suggested that local economic factors and healthcare system efficiencies might significantly influence patient experiences and perceptions of affordability in epilepsy treatment. According to Peroni *et al.*, despite similar retail prices globally, over 80% of people with epilepsy in LICs and MICs face substantial financial burdens due to low per capita income and inadequate reimbursement systems, whereas less than 20% in HICs experience better affordability due to higher incomes and stronger reimbursement mechanisms, underscoring the inequity in access to antiseizure

medications worldwide [23]. In this study, 55% of participants reported forgetfulness as a key factor in medication non-compliance, closely aligning with a study conducted in Indonesia which found a similar impact in 50% of their cohort. This highlights the critical role of cognitive dysfunction in adherence, emphasizing the need for interventions like reminder technologies or cognitive support to mitigate its effects and improve patient outcomes [24]. In the current study, 32.5% of patients identified the prolonged duration of treatment as a barrier to medication adherence, while 16.5% reported challenges related to the complexity of their medication regimens. These rates are notably higher than those reported in a study conducted in India, where 20.0% of patients experienced fatigue from taking medication over an extended period. Additionally, the Indian study found that 8.2% of patients attributed non-adherence to managing multiple medications, and 2.5% cited the complexity of the drug regimen. The combined complexity-related non-compliance in the reference study amounted to 10.7%, which remains significantly lower than the findings of the present study [22]. In the present study, the influence of household income on non-compliance with antiepileptic medications reveals significant disparities in contributing factors across different income groups. The complexity of medicine was found to be a significant barrier to medication adherence among patients from different groups, with a p-value of 0.004. This disparity may be due to limited resources, lower health literacy, or inadequate support, whereas higher income patients likely benefit from better access to mitigating resources. In comparison, the Saudi Arabian study reported that 24% of patients cited complexity as a major barrier to adherence, with a p-value of 0.034 [25]. Unemployment was significantly linked to non-compliance, particularly in the low (39.2%) and middle (42.4%) income groups, compared to the high income group (3.3%) (p = 0.001). Employment status seems crucial for medication adherence; likely due to the affordability it provides. A study conducted in Malaysia revealed that employment status was significantly associated with ASM adherence (p = 0.012), with adherence being higher among employed participants or students (56.3%) compared to unemployed, pensioners, or housewives (43.7%). Non-adherence was also more prevalent in unemployed participants (36.0%) compared to employed individuals (64.0%), emphasizing the role of employment in improving adherence [7]. These international findings support the notion that improving employment opportunities and providing financial support could positively impact adherence rates. The high cost of medication was also a major barrier, especially among the PKR < 25000 group,

where 91.9% reported cost as a reason for non-compliance, and similarly in the PKR 26-50000 (59.1%), but far less in the group earning PKR>51000 (13.3%) ($p = 0.001$). Monthly income was significantly associated with adherence status ($p = 0.008$), with adherence rates increasing from 26.2% in participants earning less than \$18 (999 birrs) to 58.3% in those earning above \$55 (3000 birrs). Conversely, non-adherence was highest in the PKR<25000 income group 39.77 (95% CI: 32.44, 47.10) and lowest in the PKR>51000 income group (41.7%), highlighting the impact of financial stability on compliance [26]. This highlighted the financial burden on lower-income patients, stressing the need for cost-reduction strategies to enhance adherence. Forgetfulness appears to be a notable factor across all income groups, with similar percentages reported among PKR<25000 group (59.5%) and PKR 26-50000 (60.6%) groups, and a lower proportion in the PKR>51000 group (43.3%). The lack of statistical significance ($p=0.094$) suggests that forgetfulness is a universally common issue, irrespective of income status. This aligns with findings from a study conducted in Norway where forgetfulness emerged as a significant factor contributing to non-compliance. Approximately 40% of participants reported sometimes or often forgetting to take their AEDs, highlighting unintentional non-compliance. Forgetfulness was independently associated with non-compliance due to memory problems, with an odds ratio (OR) of 1.529 (95% CI: 1.137-2.053, $p = 0.005$) [27]. These findings underscore the need for interventions like medication reminders to enhance adherence. The prolonged duration of treatment is also highlighted as a contributing factor, with 43.2% of patients from PKR<25000 household income, 43.9% from PKR26-50000 income, and only 6.7% from PKR>51000 income reporting it as a reason for non-compliance. The statistically significant p -value ($p=0.001$) underscores the challenges of long-term treatment, particularly for those from lower income backgrounds. Studies from international settings, such as the UAE indicated that prolonged duration of treatment did not have a statistically significant association with non-compliance ($p = 0.396$), as adherence rates remained relatively consistent across treatment durations, with slight variations: 73.7% for ≤ 1 year, 66.4% for $>1-5$ years, and 70.0% for >5 years [28]. This suggests that interventions focused on simplifying treatment plans and providing long-term support are crucial, especially for economically disadvantaged patients. The cross-tabulation of age groups influenced contributing factors to non-compliance with antiepileptic medications among the patients revealed varying levels of influence for factors such as the complexity of drugs, unemployment, high cost, forgetfulness, and prolonged duration of treatment. The complexity of medication was reported by 21.9% of patients aged 46-60, 15.7% aged 31-45, and 10.5% aged 18-30 ($p=0.216$). These findings align with those of Permatananda *et al.*, they found that patients

under 40 years old had higher adherence rates compared to those aged 40 and above ($p=0.001$), suggesting that younger patients may manage complex regimens more effectively [24]. Unemployment affected 32.9%, 31.4%, and 22.8% in these age groups, respectively, with no significant difference ($p=0.416$). The higher rates in older age groups may reflect greater employment challenges among older adults with epilepsy. However, the absence of a significant difference suggests that unemployment affects medication adherence similarly across ages. Teh *et al.*, (2020) reported that being employed or a student was significantly associated with non-adherence ($p=0.012$), indicating that employment status can impact adherence behaviors [7]. High cost was cited by 57.9% (18-30), 58.6% (31-45), and 56.2% (46-60), showing no age-related disparity ($p=0.956$). Similarly, in the study conducted in Saudi Arabia, high cost was reported as the second most common cause of non-adherence following forgetfulness, though specific age stratification was not provided. Forgetfulness, on the other hand, was the most prevalent factor contributing to non-compliance in the study, affecting 56.1% to 57.1% of participants across all age groups, with no significant differences observed ($p = 0.812$). This finding aligns with a study conducted by Mahmoud MR, where forgetfulness was identified as the leading cause of non-adherence, affecting 69.6% of patients and showing a significant association with non-compliance ($p < 0.050$) [29]. These results underscore the consistency of forgetfulness and high cost as universal barriers to medication adherence, irrespective of age stratification or geographic location. Prolonged treatment duration was more common among older patients: 37.0% (46-60), 32.9% (31-45), and 26.3% (18-30), though differences were non-significant ($p=0.434$) also seen in Indonesian study where patients with a treatment duration of less than 10 years exhibited better adherence than those with longer treatment durations ($p=0.023$) [22].

This study has several limitations that should be considered when interpreting the findings. The reliance on self-reported data introduces the possibility of recall and social desirability bias, as patients may underreport or overestimate their medication adherence. Second, the study is limited to a specific population within Pakistan, which may restrict the generalizability of the findings to other regions with different healthcare infrastructures, socioeconomic conditions, and cultural perceptions of epilepsy. Moreover, another limitation of this study is the absence of a formal validation study of the MMAS-4 for the Urdu-speaking population in Pakistan. While the scale is respected and validated internationally, different cultural nuances and language interpretations could potentially affect the accuracy of the results in this context. Confidence intervals are essential for assessing the precision and reliability of estimated effects, offering insights beyond the statistical significance indicated by p -

values. Their inclusion helps contextualize the strength and variability of observed associations, providing valuable information for clinical and policy decision-making. The initial analytical focus was primarily on identifying statistically significant associations, which led to the exclusion of confidence intervals. Recognizing this limitation, we recommend that future research includes confidence intervals to furnish a fuller statistical picture. Additionally, the study does not account for potential confounding factors such as comorbid conditions, cognitive impairments, or psychological disorders like depression and anxiety, which may independently influence adherence. The cross-sectional design also limits the ability to establish causality between non-compliance and its associated factors, making it difficult to assess long-term adherence patterns. Future research could focus on conducting a validation study of the MMAS-4 in local languages to confirm its reliability and validity in Pakistan, enhancing the robustness of adherence assessments in this population, the absence of confidence intervals in the statistical analysis is another notable limitation of the study.

CONCLUSIONS

Medication non-compliance in epilepsy is driven more by socioeconomic and behavioral factors than by clinical ones. In this study, high out-of-pocket medication costs (57.5%) and forgetfulness (55.0%) were the leading causes, followed by unemployment (29.5%), regimen complexity (16.5%), and side effects (8.3%). Clinical factors like seizure type or polytherapy showed no significant association. These findings highlight the need for both financial support (e.g., subsidies, insurance coverage) and behavioral interventions (e.g., app reminders, simplified regimens, patient education) to improve adherence, seizure control, and quality of life for epileptic patients in Pakistan.

Authors' Contribution

Conceptualization: MTR

Methodology: MM, IAM

Formal analysis: MI

Writing and Drafting: MM, IAM, HMIA, QUA, NZ, SA, R

Review and Editing: MTR, MM, IAM, HMIA, QUA, NZ, SA, R

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Micro Needling with Topical Tranexamic Acid and Mesotherapy with Intradermal Tranexamic Acid in Treatment of Melasma

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ABSTRACT

Melasma is a common hyperpigmentation disorder that poses therapeutic challenges due to its recurrent and resistant nature. Microneedling showed superior and faster pigmentation reduction, with significant MASI score improvement and no adverse effects. **Objective:** To compare the effectiveness of intradermal Tranexamic Acid (TA) via mesotherapy versus topical TA delivered through microneedling in the treatment of melasma. **Methods:** In this prospective comparative study, 100 patients were divided into two equal groups. Group A received intradermal injections of TA (100 mg/mL), and Group B was treated with the same concentration of TA via microneedling using the Dr. PEN A6 device. Each group received three treatments at two-week intervals. Outcomes were assessed at Weeks 4, 8, 12, 16, and 20 using the Melasma Area and Severity Index (MASI) and standardized clinical photography. Statistical analysis was performed using repeated measures ANOVA, with a significance threshold of $p \leq 0.050$. **Results:** The mean age was 37.7 ± 6.1 years. Group B showed greater improvement in MASI scores compared to Group A, with a 32.5% vs 18.4% reduction at Week 4 ($p = 0.170$). Group B consistently showed statistically significant improvement at Weeks 12, 16, and 20 ($p < 0.050$), and a strong trend by Week 8 ($p = 0.001$). No adverse events were reported. **Conclusion:** TA is an effective treatment for melasma. Microneedling significantly enhances its efficacy, providing faster and greater pigmentation reduction with minimal side effects.

INTRODUCTION

Melasma is an acquired pigmentary disorder commonly affecting individuals with darker skin types, particularly Asians. It presents as symmetrical, light to dark brown macules with well-defined borders, predominantly on sun-exposed areas such as the cheeks, forehead, upper lip, and temples [1]. The condition significantly affects cosmetic appearance and quality of life. To objectively assess melasma severity, Maluki and Al-Sabak introduced the Modified Melasma Area and Severity Index (mMASI) in 2015, which evaluates the extent and darkness of pigmentation

on each side of the face before and after treatment [2]. Although the exact pathogenesis of melasma remains unclear, several triggering factors have been identified, including hormonal influences (such as pregnancy or hormone therapy), Ultraviolet (UV) radiation, cosmetic products, phototoxic drugs, and anti-epileptic medications [3]. UV radiation may lead to pigmentation through photo-induced hormonal activity, inflammatory mediators, and growth factors that influence melanocyte activity [4]. A variety of treatment modalities have been



explored ranging from topical depigmenting agents and chemical peels to dermabrasion and laser therapy but their results are often inconsistent or unsatisfactory [5, 6]. Tranexamic Acid (TA), a synthetic derivative of lysine, has emerged as a promising treatment option. It is used orally, topically, intradermally (mesotherapy), or via microneedling to inhibit melanogenesis. TA acts by reversibly blocking lysine binding sites on plasminogen, thereby inhibiting the conversion of plasminogen to plasmin, which reduces inflammation and vascular factors that stimulate melanin production. Given its potential, this study aims to compare the effectiveness of intradermal TA (mesotherapy) with that of microneedling-assisted topical TA application in the management of melasma [7, 8]. In recent years, Tranexamic Acid (TA) has emerged as a promising therapeutic option for melasma. Its proposed mechanisms of action include inhibition of melanocyte proliferation, reduction in melanin synthesis, decreased dermal vascularization, and suppression of mast cell activity within the dermis [9].

Transepidermal delivery of TA through microneedling, as well as localized intradermal microinjections (mesotherapy), have shown encouraging results in recent clinical studies [10-12]. However, there is limited direct comparative evidence evaluating the effectiveness of these two delivery methods. This study aimed to address this gap by comparing the efficacy of intradermal TA (mesotherapy) and microneedling-assisted topical TA in the treatment of melasma.

METHODS

In Pakistan Emirates Military Hospital's Department of Dermatology, a prospective comparative study was carried out. The study spanned from January 2024 to June 2024, a period of six months. Adult males and females with moderate-to-severe bilaterally symmetrical melasma distribution, aged 18 to 50, were included in the target population. Diagnostic Tools for Melasma: Diagnosis of melasma was clinically confirmed using a Wood's lamp examination, which helped distinguish between epidermal and dermal melasma. Additionally, a detailed personal and medical history was taken to confirm the symmetrical distribution and moderate-to-severe classification of melasma. Consideration of comorbidities: participants with conditions that could potentially affect melasma outcomes were excluded. These included: pregnant or nursing women, patients taking oral contraceptives or hormone replacement therapy, individuals with bleeding disorders or using anticoagulants, patients with known allergies to tranexamic acid and those who had received any depigmenting treatment within the past month. Patients were selected from the Pakistan Emirates Military Hospital's Department of Dermatology after meeting the exclusion and inclusion criteria. The sample size was calculated based on a confidence level of 95%, a power of

80%, and a one-tailed test to detect a significant difference between the two treatment groups. The proportions were assumed as 0.18 for the microinjections group and 0.33 for the microneedling group. A 10% dropout rate was also considered in the final calculation. However, 200 patients were included in this investigation to allow for any variability. a sample size of 100 individuals, 50 in each treatment arm, who will present between January and June of 2024. To identify the type of melasma, a Wood's lamp examination was conducted following the acquisition of comprehensive personal and medical histories. Melasma severity was evaluated using a modified MASI grading system. Prior to treatment, the lesions of the patient were photographed in both treatment arms. About an hour before the procedure, an anaesthetic cream (5% lidocaine and 5% prilocaine) was applied with a closed dressing for maximum effectiveness. There were 100 mg/mL TXA ampoules used in the first treatment arm. The DR. PEN A6 microneedling machine was used to perform the microneedling technique, and a sterile disposable cartridge containing 36 needles was used. To cause localised bleeding, these needles were placed 2-4 mm into the targeted skin area. Making punctures in the skin in horizontal, vertical, and diagonal orientations was the needling technique. A total of 5 cc of TXA was applied topically on each patient during the microneedling treatment. After the microneedling process was finished, the skin was covered for 15 minutes with sterile gauze (SOAK) that contained 5 mL from each ampoule. Using a 1cc insulin syringe, intradermal injections of 100 mg/mL TA supplied in vials containing 100 mg/mL solutions were given to melasma lesions in the second treatment group. Every two weeks, TA injections under the skin were administered. To avoid cosmetic defects, one centimeter distances were measured with a ruler and marked with a washable marker. In order to produce a wheal-like area on the skin, 0.1 mL of solution was injected into each indicated site at an angle ranging from 5 to 15 degrees. Thirty minutes after the treatment, the areas were cleaned with an alcohol pad. After the process, ice packs were used. Weeks 0, 2, and 4 saw the conduct of the experiment three times at 2-week intervals. Weeks 4, 8, 12, 16, and 20 saw the comparison of the results. At every visit, clinical images were taken, and assessments were conducted to gauge the clinical response. These assessments included patient and physician global assessments, as well as modified Melasma Area Severity Index (MASI) scoring. The study was approved by the Institutional Review Board (IRB) of Pakistan Emirates Military Hospital. Ethical approval number: (A/28/ERC/35/24). All participants provided written informed consent, and the study was conducted in compliance with the Declaration of Helsinki guidelines. SPSS version 23.0 was used to analyse the data. To compare the demographic and clinical characteristics of the two groups, Chi-square and unpaired t-tests analyses

were used. Every follow-up was conducted using the Mann-Whitney U test to evaluate changes in lesional counts. The percentage decrease in inflammatory, non-inflammatory, and overall acne counts in both groups was also evaluated using the Mann-Whitney U test. Less than 0.050 was the threshold for a statistically significant p-value.

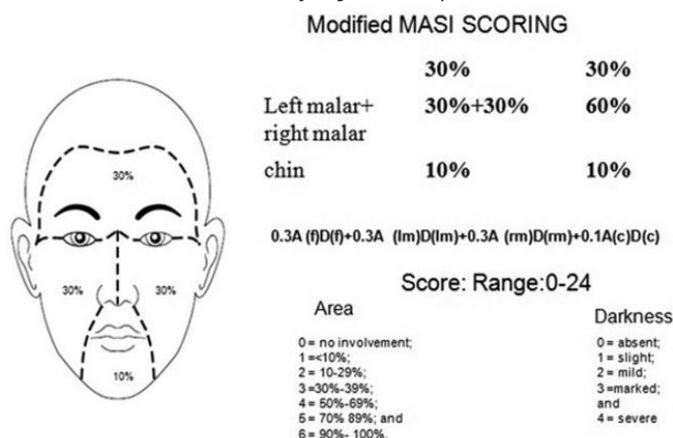


Figure 1: Modified MASI Scoring System

RESULTS

The distributions of the clinical parameters and demographic traits of melasma patients receiving treatment are shown in Table 1. A total of 100 people participated in the trial, 50 in each of the two treatment groups (Group B, microneedling) and Group A, mesotherapy. The mean age of the participants in both groups was 37.7 years; there was not any statistically significant difference ($p=0.080$) between the mean ages of Group A (37.2 years) and Group B (38.3 years). The distribution of sexes showed that 82% of participants were female overall, with 78% of them in Group A and 86% in Group B. This difference did not reach statistical significance ($p=0.290$). 60% of subjects had Type 4 skin, 40% had Type 5 skin, and the distributions of the two categories were similar ($p=0.680$). There was not any statistically significant difference ($p=0.720$) among the groups for the forms of melasma detected, which were 52% centrofacial, 46% malar, and 2% mandibular. 9 percent of the melasma patterns were epidermal, 12 percent were dermal, and 79 percent were mixed types. The distribution

of patterns did not significantly differ across the groups ($p=0.510$). For both treatment groups mesotherapy (Group A) and microneedling (Group B) Table 2 shows the mean modified Melasma Area Severity Index (MASI) scores and improvement in percentage at various time points. Group A's mean MASI score at baseline (MASI b) was 8.94 ± 2.16 , whereas Group B's mean score was 9.11 ± 4.10 . At baseline, there was not any statistically significant difference between the groups ($p=0.320$). Group A demonstrated an 18.39% improvement after 4 weeks (MASI 1) with a mean score of 5.65 ± 1.68 , while Group B demonstrated a 32.45% improvement at the same time with a mean score of 6.15 ± 2.52 . There was no statistically significant difference in the groups' percentage improvement ($p=0.170$). Group B's mean score at 8 weeks (MASI 2) was 5.41 ± 2.41 , indicating a 40.59% improvement, whereas Group A's mean score had dropped to 4.94 ± 1.73 , indicating a 28.63% improvement. Given that the difference was statistically significant ($p=0.001$), microneedling was clearly more successful at this particular time. Group A's mean score at 12 weeks (MASI 3) was 4.76 ± 1.76 , indicating a 31.32% improvement, whereas Group B's mean score at the same time was 5.21 ± 2.05 , indicating a 42.71% improvement. The greater efficacy of microneedling was further supported by the statistical significance of this difference ($p=0.010$). Group A's mean MASI score at 16 weeks (MASI 4) was 4.56 ± 1.76 , indicating a 34.21% improvement, while Group B's mean score at that same time was 5.06 ± 2.14 , indicating a 44.41% improvement. The difference was still statistically significant ($p=0.020$), indicating the continued superiority of microneedling. At 20 weeks (MASI 5), Group B's mean score was 5.06 ± 2.14 , indicating a 44.41% improvement, whereas Group A's mean score was 4.45 ± 1.69 , indicating a 35.72% improvement. The difference's statistical significance ($p=0.010$) attests to the consistent superior outcomes of microneedling. In conclusion, all time points were found to exhibit consistent superior efficacy of microneedling over mesotherapy, with statistically significant differences observed at multiple intervals. Melasma severity improved and MASI scores decreased as a result of both treatments.

Table 1: The Distributions of Demographical Characteristics and Clinical Parameters of Patients in Treatment of Melisma (n=200)

Variables	Total Mean ± SD/Frequency (%)	Group A Mesotherapy Mean ± SD/ Frequency (%)	Group B Microneedling Mean ± SD/ Frequency (%)	p-value
Age (Years)				
Age	37.7 ± 8.6	37.2 ± 9.2	38.3 ± 8.1	0.540 ^a
Sex				
Female	82 (82.0)	39 (78.0)	43 (86.0)	0.290 ^b
Male	18 (18.0)	11 (22.0)	7 (14.0)	
Fitzpatrick Skin Type				
Type 4	60 (60.0)	29 (58.0)	31 (62.0)	0.680 ^b

Type 5	40 (40.0)	21 (42.0)	19 (38.0)	
Type of Melasma				
Centro facial	52 (52.0)	28 (56.0)	24 (48.0)	0.720°
Malar	46 (46.0)	21 (42.0)	25 (50.0)	
Mandibular	2 (2.0)	1 (2.0)	1 (2.0)	
Pattern of Melasma				
Epidermal	9 (9.0)	6 (12.0)	3 (6.0)	0.510°
Dermal	12 (12.0)	5 (10.0)	7 (14.0)	
Mixed	79 (79.0)	39 (78.0)	40 (80.0)	

*SD(Standard Deviation), a(unpaired t-test was applied to measure the level of significance), b(Chi-square test was applied to measure the level of significance), c(Fisher's exact test was applied to measure the level of significance)

Comparison of mean modified MASI scores and percentage improvement between Microneedling and Mesotherapy groups (n=100)(Table 2).

Table 2: Mean modified Melasma Area Severity Index(MASI) Scores and Percentage Improvement of Both the Groups(n=100)

Variables	Group A (Mesotherapy) Mean ± SD/(%)	Group B (Microneedling) Mean ± SD/(%)	p-value
MASib			
Percentage Improvement	8.94 ± 2.16	9.11 ± 4.10	0.320 ^a
MASI 1 (4 Weeks)			
Mean	5.65 ± 1.68	6.15 ± 2.52	0.170 ^a
Percentage Improvement	18.39%	32.45%	
MASI 2 (8 Weeks)			
Mean	4.94 ± 1.73	5.41 ± 2.41	0.001 ^a
Percentage Improvement	28.63%	40.59%	
MASI 3 (12 Weeks)			
Mean	4.76 ± 1.76	5.21 ± 2.05	0.010 ^a
Percentage Improvement	31.32%	42.71%	
MASI 4 (16 Weeks)			
Mean	4.56 ± 1.76	5.06 ± 2.14	0.020 ^a
Percentage Improvement	34.21%	44.41%	
MASI 5 (20 Weeks)			
Mean	4.45 ± 1.69	5.06 ± 2.14	0.010 ^a
Percentage Improvement	35.72%	44.41%	

*SD(standard deviation), a(unpaired t-test was applied to measure the level of significance)

The percentage improvement in Melasma Area Severity Index(MASI) ratings for both treatment groups microneedling(Group B) and mesotherapy(Group A) is shown in Table 3. Comparing Group A to Group B, the data shows that a greater percentage of patients in Group A had little to no improvement. In particular, just 8% of patients in Group B saw the same result as 12% of patients in Group A who did not exhibit any improvement. In terms of percentage improvement, 26% of individuals in Group A and 18% of individuals in Group B saw improvements of less than 25%. 44% of patients in Group A showed improvement in the range of 25% to 50%, while 48% of patients in Group B showed comparable improvements. 18% of Group A individuals and 24% of Group B individuals were in the improvement range of 51% to 75%. Remarkably, 2% of individuals in Group B and none of the individuals in Group A showed recovery between 76% and 100%. Mesotherapy(Group A) was less successful in creating higher percentages of improvement than microneedling(Group B), as evidenced by the statistically significant variations in improvement percentages between the two groups(p=0.001).

Table 3: Percentage improvement and adverse event of Melasma Area Severity Index(MASI) scores in both the groups(n=100)

Variables	Group A Mesotherapy Frequency (%)	Group B Microneedling Frequency (%)	p-value
Response (%)			
No Improvement	6 (12.0)	4 (8.0)	0.001 ^a
<25	13 (26.0)	9 (18.0)	
25-50	22 (44.0)	24 (48.0)	
51-75	9 (18.0)	12 (24.0)	

76-100	-	1 (2.0)	
Adverse Event			
Itching	6 (12.0)	2 (4.0)	0.001 ^a
Burning	4 (8.0)	2 (4.0)	
Erythema	8 (16.0)	5 (10.0)	
No Adverse Events	32 (64.0)	41 (82.0)	

a (Chi-square test or Fisher's exact test was applied to measure the level of significance)

The frequency of side effects that patients in the two treatment groups microneedling (Group B) and mesotherapy (Group A) experienced is shown in Table 3. According to the data, Group A experienced unfavourable events more frequently than Group B. In particular, itching was reported by 12% of individuals in Group A and just 4% of individuals in Group B. Comparably, 8% of individuals in Group A and 4% in Group B reported experiencing burning sensations. In Group A, erythema was observed in 16% of individuals, while in Group B, it was observed in 10% of patients. Regarding total adverse events, 64% of individuals in Group A and 82% of individuals in Group B reported at least one adverse effect and no adverse event, respectively. Mesotherapy (Group A) was linked to a higher incidence of adverse effects than microneedling (Group B), as evidenced by the statistically significant ($p=0.001$) variations in the frequency of adverse events between the two groups. Figures 2 and 3 displayed the total PGA and PtGA scores for each group. Figure 2 illustrated the trends in Physician Global Assessment (PGA) and Patient Global Assessment (PtGA) scores across multiple follow-up visits in the mesotherapy group.

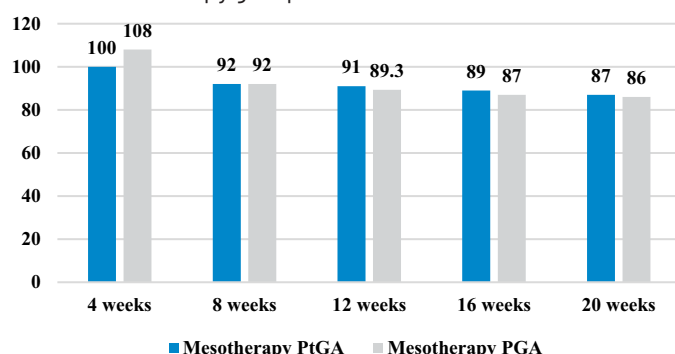


Figure 2: Total PGA and PtGA Scores at Different Visits in The Mesotherapy Group

Figure 3 displayed the progression of Physician Global Assessment (PGA) and Patient Global Assessment (PtGA) scores over the treatment period in the microneedling group.

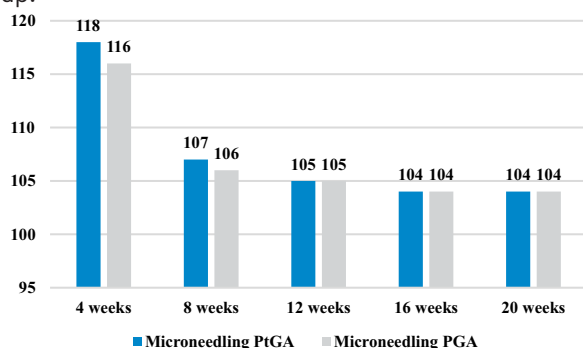


Figure 3: Total PGA and PtGA Scores at Different Visits in The Microneedling Group

DISCUSSION

The main uses of tranexamic acid are for its antihemorrhagic and antifibrinolytic properties. Topical trans-4-(aminomethyl) cyclohexanecarboxylic acid (trans-AMCHA, sometimes referred to as TA) is a plasmin inhibitor that has been demonstrated in recent studies to be able to prevent UV-induced pigmentation in animal models, including guinea pigs. By preventing plasminogen from attaching to keratinocytes, trans-AMCHA applied topically suppresses UV-induced plasmin activity in these cells. Melanocyte tyrosinase activity is subsequently decreased as a result of this action, which also lowers prostaglandin synthesis and free arachidonic acid [13]. Moreover, urokinase-type plasminogen activator, which is secreted by human keratinocytes, increases melanocyte activity in vitro. TA's ability to block this process may account for its effectiveness in lowering melasma linked to hyperpigmentation [14]. Treatment for both mixed and dermal kinds of melasma may benefit from intradermal injection of TA. Drug delivery with microneedle technology is almost painless and requires little physical intervention [15]. By making tiny holes in the skin, this method allows a wide range of medicinal substances including proteins to enter the body that would not normally be able to pass through healthy skin. Pistor offered localized microinjections, also referred to as "mesotherapy," for the first time in France [16]. In medicine, mesotherapy is a commonly used procedure that involves injecting 0.05 to 0.1 mL of highly diluted drug mixes or individual pharmaceuticals subcutaneously or intradermally into particular body parts that present health or cosmetic issues. This technique works with any intravenously injected chemical, but it does not work with alcoholic or greasy solvents. The main objective is to directly provide medication to the affected area, which minimises the need for oral medications and permits the use of lower amounts of medication. The microneedling tool is a simple, portable instrument with a handle that has a cylinder filled with tiny, 0.5–2 mm stainless steel needles. The needle-studded cylinder is rolled over the skin in different directions to create microchannels, which have therapeutic effects. The beauty industry uses this process, called "microneedling," to treat a variety of skin ailments, including as post-burn scars, acne, wrinkles, and pigmentation problems [17]. Additionally, it is applied as a component of collagen induction therapy for cosmetic rejuvenation [18]. In this study, we assessed the efficacy and safety of two different approaches to tranexamic acid (TA) administration for treating melasma: microneedling and localised microinjections (mesotherapy). The impact of both techniques was evaluated by comparing baseline, 4, 8, and 12-week treatment outcomes on the Melasma Area and Severity Index (MASI) scores, Patient Global Assessment (PtGA), and Physician Global Assessment (PGA) [19]. Over

time, MASI scores, PtGA, and PGA significantly decreased for both treatment regimens. The improvement from microneedling was higher than from microinjections, although the difference was not statistically significant. It's possible that microneedling's increased effectiveness stems from its capacity to administer medicine more evenly and deeply into the skin. During the next three-month follow-up period, all assessment scores stabilized [20].

The study's small sample size might have hampered the practical implications of the findings. Furthermore, it's possible that the brief course of treatment did not adequately reflect the long-term safety and effectiveness of both topical therapies. The study population's lack of variety may have limited the data's generalizability to larger demographic groups. Moreover, there was no evaluation of the patients' adherence to the medication, which might have affected the results.

CONCLUSIONS

Tranexamic Acid (TA) shows promise as a safe, efficient, and therapeutic drug for the treatment of melasma in light of the findings. This drug is reasonably priced and easily obtained. It can be used in a clinical context and provides almost no downtime, low adverse effects, and rather quick outcomes. The more efficient and consistent drug administration made possible by the microchannels made by microneedling may be the reason for the better therapeutic response seen in the microneedling group.

Authors' Contribution

Conceptualization: AF

Methodology: FKW, IG, WAK, NR, NUW

Formal analysis: NG

Writing and Drafting: AUB, BA

Review and Editing: AF, AUB, FKW, IG, NG, BA, NR, NUW, WAK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Urological Carcinomas in Patients Presented with Gross Hematuria

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ABSTRACT

Gross hematuria is a common urological symptom associated with both benign and malignant conditions. It is often a presenting feature of urological carcinomas, necessitating timely evaluation and diagnosis to improve outcomes. **Objectives:** To determine the prevalence of urological carcinomas and assess their association with demographic and clinical variables among patients presenting with gross hematuria. **Methods:** This descriptive cross-sectional study was conducted at the DHQ Teaching Hospital Mardan (KP) from July 2024 to January 2025. A total of 209 patients presenting with gross hematuria were included. Detailed demographic and clinical data, including age, gender, family history of cancer, anticoagulant use, urinary tract infections, history of stones, and prior urological surgeries, were recorded. All patients underwent urine cytology, ultrasound, X-ray KUB, computed tomography (CT) scan, and cystoscopy when required. Data analysis was performed using SPSS-25, and the Chi-square test was applied to determine associations. **Results:** Urological carcinoma was diagnosed in 41 (19.6%) patients. Higher prevalence was observed in older age groups (24.6% in 60–80 years) but showed no significant association with gender ($p=0.333$) or other clinical variables such as urinary tract infections ($p=0.527$) and anticoagulant use ($p=0.997$). Benign causes, including urinary tract infections (17.8%) and trauma, were common. **Conclusions:** It was concluded that urological carcinomas were prevalent in patients with gross hematuria, particularly in older age groups, highlighting the need for structured diagnostic evaluations. Early imaging, cytology, and cystoscopy are recommended to differentiate malignant from benign causes and improve outcomes.

INTRODUCTION

Gross hematuria, defined as visible blood in the urine, is a clinically significant symptom that warrants urgent urological evaluation. While it may result from benign conditions such as urinary tract infections (UTIs), nephrolithiasis, or trauma, it is also a cardinal sign of urological malignancies, including bladder cancer, renal cell carcinoma (RCC), and upper tract urothelial carcinoma (UTUC) [1, 2]. Distinguishing between benign and malignant causes is essential, as a substantial proportion of patients presenting with gross hematuria are ultimately diagnosed with cancer. Epidemiological studies have consistently

demonstrated a strong association between gross hematuria and urological malignancies. In a Spanish cohort attending a dedicated hematuria clinic, bladder tumors were identified in 31.5% of patients [1]. Similarly, a South African study found malignancy in 20% of patients evaluated for visible hematuria, with bladder cancer being the most prevalent diagnosis [2]. These findings highlight the necessity of a thorough and timely investigation in all patients presenting with this symptom, regardless of apparent risk factors. Current diagnostic guidelines recommend a multimodal approach combining urine



cytology, cystoscopy, and imaging studies. Among imaging modalities, computed tomography urography (CTU) is widely considered the gold standard for upper urinary tract evaluation due to its superior sensitivity and specificity compared to ultrasound [3]. A 2023 study comparing CTU with ultrasonography confirmed CTU's superior diagnostic accuracy in identifying both benign and malignant causes of hematuria [4]. Despite these advancements, the clinical presentation of urological malignancies can be deceptive. Upper tract urothelial carcinoma may mimic inflammatory or infectious conditions, leading to diagnostic delays [5]. Additionally, rare benign conditions such as bladder amyloidosis can radiographically resemble cancer, reinforcing the need for histological confirmation before treatment decisions are made [6]. Risk stratification remains a cornerstone of hematuria assessment. Well-established predictors such as advanced age, male gender, and smoking history have been repeatedly linked to increased cancer risk [7]. However, recent studies also emphasize that malignancies may occur in patients without traditional risk factors, suggesting that reliance on demographic risk profiles alone is insufficient [8]. Moreover, rare but clinically important scenarios, such as synchronous malignancies involving both RCC and UTUC, have been documented, supporting the use of a comprehensive diagnostic approach [9]. Although uncommon, urothelial carcinoma can even present in pediatric patients, and cases of painless gross hematuria in children have been reported as initial indicators of malignancy [10]. Furthermore, gross hematuria related to anticoagulant use may obscure serious pathology, requiring careful clinical judgment to distinguish medication effects from underlying malignancy [11]. Other rare causes, such as uretero-iliac artery fistulas, particularly in patients with prior pelvic surgery or radiotherapy, also exemplify the broad differential diagnoses in gross hematuria [12]. These diverse clinical scenarios underscore the importance of a standardized, multidisciplinary approach. The establishment of specialized hematuria clinics and adherence to structured diagnostic pathways have been shown to improve early cancer detection, reduce delays in management, and ultimately enhance patient outcomes [13]. Given the substantial proportion of urological carcinomas diagnosed in patients presenting with gross hematuria, early detection and timely intervention remain critical for improving prognosis and survival outcomes.

Despite advancements in diagnostic technologies, delays in identifying malignancies, particularly in high-risk groups, continue to pose challenges. This study aims to evaluate the prevalence of urological carcinomas and assess their association with demographic and clinical variables. The findings are expected to provide evidence for refining diagnostic pathways, enhancing risk

stratification, and improving early detection strategies in patients presenting with gross hematuria.

METHODS

This descriptive cross-sectional study was conducted to determine the prevalence of urological carcinomas and assess their association with demographic and clinical variables among patients presenting with gross hematuria. The study took place at the Department of Urology, District Headquarters (DHQ) Teaching Hospital, Mardan (Khyber Pakhtunkhwa), over seven months from July 2024 to January 2025. Before initiation, ethical approval was obtained from the hospital's institutional review board (Approval No. 1309). All participants were informed about the nature and purpose of the study, and written consent was obtained. Participant confidentiality and data privacy were strictly maintained. The sample size was calculated using a previously reported prevalence rate of 16.17% for urological carcinomas among patients with gross hematuria, as documented by Soomro et al., [14]. Using Open Epi (Version 3.01), with a 95% confidence level, 5% margin of error, and an assumed power of 80%, the required sample size was calculated to be 209 patients. A non-probability consecutive sampling technique was employed to enroll patients who fulfilled the inclusion criteria and presented during the study period. Inclusion criteria consisted of patients of either gender, aged 18 years and above, who presented with visible (gross) hematuria and consented to participate. Patients with microscopic hematuria were excluded from the study to maintain a clinically homogenous population. Gross hematuria is more strongly associated with underlying malignancies and is more likely to prompt immediate urological evaluation, whereas microscopic hematuria often results from benign causes and follows a different diagnostic protocol. Additionally, patients with bleeding disorders unrelated to urological conditions and those who declined to participate were excluded from the study. Demographic and clinical data were collected using a structured questionnaire. Variables recorded included age, gender, duration of hematuria, family history of urological carcinoma, history of urinary tract infections, previous urological surgeries, use of anticoagulant medication, and history of urinary stones. All patients underwent a standardized diagnostic evaluation, including urine cytology for detection of malignant cells, ultrasound or CT scan for identification of structural abnormalities, and cystoscopy when indicated for direct visualization of the bladder. Biopsy and histopathological confirmation were obtained in suspected cases of malignancy. The primary outcome of the study was the presence or absence of urological carcinoma, while secondary outcomes included the distribution of carcinoma types (e.g., bladder, renal, ureteral, or urethral cancer) and their relationship with clinical variables. Data were entered and analyzed using

SPSS version 25. The normality of continuous variables such as age was assessed using the Shapiro-Wilk test. Since age was found to be normally distributed, it was expressed as mean $\pm$ standard deviation. Categorical variables were summarized as frequencies and percentages. Associations between clinical variables and carcinoma presence were evaluated using the Chi-square test. A p-value of <0.050 was considered statistically significant.

RESULTS

A total of 209 patients presenting with gross hematuria were included in the study. The mean age of the participants was 50.70 ± 17.95 years, and the mean duration of gross hematuria was 30.21 ± 18.04 days. Urological Carcinomas were found in 41(20%) patients. (Figure 1).

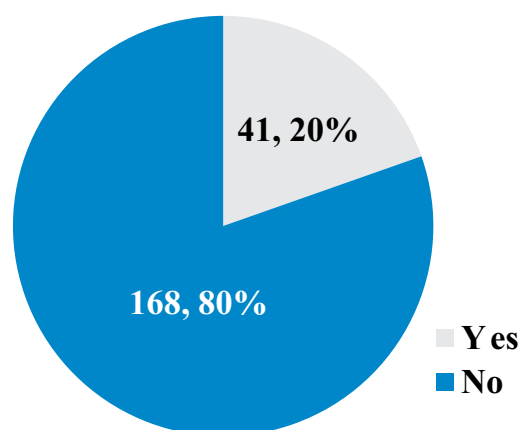


Figure 1: Frequency of Urological Carcinomas

In this study, the presence of urological carcinoma was

analyzed about various demographic and clinical variables among 209 patients. Carcinoma was more frequently observed in older age groups, with 17 (24.6%) cases occurring in patients aged 60–80 years, compared to 16 (20.5%) in the 40–59 years' group and 8 (12.9%) in the 20–39 years' group. However, this difference was not statistically significant ($p=0.233$). Gender distribution showed that 22 (22.4%) female and 19 (17.1%) male had carcinoma, but this difference also lacked statistical significance ($p=0.333$). Similarly, no significant association was found between a family history of cancer and carcinoma, as 20 (17.7%) patients with a family history and 21 (21.9%) without it had carcinoma ($p=0.449$). The use of anticoagulants did not influence carcinoma rates, with 20 (19.6%) of patients using anticoagulants and 21 (19.6%) not using anticoagulants being affected ($p=0.997$). Urinary tract infection history was also unrelated to carcinoma, with 18 (17.8%) of patients with a history of UTI and 23 (21.3%) of those without it having carcinoma ($p=0.527$). Similarly, a history of urinary stones showed no significant impact, with carcinoma present in 20 (19.0%) patients with stones and 21 (20.2%) without stones ($p=0.835$). Previous urological surgeries were also not associated with carcinoma, as 20 (18.5%) of patients with surgery and 21 (20.8%) without surgery had carcinoma ($p=0.679$). Overall, none of the analyzed variables demonstrated a statistically significant association with the presence of carcinoma, suggesting that other unmeasured factors or larger sample sizes may be required to identify meaningful trends (Table 1).

Table 1: Association of Demographic and Clinical Variables with Presence of Urological Carcinoma (n=209)

Variables	Presence of Carcinoma (Yes)	Presence of Carcinoma (No)	Total	p-value
Age Group				
20–39 Years	8 (12.9%)	54 (87.1%)	62	0.233
40–59 Years	16 (20.5%)	62 (79.5%)	78	
60–80 Years	17 (24.6%)	52 (75.4%)	69	
Gender				
Female	19 (17.1%)	92 (82.9%)	111	0.333
Male	22 (22.4%)	76 (77.6%)	98	
Family History of Cancer				
Yes	20 (17.7%)	93 (82.3%)	113	0.449
No	21 (21.9%)	75 (78.1%)	96	
Use of Anticoagulants				
Yes	20 (19.6%)	82 (80.4%)	102	0.997
No	21 (19.6%)	86 (80.4%)	107	
Urinary Tract Infection				
Yes	18 (17.8%)	83 (82.2%)	101	0.527
No	23 (21.3%)	85 (78.7%)	108	
History of Stones				
Yes	20 (19.0%)	85 (81.0%)	105	0.835
No	21 (20.2%)	83 (79.8%)	104	

Previous Urological Surgery				
Yes	20 (18.5%)	88 (81.5%)	108	0.679
No	21 (20.8%)	80 (79.2%)	101	

Note: p-values were calculated using the Chi-square test to assess associations between clinical variables and the presence of urological carcinoma

DISCUSSION

This study observed a 20% prevalence of urological carcinomas among 209 patients with gross hematuria, without statistically significant associations with age, gender, family history, anticoagulant use, urinary tract infections, urinary stones, or prior urological surgeries. These findings are consistent with, and in some cases diverge from, recent literature on this topic. Our carcinoma prevalence aligns with findings from Hamid *et al.*, who reported a 17.06% prevalence in 170 patients presenting with gross hematuria [15]. Similarly, Rashidullah *et al.*, found an 18.6% prevalence, also emphasizing that UTIs and trauma were the most common non-malignant causes of hematuria [16]. These results support the notion that gross hematuria is a key clinical indicator for further investigation of potential malignancy. Although carcinoma was more frequent in older age groups in our study, this trend was not statistically significant. In contrast, Rai *et al.*, conducted a systematic review and found age to be a consistent risk factor for urothelial malignancies, particularly bladder cancer [17]. Likewise, Takeuchi *et al.*, reported that age strongly correlates with risk, highlighting the need for risk stratification models that incorporate age more effectively in clinical pathways [18]. Gender was not a significant factor in our study, but other recent research suggests otherwise. Khadhour *et al.*, in the large multicenter IDENTIFY study, demonstrated male sex as a significant predictor for bladder cancer [19]. Rai *et al.*, also identified higher risks among males, attributing it partly to increased smoking rates and occupational exposures [17]. We found no significant association between family history and cancer, a finding that contrasts with recent findings. The Mayo Clinic cohort study by Takeuchi *et al.*, emphasized family history as an important predictive variable, especially for renal and urothelial cancers [18]. Similarly, our data did not show a difference in carcinoma rates based on anticoagulant use. This is consistent with Ryšánková *et al.*, who found that neither anticoagulants nor antiplatelet therapies significantly increased the risk of urological cancers in hematuria patients [20]. Their study of 562 patients revealed that malignancy risks were consistent across medicated and non-medicated groups. The lack of association between UTI history and carcinoma in our cohort supports the observations by Rai *et al.*, who found that UTI history was more prevalent in benign cases [17]. Khadhour *et al.*, also noted that previous UTI history was associated with a lower likelihood of malignancy in their predictive model [19]. Our study found no link between urinary stones or prior surgeries and cancer risk. This

agrees with findings from Rashidullah *et al.*, who observed that although urinary calculi were common in their cohort, they did not significantly correlate with malignancy presence [16]. More broadly, our results reinforce recent calls for multifactorial diagnostic tools. The IDENTIFY study [19] and newer algorithms like the Hematuria Cancer Risk Score (HCRS) [21] suggest that single variables such as age or UTI history may be insufficient alone, and composite models significantly outperform traditional guidelines in identifying high-risk patients.

This study is limited by its single-center design and moderate sample size, which may restrict generalizability to broader populations. In addition, the lack of stratification by tumor subtype, smoking status, and occupational exposure may have influenced the ability to detect significant associations with known risk factors. Future multicenter studies with broader variable inclusion are needed to refine risk stratification models and guide diagnostic protocols more effectively.

CONCLUSIONS

It was concluded that this study identified a 19.6% prevalence of urological carcinomas among patients presenting with gross hematuria. No statistically significant associations were found between carcinoma and variables such as age, gender, family history, UTI, or anticoagulant use. However, a higher carcinoma rate was observed in the 60–80 years' age group. We recommend that all cases of gross hematuria undergo comprehensive evaluation using urine cytology, imaging, and cystoscopy.

Authors' Contribution

Conceptualization: R

Methodology: MAC, OUR

Formal analysis: MA

Writing and Drafting: MA, S, FA, RAM

Review and Editing: MA, MAC, OUR, S, FA, RAM, R

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Evaluation of Functional Results and Local Recurrence in Enbloc Resection of Campanacci Grade 3 Giant Cell Tumor of Distal Radius and Wrist Arthrodesis Using Ulnar Translocation Technique

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ABSTRACT

Reconstruction following en-bloc resection of a distal radius GCTB of Campanacci grade 3 can be difficult. **Objective:** To examine the outcomes of patients who had ulnar translocation correction and wrist arthrodesis for Campanacci grade 3 distal radius GCTBs. **Methods:** This retrospective study was comprised of 22 patients. After obtaining informed written consent detailed demographics were recorded. A follow-up clinical evaluation was conducted to determine the functional status and any problems. The MSTs and DASH scores, which measure impairments in the musculoskeletal system, were used to assess the functional outcomes. The MSTs and DASH scores were compared before and after the operation using paired t-tests. At a significance level of P less than 0.050, statistical differences were recorded. **Results:** The included cases had mean age 30.7±6.28 years. The majority 15 (68.2%) were females and 7 (31.8%) cases were males. Mean follow up was 33.25±9.38 months. Mean length of tumor resection was 8.97±5.79 cm. Before surgery, mean MSTs was 10.84±3.35 and after surgery mean MSTs was 26.01±3.19 p value <0.050. At admission, the mean DASH score was 40.14±14.66 and after surgery decreases to 8.91±12.51 with p value <0.050. Frequency of recurrence rate was 3 (13.6%) and radioulnar synostosis was found in 2 (9.1%) cases. **Conclusion:** It was found that ulnar translocation in conjunction with wrist arthrodesis is an easy reconstructive technique that preserves function, produces outstanding results, and has few problems.

INTRODUCTION

High rates of local recurrence have been the primary reason for unsatisfactory clinical outcomes in patients of giant cell tumour of bone (GCTB), a clinically aggressive bone tumour that is histologically benign [1]. Past research suggests that the local recurrence (LR) rate in GCTB could be anything from 3% to 64% [2]. The most recommended surgical technique for treating Campanacci I and II GCTB has been curettage in conjunction with adjuvant local therapy. However, a major therapeutic dilemma is the

substantial local recurrence rate associated with Campanacci III tumours. The recurrence rate for en bloc resection is the lowest of all surgical procedures used to treat GCTB, ranging from 3% to 25% [3]. The high success rate of this surgical procedure is a direct result of this. An irregularity in the distal femur, proximal tibia, or distal radius is a hallmark of this disorder. These are the places where problems often arise. There is a correlation between the distal radius and an increased chance of local



recurrence, particularly in cases where Campanacci III tumours are encountered [4]. One initial treatment that has been supported by a number of trials is en bloc resection, which is then followed with reconstructions [5, 6]. The restoration of the wrist after en bloc resection of the distal radius bone cancer has proven to be a considerable challenge for orthopaedic oncologists. This is mostly due to the high functional demands that the wrist places on the body. A number of different ways have been investigated in order to find reconstructive methods for long bone defects [7, 8]. However, orthopaedic oncologists are not in agreement regarding the most effective form of treatment. The procedures might be categorised as either arthroplasty or arthrodesis, depending on the individual. The following procedures are included in this category: (i) complete or partial arthrodesis of the wrist; (ii) implantation of osteoarticular allografts; (IV) implantation of fibula autografts, depending on whether or not they are vascularised; and (v) replacement of the prosthesis. To the best of the knowledge, this study is the first evaluation that has been conducted to offer a comprehensive overview of the various reconstruction methods. Additionally, the indications, functional outcomes, and issues associated with each restoration process are discussed, as well as the technical refinement choices that can be utilised to improve the stability of the wrist joint. This review covers a variety of strategies, each of which has a unique mix of advantages and disadvantages. From the perspective of grip strength and long-term consequences, it seems that wrist arthrodesis is the superior alternative. On the other hand, wrist arthroplasty seems to be the superior option when it comes to the motion of the wrist. The neighbouring soft tissues become involved in Campanacci grade 3 GCTB after a cortical layer breach. Campanacci grade 3 lesions had a high recurrence incidence after intralesional excision and bone grafting. When a cortical break is present in a GCTB instance, the intralesional excision or curettage surgery is usually not an option. The recurrence rate is five times greater than with en-bloc resection, which is the reason why this [9]. The GCTB recurrence rate can be reduced to 16% with extensive resection, but functional impairment owing to patient-specific bone defects is still a possibility after surgery [10]. Therefore, it is vital to prescribe further reconstructive techniques in order to improve the quality of life following the operation and to maximise the functional outcome obtained from the procedure. Seradge originally detailed the resection of the radius GCTB's distal end [11–13]. To do this, the distal end was replaced using the ulnar translocation and the related soft tissues. When the distal end of the radius GCTB was removed, Seradge was the first to report using an ulnar translocation and its soft tissues to replace it. When treating GCTB including a cortical break, intralesional

excision or curettage is usually not an option because to the five-fold recurrence probability compared to en-bloc resection. Even though GCTB recurrence rates can be reduced to 16% with complete resection, patients may experience functional impairment after the operation as a result of bone abnormalities. Therefore, it is important to recommend additional reconstructive procedures to improve postoperative quality of life and optimize functional outcome [14].

Although tranexamic acid has shown promising results in melasma treatment, there is limited direct comparative evidence between its intradermal (mesotherapy) and microneedling-assisted topical delivery methods. This lack of head-to-head data highlights a gap in determining the most effective approach for clinical use. The aim of this study is to evaluate the results of extensive excision, reconstruction with ulna translocation and wrist arthrodesis for Campanacci grade 3 GCTB of the distal radius.

METHODS

This retrospective study was conducted at Sahiwal Medical College /Sahiwal Teaching Hospital during May 2024 to September 2024. The approved IRB reference number is 159/IRB/SLMC/SWL. People who had en-bloc tumor removal, gap reconstruction with translocation of the opposite ulna, or wrist arthrodesis after a diagnosis of Campanacci grade 3 GCTB (containing the distal radius) were evaluated. The procedures were carried out by a hand microsurgery specialist, two orthopaedic oncology surgeons, and an orthopaedic oncology surgeon. The data were collected using a non-probabilistic sequential sampling technique. With a margin of error of 7% and a 90% confidence interval, the Open Epi sample size calculator was used to compute the sample size. The proportion of Campanacci grade 3 GCTB patients treated with the ulna translocation procedure was estimated at 52%. Every case was verified by core needle biopsies. To be included, roentgenogram, MRI, or biopsy-confirmed histology had to show GCT characteristics. Wrist MRI were employed to determine the amount of bone to be removed, the lesion's size, extraosseous component, and neurovascular bundle connectivity. The MRI findings dictated the extent of radial bone resection, with a 2 cm margin of normal radius bone set aside as a precaution. All research participants received initial care at the clinic. Patients with metastasis, had history of treatment and those did not provide any written consent were excluded. Individuals underwent clinical evaluations every three to six months to ascertain their functional status and any possible consequences. Both hands' grip strength was measured using a dynamometer. The MSTS grading system and the DASH score (Disability of Arm, Shoulder, and Hand) were used to analyze the functional data. In 1993, the MSTS scoring system was developed to assess the quality of life and

functional outcome after treatment for musculoskeletal tumors. This method focused on the function of one limb. Both general patient information and traits unique to the patient's upper limb are considered in the MSTS scoring method for the upper limb. This assessment consists of six parts: manual dexterity, lifting capability, hand positioning, emotional tolerance, discomfort, and emotional tolerance. A point system is used to score each criterion. A self-administered questionnaire known as the DASH score contains 30 items that are associated with functional activities and symptoms in ADL. The patient is asked to rate each of the thirty items on a scale from one to five. A higher level of disability results in higher scores. Numerous studies have examined the DASH, looking at its validity, reliability, internal consistency, and level of clinical practice adoption [15-18]. It has been used to treat problems with the wrist, elbow, hand, and shoulder. When it comes to general upper limb surgery, the DASH is a well-respected tool for patient evaluations regardless of diagnosis. For the statistical analysis, the software used was SPSS Statistics 24.0, developed and maintained by IBM in the United States. Before and after the operation, the MSTS and DASH scores were compared using paired t-tests. When P was less than 0.050, statistical differences were deemed significant. Shapiro-Wilk or Kolmogorov-Smirnov was used for normality checking of statistical analysis.

RESULTS

The included cases had mean age 30.7 ± 6.28 years. The majority 15 (68.2%) were females and 7 (31.8%) cases were males. Left side was the most common found in 14 (63.6%) cases followed by right side in 8 (36.4%) cases. Mean follow up was 33.25 ± 9.38 months. Mean length of tumor resection was 8.97 ± 5.79 cm (table 1).

Table 1: Demographics of the Presented Cases

Variables	Mean $\pm$ SD / Frequency (%)
Mean Age (Years)	30.7 ± 6.28
Gender	
Male	7 (31.8%)
Female	15 (68.2%)
Affected Side	
Left	14 (63.6%)
Right	8 (36.4%)
Mean follow up (Months)	33.25 ± 9.38
Mean length of tumor resection (cm)	8.97 ± 5.79

Before surgery, mean MSTS was 10.84 ± 3.35 and after surgery mean MSTS was 26.01 ± 3.19 p value < 0.050 . At admission, the mean DASH score was 40.14 ± 14.66 and after surgery decreases to 8.91 ± 12.51 with p value < 0.050 . On average, the affected forearm could twist 81.9 degrees in a supination direction and 83.16 degrees in a pronation direction (table 2).

Table 2: Functional results after ulnar translocation with ulnocarpal fusion and patient characteristics associated with GCTB distal radius

Variables	Before Surgery (Mean $\pm$ SD)	After Surgery (Mean $\pm$ SD)	CI 95%	P-Value
Mean MSTS	10.84 ± 3.35	26.01 ± 3.19	0.57	< 0.050
Mean DASH Score	40.14 ± 14.66	8.91 ± 12.51	0.37	< 0.050
Supination Direction	-	81.9	-	-
Pronation Direction	-	83.16	-	-

Frequency of recurrence rate was 3 (13.6%) and radioulnar synostosis was found in 2 (9.1%) cases (table 3).

Table 3: Frequency of Recurrence after Surgery

Variables	Frequency (%)
Recurrence	
Yes	3 (13.6%)
No	19 (86.4%)
Radioulnar Synostosis	
Yes	2 (9.1%)
No	19 (90.9%)

DISCUSSION

Campanacci grade 3 GCTB of the proximal radius can be successfully treated by removing the tumor while preserving hand and wrist function, according to research. Those two passages a significant recurrence rate of 6 is linked to intralesional curettage excision, though. Therefore, treatment of Campanacci grade 3 GCTB requires extensive tumor removal [16]. Optimal limb function must be preserved for those with Campanacci grade 3 GCTB distal radius after cancer excision and bone defect rectification. Many options exist for the correction of bone defects following a substantial excision of GCTB at the distal end of the radius. Physicians can apply wrist arthrodesis, prostheses, allografts, or vascularized or non-vascularized autografts to keep the wounded wrist mobile [17]. How best to reconstruct depends on a number of factors, including the surgeon's level of experience, the availability of necessary medical resources, the patient's expectations, the length of treatment anticipated, the likelihood of complications, and the anticipated time required to complete the procedure. Concerns about the treatment's efficacy and the high recurrence rate made distal radius Campanacci III GCTB a challenging case to manage [18]. Separate risk factors for local recurrence (LR) of GCTB were found by Abraham AP et al., to be curettage and the position of the distal radius [19]. Allograft repair had a significant incidence of problems, such as infection, bone nonunion, and fractures, despite satisfactory postoperative function [20]. Although ulnar transposition decreased the occurrence of infection and nonunion in allograft bone, the most prevalent consequence was still nonunion of the proximal radio-ulnar junction. Internal fixation revision and autologous cancellous bone grafting may be necessary in this case [21]. Ulnar translocation

streamlines the treatment process by avoiding the microvascular approach; it also preserves the ulna's blood supply unharmed and does not impact the attached muscles, much like vascularized grafts. Keeping blood flowing helps to create an ideal biologic environment for healing, which speeds up the process of fusing the two pieces together. Cautious were not to sever too much soft tissue during the operation to ensure a normal healing of the ulna. Nothing has come up in the most current round of patient follow-ups that is associated with the union [22]. As part of this study, the participants were measured the grip strength using a portable dynamometer. In five of the cases, the results showed that the affected side had a residual grip strength that was 34.7-75.2 percent lower than the other side. Longer follow-up intervals were associated with an increase in postoperative grip strength, according to this study. Consistent with this result is a 2018 study by Vyas *et al.* [14] that followed 20 individuals for an average of 3.9 years and discovered that grip strength was 70% lower than the normal equivalent during that time. The respondents carried on as normal with their everyday lives despite the fact that their grip strength had decreased. Five regional issues sprung up as a direct consequence of the operation, according to these findings. Three patients experienced a return of GCT 18 months after treatment. The rebuilding process is not believed to be the cause of this local tumor recurrence [23]. Five months after the first operation, another patient developed radioulnar synostosis. The patient reported no pain and mild pronosupination movements at the follow-up appointment. The patient's functional status significantly improved following the excision of the radioulnar synostosis, as confirmed at the most recent follow-up appointment. The radioulnar synostosis can be prevented and the forearm's flexion or supination movements can be maintained by delicately separating the periosteal sleeve within the ulna at the point of the proximal osteotomy [23]. According to previous studies, 13.6% of patients who had distal radius GCTB of Campanacci grade 3 had local recurrence [24].

This study is limited by its small sample size and single-institution experience, which may affect the generalizability of outcomes. Additionally, the relatively short and variable follow-up period may underestimate late complications such as recurrence or functional decline. Future multicenter studies with larger cohorts and longer follow-up are recommended to better compare reconstruction techniques and establish standardized treatment protocols for Campanacci grade 3 GCTB of the distal radius.

CONCLUSIONS

It was found that ulnar translocation in conjunction with wrist arthrodesis is an easy reconstructive technique that preserves function, produces outstanding results, and has few problems.

Authors' Contribution

Conceptualization: BH

Methodology: AMS, TR

Formal analysis: MR

Writing and Drafting: MR, AMS, ARN, BH

Review and Editing: MR, AMS, TR, ARN, BH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article



Acute Systemic Organ Injury in Term Infants with Perinatal Asphyxia

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ABSTRACT

Perinatal asphyxia is a major contributor to neonatal morbidity and mortality. This leads to multiple organ dysfunction (MODS). **Objectives:** To assess the extent of acute organ system injury in term newborns with perinatal asphyxia, focusing on clinical and biochemical markers indicative of MODS. **Methods:** This descriptive cross-sectional study involved 50 term newborns diagnosed with perinatal asphyxia. Clinical manifestations and biochemical markers, including renal and liver function tests, were analyzed to evaluate the extent of organ dysfunction. Fifty term newborns diagnosed with perinatal asphyxia were enrolled through non-probability convenience sampling. Clinical assessments included evaluations of the neurological, cardiovascular, respiratory, renal, and hepatic systems. Biochemical tests measured serum creatinine, serum ALT, and CKMB levels to assess kidney, liver, and myocardial function, respectively. Data were analyzed using descriptive statistics and Chi-square tests to examine the relationship between perinatal asphyxia and multi-organ injury, with a significance level of $p \leq 0.05$. **Results:** The severity of perinatal asphyxia was significantly correlated with the incidence of organ damage. Serum creatinine levels were elevated in 18 (36%) neonates, ALT levels were elevated in 20 (40%) neonates, and CKMB levels were elevated in 23 (46%) neonates. In some cases, early intervention was linked to improved neurological outcomes. **Conclusions:** This study emphasizes the critical need for early diagnosis and prompt intervention to prevent extensive organ damage in newborns with perinatal asphyxia. The severity of organ dysfunction is closely related to the degree of asphyxia, highlighting the importance of comprehensive monitoring and targeted treatment strategies. Further research is essential to develop better protective interventions for these infants.

INTRODUCTION

Perinatal asphyxia is defined as inadequate blood flow or gas exchange in the fetus or newborn during the perinatal period (before, during, and after delivery) [1, 2]. This critical event triggers a series of pathophysiological processes due to impaired oxygen and nutrient delivery, leading to systemic and neurological complications [3, 4]. These complications can vary in severity, depending on the duration and intensity of the asphyxia, and can cause lasting damage to multiple organ systems, including the brain, kidneys, liver, and heart [5-8]. Several studies have demonstrated the widespread effects of perinatal asphyxia on organ systems, but the extent of involvement varies. For instance, a study of 46 cases showed that all patients (100%) had central nervous system involvement, while 80% exhibited liver damage characterized by

elevated ALT levels [9, 10]. Cardiac dysfunction, as evidenced by elevated cardiac enzymes, was present in 78% of cases, and renal injury, as indicated by elevated serum creatinine levels, was observed in 72% of cases [11]. Similarly, another study of 60 newborns found that 95% had involvement of at least one organ system, with cardiovascular dysfunction being the most common (95%), followed by renal injury (37%), liver dysfunction (22%), and central nervous system involvement (20%) [12]. A separate study of 56 newborns with perinatal asphyxia found that 22 of them had liver injury, as evidenced by elevated ALT levels [13]. Further research indicates that the mortality rate associated with perinatal asphyxia remains substantial. In a cohort of 267 neonates, 18% exhibited perinatal asphyxia, with a case fatality rate of 37.5% [14]. Additionally, a study



on 152 asphyxiated neonates revealed that renal involvement occurred in 64%, respiratory dysfunction in 45%, cardiovascular impairment in 32%, and liver injury in 16% [15].

Although perinatal asphyxia is known to cause multi-organ dysfunction in neonates, the pattern and extent of acute organ involvement remain variable across studies. There is limited local evidence identifying the predominant organ injuries and associated risk patterns in term neonates, necessitating further investigation. This study aims to provide a detailed analysis of acute systemic organ injuries in term neonates affected by perinatal asphyxia, aiming to identify potential risk factors that could guide improved clinical interventions and therapeutic strategies.

METHODS

This descriptive cross-sectional study was conducted from March 2023 to October 2023 at Bacha Khan Medical Complex, District Sawabi, Khyber Pakhtunkhwa. The study included 50 neonates diagnosed with perinatal asphyxia. Non-probability convenience sampling was used to select the participants. Ethical approval was obtained from the institutional ethical review board with approval No. 2509/PF/GKMC. Written informed consent was obtained from the parents or legal guardians of all participating neonates. Data were collected through a pre-designed questionnaire that included both clinical assessments and laboratory investigations. The inclusion criteria for the study were term neonates (gestational age between 37 and 42 weeks) diagnosed with perinatal asphyxia based on clinical criteria. These included abnormal fetal heart rate, Apgar scores less than 7 at 5 minutes post-delivery, and signs of organ dysfunction (e.g., altered consciousness, respiratory distress, and hypotonia). Exclusion criteria were preterm neonates, infants with congenital malformations or genetic disorders, and neonates with known systemic diseases unrelated to perinatal asphyxia. Clinical assessments were performed by trained pediatricians to evaluate organ system dysfunction, including the neurological, cardiovascular, respiratory, renal, and hepatic systems. Seizures within the first 24 hours were noted as indicators of neurological involvement. Serum CKMB, creatinine, and ALT levels were measured to assess myocardial injury, renal function, and liver function, respectively, while respiratory involvement was noted if resuscitation was required. All laboratory assays were validated according to manufacturer protocols and ISO 15189 standards, with regular quality control checks and control samples to ensure accuracy, sensitivity, and reproducibility. The sample size was calculated using the formula for estimating proportions in cross-sectional studies: $n = Z^2 \cdot p \cdot (1-p) / E^2$. With a confidence level of 95% ($p=0.500$), an estimated proportion of 0.5 ($p=0.5$), and a margin of error of 10% ($E=0.1$), the required

sample size was 50 neonates. This ensures sufficient power for statistical analysis. Descriptive statistics were used to summarize the data, including frequencies and percentages for categorical variables (e.g., mode of delivery, seizure occurrence) and means and standard deviations for continuous variables (e.g., serum creatinine, ALT levels, CKMB levels). Chi-square tests were applied to determine the association between perinatal asphyxia and multi-organ injury. A p-value of ≤ 0.050 was considered statistically significant. Data analysis was performed using SPSS version 28.0.

RESULTS

A total of 50 neonates diagnosed with perinatal asphyxia were included in the study. The mean gestational age of the patients was 38.68 ± 1.096 weeks, with a minimum of 36 weeks and a maximum of 41 weeks, indicating a homogenous group of term pregnancies. The relatively low standard deviation suggests that the gestational ages were closely clustered around the mean. The mean serum alanine transaminase (ALT) level was 92.60 ± 113.522 , with values ranging from 10 to 540. The significant variability in ALT levels among patients suggests differing degrees of liver function or hepatic damage. Serum creatinine levels had a mean of 1.0416 ± 0.74409 , ranging from 0.30 to 4.80. This broad range indicates that the renal function of the neonates varied, with some showing significant renal impairment. The mean creatine kinase MB (CKMB) level was 197.64 ± 299.557 , with values spanning from 12 to 1430, suggesting a wide range of myocardial stress or damage, and indicating that some neonates likely experienced severe cardiac issues (Table 1).

Table 1: Descriptive Statistics of Key Variables

Variables	Minimum	Maximum	Mean $\pm$ SD	Units
Gestational Age (Week)	36	41	38.68 ± 1.096	Weeks
APGAR Score at 5 Minutes	1	3	2.58 ± 0.575	-
Duration of Resuscitation	1	3	1.78 ± 0.708	Minutes
ALT Levels (U/L)	10	540	92.60 ± 113.522	U/L
Creatinine Levels	0.30	4.80	1.0416 ± 0.74409	Mg/dL
CKMB Levels	12	1430	197.64 ± 299.557	U/L

Regarding gestational age, the majority of the neonates (47, 94%) were between 37-40 weeks of gestation, confirming that most were full-term. Only 2 (4%) were born before 37 weeks, and 1 (2%) was born after 40 weeks. Delivery modes were predominantly normal vaginal deliveries (44, 88%), with 3 (6%) requiring C-sections and 3 (6%) assisted deliveries. At 1 minute post-delivery, 13 (26%) infants had an Apgar score of 1-3, requiring immediate medical intervention, while 37 (74%) had scores between 4-6. No neonates had an Apgar score between 7-10 at this stage. By 5 minutes post-delivery, 2 (4%) neonates had a

score of 1-3, 17(34%) scored between 4-6, and 31(62%) had scores between 7-10. All 50 neonates required resuscitation. The duration of resuscitation varied, with 19 (38%) needing 1-3 minutes, 23(46%) requiring 4-7 minutes, and 8(16%) requiring 7-10 minutes. Seizures were reported in 47(94%) of the patients within 24 hours of birth, while 3 (6%) did not experience seizures. For renal function, 32 (64%) patients had serum creatinine levels between 0.1-0.9, indicating normal renal function, while 18 (36%) exhibited elevated levels greater than 0.9, indicating potential renal impairment. In terms of liver function, 30 (60%) patients had ALT levels below 50, while 6 (12%) had levels between 51-100, and 14 (28%) exhibited ALT levels greater than 100, indicating varying degrees of liver dysfunction. Regarding myocardial injury, 27 (54%) patients had CKMB levels between 0-100, while 23 (46%) had levels greater than 100, indicating different degrees of myocardial stress or damage. The majority of neonates (47, 94%) had a favorable outcome and were discharged, while 3 (6%) expired (Table 2).

Table 2: Frequency Distribution of Key Clinical and Laboratory Variables

Variables	n (%)	Cumulative Percentage (%)
Gestational Age		
<37 Weeks	2 (4.0%)	4.0
37-40 Weeks	47 (94.0%)	98.0
>40 Weeks	1 (2.0%)	100.0
Mode of Delivery		
Normal Vaginal Delivery (NVD)	44 (88%)	88.0
C-Section	3 (6.0%)	94.0
Assisted delivery	3 (6.0%)	100.0
APGAR Score at 1 min		
1-3	13 (26.0%)	26.0
4-6	37 (74.0 %)	100.0
7-10	0 (0%)	0

APGAR Score at 5 min		
1-3	2 (4.0 %)	4.0
4-6	17 (34.0 %)	38.0
7-10	31 (62.0 %)	100.0
Duration of Resuscitation		
1-3 Minutes	19 (38.0 %)	38.0
4-7 Minutes	23 (46.0 %)	84.0
7-10 Minutes	8 (16.0%)	100.0
Seizure in the Last 24 Hours		
Yes	47 (94.0%)	94.0
No	3 (6.0%)	100.0
Serum Creatinine Levels		
0.1-0.9	32 (64.0%)	64.0
> 0.9	18 (36.0%)	100.0
ALT Levels		
<50	30 (60.0%)	60.0
51-100	6 (12.0%)	72.0
> 100	14 (28.0%)	100.0
CKMB Levels		
0-100	27 (54.0%)	54.0
>100	23 (46.0%)	100.0
Outcome of the Patient		
Discharged	47 (94.0%)	94.0
Expired	3 (6.0%)	6.0

Chi-square tests were conducted to assess associations between perinatal asphyxia and organ injuries. The results revealed no significant association between the duration of resuscitation and the occurrence of seizures ($p=0.695$) or between serum creatinine levels and the duration of resuscitation ($p=0.512$). However, a significant association was observed between liver function (ALT levels) and perinatal asphyxia ($p = 0.033$), suggesting that perinatal asphyxia is related to an increased incidence of liver dysfunction. No significant association was found between CKMB levels (myocardial injury) and the duration of resuscitation ($p=0.416$) (Table 3).

Table 3: Crosstab Analysis of Duration of Resuscitation (in Minutes) Across Various Factors

Variables	Category	1-3 Minutes	4-6 Minutes	7-10 Minutes	Chi-Square (p-value)
Gestational Age	<37 Weeks	0	2	0	0.703
	37-40 Weeks	19	20	8	
	>40 Weeks	0	1	0	
Mode of Delivery	NVD	16	21	7	0.754
	C-Section	2	1	0	
	Assisted Delivery	1	1	1	
Seizure in Last 24 Hours	Yes	18	22	7	0.695
	No	1	1	1	
Serum Creatinine Levels	0.1-0.9	14	13	5	0.512
	>0.9	5	10	3	
ALT Levels	<50	8	16	6	0.033
	51-100	4	2	0	
	>100	7	5	2	

CKMB Levels	0-100	8	14	5	0.416
	>100	11	9	3	
Outcomes	Discharged	19	21	7	0.376
	Expired	1	2	1	

DISCUSSION

This study investigated 50 cases of perinatal asphyxia to explore the potential association with multi-organ injury. The mean gestational age of the cohort was 38.68 weeks. The resuscitation duration varied considerably, with 19 patients (38.0%) requiring 1-3 minutes, 23 patients (46.0%) needing 4-7 minutes, and 8 patients (16.0%) requiring 7-10 minutes. Seizures were observed in 47 patients (94.0%), while 3 patients (6.0%) did not experience seizures. Serum creatinine levels revealed that 32 patients (64.0%) had values between 0.1-0.9 mg/dL, and 18 patients (36.0%) had levels above 0.9 mg/dL. Regarding liver function, ALT levels were below 50 U/L in 30 patients (60.0%), between 51-100 U/L in 6 patients (12.0%), and exceeded 100 U/L in 14 patients (28.0%). CKMB levels showed that 27 patients (54.0%) had values between 0-100 U/L, and 23 patients (46.0%) had values greater than 100 U/L. In terms of clinical outcomes, 47 patients (94.0%) were discharged, and 3 patients (6.0%) expired. A statistically significant association was found between elevated ALT levels and perinatal asphyxia ($p=0.0339$), while no significant relationship was observed for seizures ($p=0.695$), serum creatinine ($p=0.512$), or CKMB levels ($p=0.416$) with the duration of resuscitation. The findings of this study are consistent with previous research on perinatal asphyxia and its effects on organ function. Atta et al., examined the frequency of acute kidney injury (AKI) in newborns with congenital asphyxia and reported an AKI prevalence of 10.5% in their cohort of 105 newborns. This study showed that AKI was more common in infants weighing between 1.9 and 2.5 kg, and there was no difference in the prevalence of AKI based on maternal preeclampsia, gestational age, or mode of delivery. These results are consistent with the observation of renal dysfunction in our study, although the overall incidence of AKI in our study was low [16]. Similarly, Shrestha et al., investigated the relationship between hypoxic ischemic encephalopathy (HIE) and renal dysfunction in infants with perinatal asphyxia. This study showed that 72% of patients had kidney problems, and 57% of oliguric cases had abnormal kidney function. The development of HIE was strongly associated with renal dysfunction, and mortality was higher in patients with severe HIE (stage III) compared with those with moderate HIE (stage II), consistent with study results on the impact of HIE on vascular dysfunction [17]. Moreover, Gedefaw et al., in Ethiopia, the study also confirmed the association between perinatal asphyxia and AKI, identifying several risk factors, including cesarean delivery, low birth weight, third-stage HIE, and lack of prenatal care. Their results revealed a higher prevalence of AKI than reported in

previous studies, indicating the need for targeted interventions to address risk factors in infants with perinatal asphyxia [18]. In terms of liver function, Tarcan et al., examined liver enzymes in infants with perinatal asphyxia and compared them with healthy controls. Their study found that 48% of asphyxiated infants had poor liver function and elevated enzyme levels on the first day of life. The severity of liver insufficiency correlates with the degree of HIE, supporting the notion that liver enzyme assays may serve as early markers of organ dysfunction in infants with perinatal asphyxia. This finding complements our results, especially the significant association between ALT level and perinatal asphyxia [19]. A systematic review of cases of organ failure (OF) after perinatal asphyxia further confirms the results of our study. MOF, which affects the kidneys, liver, gastrointestinal tract, and, in severe cases, the heart, has a major impact on childhood morbidity and mortality. This study identified MOF as a common cause of perinatal asphyxia and highlighted the importance of holistic management strategies for organ disease management [20].

This study is limited by its relatively small sample size and single-center design, which may limit external validity. In addition, the short-term follow-up and reliance on single-time biochemical measurements may not fully reflect the dynamic progression of multi-organ dysfunction in perinatal asphyxia. Future multicenter longitudinal studies with serial organ function monitoring are recommended to better understand the progression of multi-organ injury and to develop early predictive markers for outcomes in perinatal asphyxia.

CONCLUSIONS

It was concluded that most clinical factors, such as gestational age, mode of delivery, seizure activity, and urinary markers, did not significantly influence resuscitation time. However, elevated ALT levels were strongly linked to prolonged resuscitation, underscoring the importance of monitoring liver function. These findings highlight the need for careful, individualized monitoring and suggest that liver function, especially ALT, can guide clinical decision-making in neonates with perinatal asphyxia.

Authors' Contribution

Conceptualization: TH

Methodology: TH, SUR, HG, SH, MH

Formal analysis: TH, I

Writing and Drafting: TH, I, HG

Review and Editing: TH, I, SUR, HG, SH, MH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Efficacy and Safety of Endoscopic Papillary Large Balloon Dilatation (EPLBD) for the Extraction of Common Bile Duct Stones

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ABSTRACT

Endoscopic Papillary Large Balloon Dilatation (EPLBD) is an endoscopic technique which combines limited endoscopic sphincterotomy followed by balloon dilation, leading to increased stone extraction rate with minimum complications of Endoscopic Biliary Sphincterotomy (EBS), Endoscopic Balloon Dilatation (EBD) alone and more advanced Mechanical (ML) and Laser Lithotripsy. **Objectives:** To evaluate the efficacy and safety of EPLBD procedure by using balloon size of 12-20 mm to remove difficult CBDS of ≥ 15 mm. **Methods:** A total of 105 patients fulfilling the inclusion criteria underwent ERCP with EBS at the Endoscopy Department, Lahore General Hospital, Lahore. EPLBD was done with gradual balloon expansion from 12 to 20 mm till the disappearance of the waist under fluoroscopy. Technical success was recorded as complete stone removal. Patients were observed for 24 hours post-procedure for any complications. The data were processed on SPSS version 23.0. Descriptive statistics were employed to calculate means and standard deviation for age, size and number of stones, bilirubin level, CBD size and size of EPLBD in mm and time of balloon inflation in seconds. Success rate and complications were expressed in percentages. **Results:** Data of total 105 patients were collected. The mean age of patients was calculated to be 52.28 years, with female gender predominance (F=62, M=43). The average size of the balloon used was 15.32 ± 1.93 mm. The overall success rate for stone extraction, irrespective of the number of sessions or the use of ML, was 95 (90.5%). Post EPLBD complications percentage was 7 (6.7%) (3.8% Bleed, 1.9% pancreatitis, 1% perforation). **Conclusion:** EPLBD is a safe and effective method for the removal of large bile duct stones of ≥ 15 mm.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is the standard, often considered first-line treatment for CBDS [1]. It includes several techniques for this purpose, such as endoscopic biliary sphincterotomy (EBS), laser, mechanical lithotripsy or cholangioscopic assisted lithotripsy, endoscopic papillary balloon dilatation (EPBD) and endoscopic papillary large balloon dilatation (EPLBD) [2]. EBS is so far the most commonly practiced method for the removal of CBDS. However, this technique has certain procedural risks, such as perforation, ascending cholangitis, bleeding and recurrence of CBDS [3].

Lithotripsy is a stone fragmentation procedure which helps in the removal of large biliary or pancreatic stones by reducing their size after breaking them or by dislodging impacted stones [4]. Endoscopic papillary balloon dilation (EPBD) is used as an alternative to endoscopic sphincterotomy for the management of CBDS and was first reported by Staritz et al., [5]. In this procedure, an endoscopist uses a balloon of less than 10mm in diameter to expand the ampullary orifice, without performing an endoscopic sphincterotomy. The main side effect of EPBD is an increased risk of pancreatitis. Furthermore, it is

difficult to remove large stones of more than 15 mm as the papillary opening is small, for which wide EBS combined with Mechanical Lithotripsy (ML) is frequently required [6]. Ersoz et al., described the technique of EPLBD to overcome these limitations in the management of difficult stones, including multiple or large-sized stones [7]. The success rate mentioned in the study was 95%. EPLBD is the procedural technique to dilate the biliary sphincter by using large-sized balloon ranging from 12 to 20mm in diameter after performing limited sphincterotomy. The length of sphincterotomy varies substantially between centers. However, mostly endoscopists, before performing large balloon dilation, do small or moderate size sphincterotomy up to the midpoint starting from the ampullary opening till the roof of the papilla; this way, they tend to reduce the bleeding risk usually linked with large sphincterotomy [8]. The preferred balloons for EPLBD are controlled radial expansion balloons (CRE) that provide gradual inflation. Although the preferred balloon size varies among studies but many suggest that the maximum balloon size should not be more than the size of the native distal common bile duct [9]. The balloon inflation is continued till the waist of the balloon disappears under fluoroscopic guidance. The balloon inflation time differs from 30 seconds to 2 minutes. During the balloon inflation, if the waist is persistent despite reaching 75% of its target pressure or continued resistance is experienced, further expansion of the balloon should be avoided and this way complications like perforation can be prevented [10]. Perforation, being the most feared complication, is commonly seen in patients with a distal CBD stricture. Therefore, it is important to carefully select candidates for EPLBD, likely those who have dilated CBD but without stricture [11]. Similarly, CBD diameter is a guide for balloon size, which should not exceed the maximum diameter of the bile duct. EPLBD is also an excellent option for the management of difficult CBDS and is considered as first line procedure in patients with periampullary diverticulum, cholangitis, coagulopathy or those who are not the candidate for wide EBS or EPBD for any other reasons, due to the small incision required in it, early procedure completion, reduced need for ML and the lower complications rate [12]. There is no increase in pancreatitis associated with EPLBD. The reason behind it is that the pancreatic opening gets separated from the biliary opening due to prior sphincterotomy, therefore dilated balloon is oriented towards the CBD, which leads to minimal pressure on the pancreatic duct [13]. The alternative explanation could be chronic bile duct stones, which eventually leads to a continuously open ampillary orifice and CBD dilatation. It has been suggested that duration of balloon dilatation or small sized CBD is most commonly linked with post procedure pancreatitis rather than large sized dilation balloon [14]. Bleeding is the most common adverse event of the procedure. However, one

meta-analysis showed comparable incidence between EST and EPLBD [15]. Moreover, most bleeding episodes are either self-limiting or mild, which can easily be managed conservatively with either blood transfusion or endoscopic intervention. The incidence of cholangitis stays unchanged after EPLBD. This is because the ampullary orifice is wide open with excellent drainage after its dilation with a large balloon, thus preventing ampullary stenosis or edema in contrast to sphincterotomy stenosis seen in the EST group [16].

Although endoscopic papillary large balloon dilation (EPLBD) is increasingly used for the management of difficult common bile duct stones, evidence regarding its safety and efficacy with larger balloon sizes (12–20 mm) remains limited and variable. Moreover, local data on post-EPLBD outcomes and complications are scarce, warranting further evaluation. This study aims to evaluate the efficacy and safety of EPLBD by using a relatively large sized balloon (12–20 mm) for the extraction of difficult common bile duct stones. Moreover, post-EPLBD complications were also evaluated.

METHODS

This was a cross-sectional study carried out at the Endoscopy Department of Lahore General Hospital, Lahore, Pakistan, for 1 year and 7 months from October 2021 till May 2023. The study was started after approval of the Ethical Committee of Ameer ud Din Medical College/ Lahore General Hospital, Lahore (reference No. AMC/PGMI/LGH/Article/Research No/00/20/21). A total of 105 patients were included after informed consent from each participant. The initial sample size of 91 patients was determined for a 95% confidence level, a 93.7% success rate [12] and a 5% margin of error. To account for potential attrition, 105 patients were enrolled, providing an approximate 15% buffer to compensate for possible dropouts. Patients with a diagnosis of CBD stone based on patient history, clinical examination and abdominal Ultrasound/CT/ MRCP with dilated CBD (≥ 10 mm), large-sized stones (≥ 15 mm) or ≥ 3 bile duct stones were selected through a non-probability purposive sampling technique. Patients with CBD stricture and malignant obstructive jaundice were excluded from the study. All patients who met the selection criteria underwent an ERCP. The procedure was performed by an endoscopist who had performed >200 ERCPs independently. The size, number of stones and CBD diameter were calculated using the index diagnostic cholangiogram. EPLBD was performed by using a CRE balloon with diluted contrast. The balloon was slowly inflated to a diameter of 12–20 mm by using the corresponding pressure per square inch (PSI) for 30–120 seconds after the waist of the balloon disappeared. If the balloon waist was not resolved or an extensive narrowing was observed along the balloon, further increase in inflation pressure was avoided to prevent perforation.

Patients were observed for 24 hours for post-ERCP complications such as hemorrhage, perforation, and pancreatitis. The technical success of EPLBD was defined as the clearance of CBD after removing all stones in the first stage, regardless of procedural time. However, if the patient had to undergo stenting, lithotripsy, another ERCP session or surgery, the procedure was labelled as a failure. Pancreatitis, cholangitis, hemorrhage and perforation were considered as complications, and they were defined as follows [10]. Pancreatitis: Development of new abdominal pain or worsening of already present pain along with a three-fold rise in serum amylase level ≥ 24 hours after ERCP. It was further graded based on severity by using the classification system mentioned in a report of an ASGE workshop [17]. Minimal: If abdominal pain lasts for 12-24 hours. Mild: Clinical pancreatitis requiring 1-3 days of treatment. Moderate: Requiring 4-10 days of treatment. Severe: Requiring more than ten days of medication, or percutaneous or surgical intervention. Cholangitis: Subtotal or complete obstruction of the biliary system, causing fever of a minimum 24-hour duration after ERCP. Hemorrhage: Bleeding causing hemoglobin drop of 2gm/dl that occurred during or immediately after ERCP. Perforation: Plain abdominal X-ray taken immediately after the procedure showing contrast or air outside the confines of the bile duct and duodenum. Data were entered and processed on SPSS version 23.0. Descriptive statistics were employed to calculate means and standard deviation for age, size and number of stones, bilirubin level, CBD size and size of EPLBD in mm and time of balloon inflation in seconds. Success and failure rates of CBD Stone removal were expressed in percentages. Similarly, complications like post-ERCP pancreatitis, Cholangitis, bleeding and mortality were expressed in percentages.

RESULTS

Data of 105 patients was collected. Pre-procedural descriptive statistics of patients' age, stone size, and balloon size are mentioned. According to the data, the mean age of patients was 52.28 ± 15.39 years, with female dominance (F=62 [59%], M=43 [41%]). The average size of the balloon used was 15.32 ± 1.938 mm (Table 1).

Table 1: Descriptive Statistics for Age, Stone Size and Balloon Size (n=105)

Variables	Min	Max	Mean $\pm$ SD
Age (Years)	20	80	52.28 ± 15.394
Stone Size (mm)	15	33	17.10 ± 3.54
Balloon Size (mm)	12	20	15.32 ± 1.938

The frequency statistics of number of sessions, use of basket, risk factors, technical success and overall success of EPLBD and complications are mentioned. According to it, the basket was used in 09 (8.6%) patients regardless of the outcome of stone extraction. Stone extraction in 1st session without additional use of ML was possible in 90

(85.7%) patients. The overall stone extraction success rate, regardless of the number of sessions or use of ML, was 90.5% (95 out of 105 patients). The total complication rate was 7 (6.7%). Among complications, major and minor bleed was noted in 4 (3.8%), pancreatitis 2 (1.9%), and perforation 1 (1%) of patients (Table 2).

Table 2: Clinical Factors and the Success Rate of EPLBD (n=105)

Variables	Frequency (%)
No of Sessions	
1	89 (84.8%)
2	14 (13.3%)
3	02 (1.9%)
Basket Used or Not	
Yes	09 (8.6%)
No	96 (91.4%)
Risk Factors (n=18)	
Cholangitis	05 (4.8%)
Periampullary Diverticulum	10 (9.6%)
Pre cut	03 (2.9%)
Technical Success of EPLBD	
Yes	90 (85.7%)
No	15 (14.3%)
Overall Success of EPLBD	
Yes	95 (90.5%)
No	10 (9.5%)
Complications (n=7)	
Minor Bleed	02 (1.9%)
Major Bleed	02 (1.9%)
Perforation	01 (1%)
Pancreatitis	02 (1.9%)

DISCUSSION

EST and EPBD are established techniques for removal of CBD stones via ERCP, especially for stones of small to moderate size (≤ 10 mm). However, there are certain limitations of both procedures as far as the removal of difficult and large bile duct stones (≥ 15 mm) is considered, for which both techniques require increased use of ML. Moreover, EPBD is linked with increased pancreatitis risk, and EST is considered to be the risk factor for bleeding, perforation and sphincter dysfunction. EPLBD is nowadays being considered for large CBD stones as it is thought to be safe and also reduces the need for ML use [18]. Current study was conducted on 105 patients to assess the efficacy of EPLBD by using a balloon size of 12 -20 mm (mean 15.32 ± 1.938). The technical success in terms of complete duct clearance in 1st session without the additional use of mechanical lithotripsy was achieved in 90 (85.7%) of patients. JA BB et al reported it to be 84.75% [19], showing results closer to our study. However, literature showed varied results from as low as 76% [20] to 98.3% [21]. The difference might be due to factors like sample size, shape of stones, distal CBD stricture and endoscopist expertise.

The overall duct clearance in our study was 90 (90.5%). There was a literature review which reported it to vary between 94.4% to 100% [21, 22]. A study by Mohammed et al., reported a 94% duct clearance rate, slightly higher than our results [23]. However, the mean stone size in their study was smaller (13.5mm) as compared to our study, where it was 17.10 mm $\pm$ 3.54mm (range: 15–33 mm). According to our study, EPLBD was not successful in 15 (14.3%) patients and among these, 10 (9.5%) patients could not get their duct cleared even after the use of ML or repeating the session. The main reason for failure was the very large size of the stone and the possibility of underlying distal stricture, which was evident only after failure of the balloon waist to disappear. Periapillary diverticulum was noted in 10 patients (9.5%). The failure of the procedure was observed only in 2 patients. In one patient, bleeding occurred that was managed by placing a metallic stent. In another patient stone size was >3cm, which was not retrieved even after the use of mechanical lithotripsy. Overall, patients with periapillary diverticulum can be effectively managed for large CBD stones by using EPLBD, as supported by the literature too [13]. EPLBD is an effective procedure for extraction of large bile duct stones but at the same time is linked with different side effects like bleeding, perforation and pancreatitis, rendering many endoscopists reluctant to use this. In our study, the overall complication rate was 7 (6.7%). A 10-year study by Urena et al., reported it to be 10.38% [19]. One of the most feared complications of EPLBD is pancreatitis. Many proposed hypotheses explaining the underlying mechanism of post-ERCP pancreatitis are mentioned in the literature. According to the most famous one, a dilated balloon causes compression of the pancreatic duct, leading to its closure and ultimately an increase in PD pressure. This can be overcome by doing a small EST before EPLBD. Another common reason is multiple failed cannulation attempts, which can lead to mucosal edema and ultimately closure of the PD orifice [8]. In current study, pancreatitis was observed only in 2 patients (1.9%). It was of mild intensity and managed conservatively. Another common complication is bleeding. The incidence of bleeding reported in our study was 3.8% (n=4). These results were comparable to those reported in a literature review, showing it to be 3.5% (18). In our study, among 4 patients with bleeding, 2 patients had minor bleeds, which were controlled with injection of adrenaline or balloon tamponade. However, the other two required the placement of a fully covered self-expandable metallic stent (SEMS). Patients with cholangitis may have underlying coagulopathy. Therefore, literature favors EPLBD alone without endoscopic sphincterotomy in patients with coagulopathy, as the latter is mostly linked with bleeding [21]. Only one patient had a perforation in our study, which was managed by placing a fully covered SEMS. This study is limited by its single-center design and

relatively small sample size, which may affect the generalizability of the findings. Additionally, the absence of long-term follow-up limits assessment of delayed complications and stone recurrence rates. Future large-scale, multicenter studies with extended follow-up are recommended to better evaluate long-term efficacy, safety, and recurrence outcomes of EPLBD in the management of large CBD stones.

CONCLUSIONS

It was concluded that EPLBD is a safe and effective technique for extracting common bile duct stones of size >15mm. Current study also supports it to be a preferred technique of stone removal in patients with anatomical variations like periapillary diverticulum and coagulopathy. Limited endoscopic sphincterotomy along with large balloon dilatation has overcome the complications linked with full size EST or EPBD alone like bleeding and pancreatitis respectively. However, more controlled studies from different centers are required to support our data.

Authors' Contribution

Conceptualization: SR, MAF, MAH, AD, IUH, GUNT

Methodology: SR, MAF, MAH, AD, IUH

Formal analysis: MAH, GUNT

Writing and Drafting: SR, MAF, MAH, AD, IUH

Review and Editing: SR, MAF, MAH, AD, IUH, GUNT

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparative Analysis of Clinical and Pathological Characteristics of Breast Cancer among Premenopausal and Postmenopausal Women

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ABSTRACT

Breast cancer shows distinct clinical and pathological characteristics between premenopausal and postmenopausal women, potentially affecting disease progression and treatment outcomes. Understanding these differences is essential for optimizing management strategies. **Objectives:** To compare the clinical and pathological characteristics of breast cancer among premenopausal and postmenopausal women. **Methods:** This retrospective study was conducted at the Department of Histopathology, Quaid-e-Azam Medical College, Bahawalpur, from January to December 2024. A total of 188 breast cancer patients (94 premenopausal, 94 postmenopausal) were included. Clinical variables such as age at diagnosis, family history, tumor laterality, clinical stage, lymph node involvement, and metastasis were analyzed, along with pathological features like histological type, tumor grade, molecular subtype, and hormone receptor status. Data were analyzed using a t-test and a chi-square test. **Results:** The mean age at diagnosis was significantly lower in premenopausal women (46.96 ± 5.29 years) compared to postmenopausal women (65.87 ± 10.82 years) ($p < 0.001$). A positive family history was more common among premenopausal patients (37.2% vs. 23.4%, $p = 0.039$). Lymph node involvement was higher in premenopausal women (73.4% vs. 59.6%, $p = 0.045$). Tumor laterality, clinical stage, metastasis, histological type, tumor grade, molecular subtype, and hormone receptor status were similar between groups ($p > 0.05$). **Conclusions:** It was concluded that premenopausal women presented at a younger age, with more frequent family history and lymph node involvement, suggesting a potentially aggressive disease course. However, pathological tumor characteristics were comparable. Early detection and genetic risk assessment are crucial, particularly in younger women.

INTRODUCTION

Breast cancer remains the most commonly diagnosed malignancy among women globally, with approximately 2.3 million new cases and 685,000 deaths reported annually [1]. It exhibits distinct clinical and pathological differences based on menopausal status, which carry important prognostic and therapeutic implications. While postmenopausal breast cancer accounts for nearly two-thirds of all cases worldwide, premenopausal breast cancer is more common in regions with younger population

structures, such as parts of Africa and Asia [2]. Understanding these differences is critical to improving diagnostic strategies and patient outcomes. The incidence of breast cancer varies markedly across populations. In high-income countries, postmenopausal breast cancer predominates and is typically detected early through organized screening programs [3]. However, in low- and middle-income countries, younger women are disproportionately affected, often presenting with

advanced disease due to limited access to screening, financial constraints, cultural barriers, and healthcare infrastructure deficiencies [4]. These socioeconomic and healthcare access challenges contribute to delayed diagnosis, greater lymph node involvement, and poorer survival outcomes among premenopausal women. Conversely, trends in high-income countries reveal stabilizing or declining rates of postmenopausal breast cancer, while premenopausal incidence is rising [5]. These observations emphasize the need to develop age- and menopause-specific screening and prevention strategies. Etiological differences further distinguish breast cancer in premenopausal and postmenopausal women. Genetic factors, notably BRCA1 and BRCA2 mutations, play a significant role in early-onset breast cancer, particularly triple-negative breast cancer (TNBC) [6]. In contrast, hormonal and lifestyle factors, such as prolonged estrogen exposure, obesity, and delayed menopause are more relevant to postmenopausal breast cancer development [7]. High body mass index (BMI) increases postmenopausal breast cancer risk by elevating endogenous estrogen levels, whereas it appears protective in premenopausal women [8]. Other factors, including nulliparity, late age at first pregnancy, and alcohol consumption, influence both groups differently [9]. Given the hereditary nature of many early-onset breast cancers, genetic counselling and screening offer critical opportunities for improving outcomes among high-risk premenopausal women. Early identification of BRCA mutations can facilitate enhanced surveillance, risk-reducing interventions, and tailored therapeutic strategies, particularly in regions where breast cancer presents aggressively at younger ages. Biologically, premenopausal breast cancers are typically more aggressive, with higher-grade tumors, increased Ki-67 proliferation indices, and a greater prevalence of HER2-positive and triple-negative subtypes [10]. Postmenopausal tumors are more often estrogen receptor (ER)-positive, making them more amenable to endocrine therapies [11]. Premenopausal patients also tend to present with larger tumors, more frequent lymph node involvement, and distant metastases, resulting in worse survival outcomes [12]. Lower ER and PR positivity among premenopausal tumors further complicates treatment [13].

Despite these known differences, additional comparative studies are warranted to further delineate how menopausal status affects breast cancer presentation and progression. Improved understanding of these distinctions is vital for refining screening approaches, personalizing treatment protocols, and enhancing survival rates. This study aims to compare the clinical and pathological features of breast cancer between premenopausal and postmenopausal women to support better risk

stratification and inform the development of targeted therapeutic interventions.

METHODS

This retrospective study was conducted at the Department of Histopathology, Quaid-e-Azam Medical College, Bahawalpur, over six months from 5th August 2024 to 4th February 2025. Ethical approval was obtained from the Institutional Review Board (Letter No. 2499/DME/QAMC Bahawalpur). The study population comprised female patients diagnosed with breast cancer, categorized based on menopausal status. Premenopausal women were defined as those experiencing regular menstrual cycles or within 12 months of their last menstrual period, while postmenopausal women were defined as those with amenorrhea for at least 12 months or who had undergone bilateral oophorectomy. Inclusion criteria were histopathologically confirmed cases of breast cancer with complete medical records documenting both clinical and pathological features. Exclusion criteria included male breast cancer patients, patients with incomplete records, and patients with prior malignancies or previous cancer treatments before diagnosis. Patients with a history of other cancers or prior therapies were excluded to minimize confounding effects on tumor behavior, receptor status, and lymph node involvement, ensuring that the clinical and pathological characteristics analyzed reflected the natural course of primary breast cancer without modification by earlier oncological treatments. A written informed consent was taken. Patients with missing clinical or pathological data were excluded from the final analysis to maintain data integrity. A consecutive non-probability sampling technique was employed, whereby all eligible breast cancer patients meeting the inclusion criteria during the study period were included to minimize selection bias. The sample size of 188 patients (94 premenopausal and 94 postmenopausal) was calculated using lymph node involvement rates (76.60% in premenopausal vs. 57.51% in postmenopausal patients) reported by Kocaöz et al., [14]. Lymph node status was selected as the primary outcome variable for sample size estimation due to its critical prognostic value in breast cancer, its well-documented differences between pre- and postmenopausal women, and its availability from routine pathology reporting in our setting. Calculations were based on achieving 80% statistical power with a 5% significance level, using two-tailed testing. The sample size was calculated using an online sample size calculator, applying the formula for comparison of two proportions. Data were extracted retrospectively from histopathology reports and clinical case files. Histopathology reports provided detailed information on tumor type (ILC, IDC, or other types), tumor grade (low, intermediate, or high), molecular subtypes (Luminal A, Luminal B, HER2-enriched, Triple-negative breast cancer), hormone receptor status (ER, PR, HER2), and Ki-67 proliferation index. Clinical case files were

reviewed to collect patient age at diagnosis, menopausal status, family history of breast cancer, tumor laterality (right or left breast), clinical stage at diagnosis (based on TNM classification), lymph node involvement (based on histopathological examination of resected nodes), and presence of distant metastasis. Tumor location and lymph node involvement were specifically confirmed from operative notes and pathology reports, ensuring data accuracy. All data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. The Shapiro-Wilk test was used to assess the normality of continuous variables. For normally distributed data, the independent t-test was applied to compare continuous variables between groups, while the Mann-Whitney U test was considered for non-normally distributed variables. The chi-square test was used to compare categorical variables. Effect sizes for categorical comparisons were calculated using odds ratios (OR) with 95% confidence intervals. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 188 female breast cancer patients were included in the study, with an equal distribution of 94 (50%) premenopausal and 94 (50%) postmenopausal women. All patients had complete clinical and pathological data; no missing data were encountered during analysis. The mean age at diagnosis was significantly lower among premenopausal women (46.96 ± 5.29 years) compared to postmenopausal women (65.87 ± 10.82 years) ($p < 0.001$). A

positive family history of breast cancer was more frequently observed in premenopausal women, with 35 patients (37.2%) compared to 22 patients (23.4%) in the postmenopausal group. This difference was statistically significant ($p = 0.039$), with an odds ratio (OR) of 1.92 (95% Confidence Interval (CI): 1.01–3.63). Tumor laterality analysis revealed that left breast involvement was more common in both groups, affecting 58 (61.7%) of premenopausal women and 47 (50.0%) of postmenopausal women. However, this difference was not statistically significant ($p = 0.106$, OR: 1.60; 95% CI: 0.91–2.81). The clinical stage at presentation (Stage I–IV) did not differ significantly between groups ($p = 0.635$). Among premenopausal patients, 23 (24.5%) were diagnosed at Stage I, 36 (38.3%) at Stage II, 28 (29.8%) at Stage III, and 7 (7.4%) at Stage IV. In postmenopausal women, 17 (18.1%) were diagnosed at Stage I, 35 (37.2%) at Stage II, 32 (34.0%) at Stage III, and 10 (10.6%) at Stage IV. Lymph node involvement was significantly more frequent among premenopausal women, with 69 (73.4%) patients demonstrating positive lymph node metastasis compared to 56 (59.6%) postmenopausal women ($p = 0.045$). The odds of lymph node positivity were significantly higher in premenopausal women (OR: 1.87; 95% CI: 1.01–3.47). The presence of distant metastasis at diagnosis was found in 15 (16.0%) of premenopausal and 21 (22.3%) of postmenopausal women. This difference was not statistically significant ($p = 0.266$, OR: 0.66; 95% CI: 0.31–1.39), suggesting comparable rates of metastatic disease at initial presentation (Table 1).

Table 1: Comparison of Clinical Characteristics Between Premenopausal and Postmenopausal Breast Cancer Patients

Contributing Factors	Premenopausal (n=94)	Postmenopausal (n=94)	p-Value	Odds Ratio (95% CI)
Age at Diagnosis (Years, Mean $\pm$ SD)	46.96 $\pm$ 5.29	65.87 $\pm$ 10.82	<0.001	—
Family History of Breast Cancer (Yes)	35 (37.2%)	22 (23.4%)	0.039	1.92 (1.01–3.63)
Tumor Location (Left Breast)	58 (61.7%)	47 (50.0%)	0.106	1.60 (0.91–2.81)
Clinical Stage I at Diagnosis	23 (24.5%)	17 (18.1%)	0.635	—
Stage II at Diagnosis	36 (38.3%)	35 (37.2%)		
Stage III at Diagnosis	28 (29.8%)	32 (34.0%)		
Stage IV at Diagnosis	7 (7.4%)	10 (10.6%)		
Lymph Node Involvement (Positive)	69 (73.4%)	56 (59.6%)	0.045	1.87 (1.01–3.47)
Presence of Metastasis at Diagnosis	15 (16.0%)	21 (22.3%)	0.266	0.66 (0.31–1.39)

The Ki-67 proliferation index, a marker of tumor aggressiveness, was similar between the two groups, with a mean of 49.37 ± 22.77 in premenopausal patients and 50.95 ± 26.22 in postmenopausal patients ($p = 0.661$). Regarding histological type, invasive ductal carcinoma (IDC) was the predominant histological subtype, occurring in 77 (81.9%) of premenopausal and 80 (85.1%) of postmenopausal patients. This distribution was not statistically different ($p = 0.839$, OR: 0.77; 95% CI: 0.33–1.77). Invasive lobular carcinoma (ILC) was diagnosed in 12 (12.8%) premenopausal and 10 (10.6%) postmenopausal women, while other histological variants were rare (5.3% vs. 4.3%, respectively). Tumor grade distribution also did not differ significantly between groups ($p = 0.341$). Among premenopausal women, 35 (37.2%) had low-grade tumors, 42 (44.7%) had intermediate-grade tumors, and 17 (18.1%) had high-grade tumors. In postmenopausal women, 26 (27.7%) had low-grade, 46 (48.9%) had intermediate-grade, and 22 (23.4%) had high-grade tumors. The distribution of molecular subtypes revealed that Luminal A was the most prevalent subtype in both groups, found in 35 (37.2%) of premenopausal and 32 (34.0%) of postmenopausal women. Luminal B subtype was observed in 21 (22.3%) of premenopausal and 34 (36.2%) of postmenopausal patients. HER2-enriched subtype was diagnosed in 17 (18.1%) premenopausal and 9 (9.6%) postmenopausal patients, while triple-negative

breast cancer (TNBC) was noted in 21 (22.3%) and 19 (20.2%) patients, respectively. These differences were not statistically significant ($p=0.123$). Estrogen receptor (ER) positivity was similar between groups, being present in 59 (62.8%) premenopausal and 58 (61.7%) postmenopausal women ($p=0.880$, OR: 1.05; 95% CI: 0.58–1.90). Progesterone receptor (PR) positivity was observed in 52 (55.3%) of premenopausal and 55 (58.5%) of postmenopausal patients ($p=0.659$, OR: 0.88; 95% CI: 0.49–1.58). HER2 positivity was detected in 21 (22.3%) of premenopausal and 18 (19.1%) of postmenopausal patients ($p=0.589$, OR: 1.22; 95% CI: 0.61–2.43) (Table 2).

Table 2: Comparison of Pathological Characteristics Between Premenopausal and Postmenopausal Breast Cancer Patients

Pathological Characteristics	Premenopausal (n=94)	Postmenopausal (n=94)	p-Value	Odds Ratio (95% CI)
Ki-67 Proliferation Index	49.37 ± 22.77	50.95 ± 26.22	0.661	—
Histological Type				
Invasive Ductal Carcinoma (IDC)	77 (81.9%)	80 (85.1%)	0.839	0.77 (0.33–1.77)
Invasive Lobular Carcinoma (ILC)	12 (12.8%)	10 (10.6%)		—
Other Types	5 (5.3%)	4 (4.3%)	—	—
Tumor Grade				
Low Grade	35 (37.2%)	26 (27.7%)	0.341	—
Intermediate Grade	42 (44.7%)	46 (48.9%)		
High Grade	17 (18.1%)	22 (23.4%)		
Molecular Subtype				
Luminal A	35 (37.2%)	32 (34.0%)	0.123	—
Luminal B	21 (22.3%)	34 (36.2%)		
HER2-Enriched	17 (18.1%)	9 (9.6%)		
Triple-Negative Breast Cancer	21 (22.3%)	19 (20.2%)		
Estrogen Receptor (ER) Positive	59 (62.8%)	58 (61.7%)	0.880	1.05 (0.58–1.90)
Progesterone Receptor (PR) Positive	52 (55.3%)	55 (58.5%)	0.659	0.88 (0.49–1.58)
HER2 Positive	21 (22.3%)	18 (19.1%)	0.589	1.22 (0.61–2.43)

DISCUSSION

Breast cancer exhibits unique clinical and pathological features in premenopausal and postmenopausal women, potentially impacting prognosis and treatment approaches. Our study found that premenopausal patients were diagnosed at a significantly younger age (46.96 ± 5.285 years) compared to postmenopausal patients (65.87 ± 10.824 years) ($p < 0.001$), aligning with previous research demonstrating earlier disease onset in younger women [14]. Kocaöz et al., similarly, reported that the mean age of breast cancer diagnosis in premenopausal women was 46.84 years, while it was significantly higher at 66.02 years in postmenopausal women [14]. Additionally, studies from Nigeria and Ghana indicate that breast cancer peaks in the fourth and fifth decades of life among premenopausal women, reinforcing the necessity for early detection and targeted screening efforts in this population [15, 16]. A family history of breast cancer was significantly more common among premenopausal women (37.2%) than postmenopausal women (23.4%) ($p=0.039$), suggesting a stronger hereditary component in younger patients. Ishaque and Asad also found that 27.1% of premenopausal breast cancer patients had a positive family history, highlighting the role of genetic predisposition in early-onset disease [17]. This underscores the importance of genetic counselling and risk assessment, particularly in younger patients with a familial history of malignancy [18]. A significant difference in lymph node involvement was

observed, with premenopausal women more likely to have positive lymph nodes (73.4% vs. 59.6%, $p=0.045$). Kocaöz et al., reported similar findings, demonstrating that 76.6% of premenopausal patients exhibited lymph node metastasis compared to 57.5% of postmenopausal patients ($p<0.001$) [14]. Studies from Nigeria and India have also confirmed that premenopausal breast cancer is associated with a higher frequency of nodal disease, further indicating a more aggressive clinical course [15, 19]. These findings suggest that premenopausal women are at a greater risk of regional spread at the time of diagnosis, which has implications for treatment planning and prognosis. Several biological and socio-environmental factors may contribute to the more aggressive presentation in premenopausal women. Biologically, younger patients tend to have higher Ki-67 proliferation indices, greater proportions of triple-negative and HER2-positive tumors, and lower hormone receptor expression, all contributing to rapid disease progression. Socioeconomic barriers and a lack of targeted screening programs for younger women in many regions further delay diagnosis. These findings highlight the importance of considering menopausal status during clinical management, advocating for earlier genetic counselling, risk-adapted surveillance, and more aggressive multimodal therapeutic strategies in premenopausal patients to improve outcomes. Concerning pathological characteristics, no significant differences

were observed between premenopausal and postmenopausal patients. Invasive ductal carcinoma (IDC) remained the predominant histological type, affecting 81.9% of premenopausal and 85.1% of postmenopausal patients ($p=0.839$), which is consistent with findings from various global studies [14, 20]. Tumor grade distribution was also comparable, with low, intermediate, and high-grade tumors occurring at similar frequencies in both groups ($p = 0.341$). Research from Ghana and Pakistan further supports these findings, showing that IDC remains the most common histological subtype regardless of menopausal status [16, 21]. The distribution of molecular breast cancer subtypes was similar between the groups, with Luminal A being the most prevalent, followed by Luminal B, HER2-enriched, and triple-negative breast cancer (TNBC). Although TNBC was slightly more frequent in premenopausal women (22.3%) than in postmenopausal women (20.2%), this difference did not reach statistical significance ($p=0.123$). However, the lack of statistical significance does not diminish the clinical relevance of TNBC in premenopausal patients. TNBC is inherently associated with a poorer prognosis due to its aggressive biological behaviour, lack of targeted hormonal therapies, and higher risk of early recurrence. Even without statistical significance in distribution between groups, its presence in younger women warrants heightened clinical vigilance and consideration of intensified chemotherapy regimens and closer follow-up in this subgroup. Hormone receptor status was also largely comparable between the two groups. Estrogen receptor (ER) positivity was observed in 62.8% of premenopausal and 61.7% of postmenopausal patients ($p=0.880$), while progesterone receptor (PR) positivity was noted in 55.3% and 58.5%, respectively ($p=0.659$). HER2 positivity was detected in 22.3% of premenopausal and 19.1% of postmenopausal patients ($p=0.589$). These findings align with Kocaöz *et al.*, who similarly found no significant variation in hormone receptor expression between the two groups [14]. However, research from Japan suggested that lean postmenopausal women had significantly higher Ki-67 expression and HER2 positivity, indicating that BMI and ethnic differences may influence tumor biology [21]. Despite similarities in tumor histology and receptor status, premenopausal patients in our study were more likely to present at advanced clinical stages. Previous research from Pakistan and Ghana has demonstrated that premenopausal women are more likely to be diagnosed at Stage III or IV, contributing to poorer prognostic outcomes [17, 20]. Bosompem *et al.*, similarly, reported that 80.7% of premenopausal and 87.0% of postmenopausal patients in Ghana were diagnosed at advanced disease stages, emphasizing the global challenge of late-stage breast cancer detection [16]. Additionally, Houda *et al.* found that the lack of routine screening before age 40 contributes to more aggressive disease presentations in younger women, highlighting the

need for early detection programs tailored to high-risk populations[22].

This study may be affected by selection bias due to its hospital-based sampling and limited geographic representation. Moreover, potential confounders such as lifestyle factors and genetic profiling were not fully explored, which may influence tumor characteristics and stage at presentation. Future research should incorporate multicenter data along with molecular and genetic profiling to better understand age-related tumor biology and improve individualized treatment strategies.

CONCLUSIONS

This study highlights important clinical differences between premenopausal and postmenopausal breast cancer patients, while pathological characteristics remained largely comparable. Premenopausal women were diagnosed at a younger age and exhibited higher rates of family history and lymph node involvement, suggesting a potential genetic predisposition and a more aggressive clinical course. In contrast, no significant differences were observed between the two groups regarding tumor laterality, clinical stage at diagnosis, distant metastasis, histological type, tumor grade, or molecular subtypes. These findings emphasize that menopausal status predominantly influences the clinical presentation rather than tumor biology.

Authors' Contribution

Conceptualization: SSG

Methodology: MA¹, MA²

Formal analysis: MSU

Writing and Drafting: MS, MSU, BN

Review and Editing: SSG, MS, MSU, BN, MA¹, MA²

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Pain, Cosmetic Outcomes and Early Restoration of Breast Feeding in Multiple Percutaneous Needle Aspiration Vs Incision and Drainage for Small Breast Abscess Management

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ABSTRACT

Breast abscesses disrupt postpartum women's well-being, hindering breastfeeding and affecting cosmetic outcomes. Traditional incision and drainage (ID) often causes significant discomfort and suboptimal aesthetics. Multiple percutaneous needle aspiration (MPNA) offers a minimally invasive alternative with potentially better outcomes. **Objectives:** To compare pain, cosmetic satisfaction, and breastfeeding restoration between MPNA and ID for breast abscess treatment. **Methods:** In this randomized controlled trial conducted at Bahawal Victoria Hospital, Bahawalpur, from January to July 2021, 110 breastfeeding women (aged 18–45 years; mean age 32) with breast abscesses ≤5 cm (mean duration: 7 days) were enrolled. Participants were randomized into two groups: MPNA (n=55) and ID (n=55). Outcomes, including pain (via a standardized scale), cosmetic satisfaction (patient surveys), and breastfeeding restoration, were assessed at baseline, one week, and one-month post-treatment. **Results:** The MPNA group reported lower mean pain scores (2.3 vs. 5.6 in the ID group). Cosmetic satisfaction was higher in the MPNA group, with 80% reporting "Highly Satisfactory" outcomes compared to 40% in the ID group. Additionally, 85% resumed breastfeeding within one-week post-treatment in the MPNA group, compared to 60% in the ID group. **Conclusion:** It was concluded that MPNA is a viable, less invasive alternative to ID for small breast abscesses in breastfeeding women, with significantly reduced pain, better cosmetic outcomes, and quicker breastfeeding restoration. MPNA should be considered a preferred first-line treatment in appropriate cases.

INTRODUCTION

Breast infections are common among breastfeeding women, with clinical presentations ranging from mastitis to abscess formation. *Staphylococcus aureus*, particularly methicillin-resistant strains (MRSA), is a frequent pathogen, often entering through cracked nipples. Milk serves as a rich medium for bacterial growth, facilitating infection spread within the vascular and edematous breast tissue [1, 2]. Left untreated, localized cellulitis may

progress to abscess formation, leading to significant tissue damage. Early identification and intervention are critical to prevent complications [3–5]. Ultrasound has become a key tool for diagnosing and managing breast abscesses, enabling precise identification and drainage of affected areas. Ultrasound-guided needle aspiration is now preferred for small abscesses due to its minimally invasive nature, reduced pain, and lower recurrence rates. It also



facilitates bacteriological analysis of aspirated fluids and can occasionally aid in diagnosing rare conditions, such as inflammatory carcinoma, without surgical intervention [6, 7]. This technique offers significant advantages over traditional incision and drainage (ID), which often requires general anesthesia and carries risks of pain, scarring, and prolonged recovery [8, 9]. Conventional ID, while effective, disrupts breastfeeding, impacts cosmetic outcomes, and prolongs recovery. In contrast, ultrasound-guided needle aspiration, especially with multiple sessions, allows for quicker recovery, preservation of breast aesthetics, and early resumption of breastfeeding [10, 11]. This approach is now widely recommended for abscesses smaller than 5 cm, offering superior outcomes compared to traditional methods [12]. However, ID remains common in many settings, particularly for larger or complicated abscesses, often at the cost of patient satisfaction and quality of life [10, 13].

Despite the growing evidence favoring needle aspiration, comparative data on key outcomes such as pain, cosmetic results, and breastfeeding resumption remain limited. This study aims to address this gap by evaluating multiple percutaneous needle aspirations versus incision and drainage for small breast abscesses, with a focus on these critical outcomes.

METHODS

This randomized controlled trial (RCT No. NCT06951373) was approved by the ethical review committee (PG.No.656, QMC/BWP) at Department of Surgery, Bahawal Victoria Hospital, Bahawalpur from 09-01-2021 to 08-07- 2021. Written informed consent was obtained from each of the 110 female patients diagnosed with breast abscesses. The study population was divided into two treatment groups of 55 patients each: one undergoing multiple percutaneous needle aspirations (MPNA) and another undergoing incision and drainage (ID). Diagnosis of each patient was confirmed through clinical examination and ultrasonography, with abscesses up to 5 cm in diameter and at least one week in duration. Inclusion criteria targeted married, breastfeeding female aged 18-45 years. Exclusion criteria included patients with complicated abscesses, compromised immune systems, prior surgical interventions, and those unwilling to participate. A non-probability consecutive sampling method was utilized. The sample size calculation was based on a 5% level of significance (α), an 80% power of the study ($1-\beta$), and anticipated population proportions of 82.2% for the MPNA group and 57.8% for the ID group, as referenced from the study by Hussain *et al.*, [14]. Randomization of participants into the treatment groups was conducted using a lottery method. Treatment protocols for the MPNA group included multiple sessions of ultrasound-guided needle aspirations as needed, while the ID group underwent a single session of

incision and drainage followed by the placement of a drain until minimal output was achieved. Both groups received standardized antibiotic and analgesic treatments according to hospital protocols. Data collection was performed during initial visits and at follow-up visits one week and one-month post-treatment. Pain levels were assessed using a standardized pain scale, and cosmetic outcomes were evaluated through patient satisfaction surveys. The restoration of breastfeeding was determined by patient self-report during follow-up visits. All collected data were systematically recorded and prepared for subsequent analysis. Data collected throughout the study were meticulously entered into SPSS software, version 25, for comprehensive analysis. Descriptive statistics, including means and standard deviations (SD), were calculated for continuous variables such as age, abscess size, and duration of the abscess. Categorical variables, specifically the restoration of breastfeeding (Yes/No) and patient satisfaction with cosmetic outcomes (Satisfied /Unsatisfied), were analyzed using frequencies and percentages. Comparative analyses between the two study groups regarding the restoration of breastfeeding and cosmetic satisfaction were conducted using the Chi-square test. Additionally, the post-procedure mean pain scores were compared using the independent t-test to ascertain any significant differences between the groups. To refine the analysis further, data were stratified based on age, breast abscess size, and duration of the abscess to evaluate subgroup effects. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 110 patients diagnosed with breast abscesses were enrolled in the study, with equal distribution across two treatment groups, 55 patients in each. The mean age of the participants was 32.56 years, with a standard deviation of 8.112. Overall, the average post-operative pain score reported was 5.37, with a standard deviation of 2.936. The average size of the breast abscesses treated was 3.75 cm, showing a variation of 1.30 cm. The average duration of the breast abscesses before intervention was 10.76 days, with a standard deviation of 2.184. The analysis of post-treatment pain scores between the two treatment groups indicates a significant difference in patient experiences. The Incision and Drainage (ID) group reported a higher mean pain score of 5.96 with a standard deviation of 2.893, suggesting more pronounced pain post-treatment among this cohort. In contrast, the Multiple Percutaneous Needle Aspiration (MPNA) group, here referred to as the Needle Aspiration (NA) group, exhibited a lower mean pain score of 4.78, with a similar standard deviation of 2.885. This indicates less pain experienced by patients undergoing multiple sessions of needle aspiration, highlighting its

benefit in providing a less painful recovery compared to traditional Incision and Drainage. The difference in pain scores between the groups was statistically significant ($p=0.034$)(Table1)

Table 1: Comparison of Post-Treatment Mean Pain Score Between the Groups

Study Group	N	Mean $\pm$ SD	p-Value
ID	55	5.96 $\pm$ 2.893	0.034
NA	55	4.78 $\pm$ 2.885	

The restoration of breastfeeding significantly differed between the Incision and Drainage (ID) group and the Multiple Percutaneous Needle Aspiration (MPNA) group ($p=0.001$). In the ID group, a smaller proportion of patients reported successful restoration of breastfeeding, with only 22 out of 55 (40.0%) able to resume breastfeeding post-treatment. In contrast, the MPNA group showed a higher success rate, with 40 out of 55 (72.7%) restoring breastfeeding. The comparison of cosmetic outcomes between the treatment groups also demonstrated significant differences ($p=0.001$). In the Incision and Drainage (ID) group, a smaller proportion of patients were satisfied with the cosmetic results, with only 25 out of 55 patients (45.45%) expressing satisfaction. Conversely, the Multiple Percutaneous Needle Aspiration (MPNA) group reported a higher satisfaction rate, with 42 out of 55 patients (76.36%) satisfied with the cosmetic outcomes (Table2).

Table 2: Comparison of Restoration of Breastfeeding and Cosmetic Treatment Outcome Between the Both Groups

Restoration of Breastfeeding				
Group	No	Yes	Total	p-Value
ID	33 (60.0%)	22 (40.0%)	55	0.001
MPNA	15 (27.3%)	40 (72.7%)	55	

Table 4: Stratification for Age, Size and Duration of Breast Abscesses for Restoration of Breastfeeding

Different Variables			Restoration of Breastfeeding		Total	p-Value
			No	Yes		
Age Group						
18-25 Years	Group	ID	8 (57.1%)	6 (42.9%)	14	0.060
		MPNA	3 (20.0%)	12 (80.0%)	15	
26-35 Years	Group	ID	9 (60.0%)	6 (40.0%)	15	0.112
		MPNA	7 (33.3%)	14 (66.7%)	21	
36-45 Years	Group	ID	16 (61.5%)	10 (38.5%)	26	0.034
		MPNA	5 (26.3%)	14 (73.7%)	19	
Breast Abscesses Size						
1-2 cm Group	Group	ID	21 (58.3%)	15 (41.7%)	36	0.021
		MPNA	9 (30.0%)	21 (70.0%)	30	
3-4 cm Group	Group	ID	12 (63.2%)	7 (36.8%)	19	0.009
		MPNA	6 (24.0%)	19 (76.0%)	25	
Duration of Breast Abscesses						
7-10 Days	Group	ID	15 (57.7%)	11 (42.3%)	26	0.062
		MPNA	6 (30.0%)	14 (70.0%)	20	

Cosmetic Treatment				
Group	Satisfied	Unsatisfied	--	0.001
ID	25 (45.45%)	30 (54.55%)	55	
MPNA	42 (76.36%)	13 (23.64%)	55	

Mean $\pm$ SD for age, size of abscess, and duration of Breast abscesses was analyzed (Table 3).

Table 3: Stratification of Mean Pain Score for Age, Size and Duration of Breast Abscesses

Different Variables	Group	Mean ± SD	N	p-Value
Age groups				
18-25 Years	ID	5.57 ± 3.390	14	0.218
	MPNA	4.13 ± 2.748	15	
26-35 Years	ID	6.40 ± 2.898	15	0.273
	MPNA	5.33 ± 2.799	21	
36-45 Years	ID	5.92 ± 2.682	26	0.159
	MPNA	4.68 ± 3.110	19	
Breast Abscess Size Groups				
Small (1-3 cm Group)	ID	7.11 ± 2.747	19	0.184
	MPNA	5.79 ± 2.778	14	
Large (4 cm to 5 cm Group)	ID	5.36 ± 2.820	36	0.160
	MPNA	4.44 ± 2.873	41	
Duration of Breast Abscess Group				
7-10 Days	ID	5.77 ± 2.984	26	0.297
	MPNA	4.85 ± 2.852	20	
11-14 Days	ID	6.14 ± 2.850	29	0.059
	MPNA	4.74 ± 2.944	35	

Stratification for the restoration of breastfeeding outcomes for age, size of abscess, and duration of Breast abscesses was mentioned (Table 4).

11-14 Days	Group	ID	18 (62.1%)	11 (37.9%)	29	0.003
		MPNA	9 (25.7%)	26 (74.3%)	35	

Stratification for Restoration of Cosmetic treatment outcome for age, size of abscess, and duration of Breast abscesses was mentioned (Table 5).

Table 5: Stratification for Age, Size and Duration of Breast Abscesses for Cosmetic Treatment

Different Variables			Cosmetic treatment		Total	p-value
			Satisfied	Unsatisfied		
Age Group						
18-25 Years	Group	ID	7 (50.0%)	7 (50.0%)	14	0.196
		MPNA	11 (73.3%)	4 (26.7%)	15	
26-35 Years	Group	ID	8 (53.3%)	7 (46.7%)	15	0.418
		MPNA	14 (66.7%)	7 (33.3%)	21	
36-45 Years	Group	ID	10 (38.5%)	16 (61.5%)	26	0.001
		MPNA	17 (89.5%)	2 (10.5%)	19	
Breast Abscesses Size Groups						
1-2 cm Group	Group	ID	11 (30.6%)	25 (69.4%)	36	0.001
		MPNA	21 (70.0%)	9 (30.0%)	30	
3-4 cm Group	Group	ID	14 (73.7%)	5 (26.3%)	19	0.467
		MPNA	21 (84.0%)	4 (16.0%)	25	
Duration of Breast Abscesses						
7-10 Days	Group	ID	11 (42.3%)	15 (57.7%)	26	0.027
		MPNA	15 (75.0%)	5 (25.0%)	20	
11-14 Days	Group	ID	14 (48.3%)	15 (51.7%)	29	0.017
		MPNA	27 (77.1%)	8 (22.9%)	35	

DISCUSSION

This study bridges a critical gap in the literature by providing a comprehensive comparison of multiple needle aspiration (MPNA) versus incision and drainage (ID) for managing small breast abscesses, focusing on pain management, restoration of breastfeeding, and cosmetic outcomes. While existing studies have independently highlighted the benefits of needle aspiration or incision and drainage, few have offered a detailed, head-to-head comparison of these outcomes, particularly in the context of multiple percutaneous procedures. One of the key contributions of our study is the nuanced analysis of postoperative pain outcomes. Although Singh *et al.*, and similar studies reported lower pain scores with needle aspiration, these works did not extensively examine the cumulative impact of multiple aspirations in reducing patient discomfort [13]. Our findings build on this by demonstrating a consistent reduction in pain scores across repeated NA sessions, emphasizing its role as a gentler, less invasive alternative to traditional surgical techniques. Furthermore, this study addresses the underexplored relationship between treatment modality and breastfeeding restoration. While Hussain *et al.*, observed higher breastfeeding resumption rates with NA compared to ID, our study contributes by quantifying this benefit specifically in the context of multiple needle aspirations, highlighting an improvement in early breastfeeding restoration to 72.7% in our cohort [14]. This evidence underscores the role of MPNA in minimizing

recovery time and surgical trauma, directly facilitating maternal-infant bonding and improved breastfeeding outcomes. Cosmetic outcomes, a major determinant of patient satisfaction, have been inconsistently reported in prior studies. Our findings, with 76.36% of MPNA patients reporting satisfaction compared to 45.45% in the ID group, not only align with Karim *et al.*, but also extend their conclusions by emphasizing the consistent aesthetic advantages offered by multiple aspirations in preserving breast tissue integrity [15]. Additionally, healing times—a critical indicator of overall recovery is often overlooked in comparative studies. While Manzoor *et al.*, reported shorter healing times with NA, our study reinforces these findings by demonstrating that the MPNA approach, when guided by ultrasound, effectively reduces recovery duration without increasing recurrence rates [16]. Voruganti *et al.*, similarly found that ultrasound-guided aspirations led to better healing outcomes, reduced scarring, and improved patient comfort compared to incision and drainage [17]. Likewise, Randhawa *et al.*, reported significantly better cosmetic outcomes, less postoperative discomfort, and higher patient satisfaction with needle aspiration than with ID [18]. Our study uniquely synthesizes insights from individual reports and meta-analyses, including Zhou *et al.*, and Bing and Jie, by contextualizing the benefits of ultrasound-guided MPNA in a clinical setting [19, 20]. This approach provides a clearer understanding of how minimally invasive techniques can be

integrated into routine practice, offering better patient outcomes compared to the traditional reliance on ID. In summary, this study fills a critical void in the literature by systematically evaluating MPNA as a comprehensive, patient-centered alternative to ID. The findings support the adoption of MPNA as a first-line treatment for small breast abscesses, particularly for patients prioritizing reduced pain, aesthetic preservation, and early breastfeeding restoration. This evidence paves the way for updated clinical guidelines and underscores the importance of minimally invasive, ultrasound-guided interventions in modern breast abscess management.

This study is limited by its relatively small sample size and single-center design, which may limit the generalizability of the findings. Additionally, the short follow-up period may not fully capture long-term recurrence rates and sustained breastfeeding outcomes. Future large-scale, multicenter randomized trials with extended follow-up are recommended to validate the long-term efficacy of MPNA and to establish standardized treatment protocols for breast abscess management.

CONCLUSIONS

The findings of this randomized controlled trial clearly demonstrate the advantages of Multiple Percutaneous Needle Aspiration (MPNA) over traditional Incision and Drainage (ID) for the treatment of breast abscesses in breastfeeding women. The MPNA group experienced significantly lower pain scores, higher rates of breastfeeding restoration, and greater cosmetic satisfaction compared to the ID group. These results suggest that MPNA, being a less invasive and more patient-friendly approach, should be considered a preferred first-line treatment for small breast abscesses in lactating women. This study underscores the importance of adopting minimally invasive techniques in clinical practice to enhance patient outcomes and satisfaction, thereby supporting quicker recovery and better overall maternal health.

Authors' Contribution

Conceptualization: AA¹

Methodology: AA¹, AA²

Formal analysis: SA

Writing and Drafting: SA, SN, AK, NA

Review and Editing: AA¹, SA, SN, AA², AK, NA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Factors Affecting Parental Satisfaction with Ponseti Treatment in Children with Clubfoot

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ABSTRACT

Clubfoot, also known as congenital talipes equinovarus (CTEV), is a common lower-limb developmental disorder. **Objectives:** To assess the factors affecting parental satisfaction with Ponseti treatment in children with clubfoot presenting at a tertiary care hospital. **Methods:** It was a cross-sectional study carried out in the Department of Orthopaedics, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan, from January 2024 to December 2024. We enrolled the 150 parents (either mother or father of children aged more than 18 years) of children diagnosed with clubfoot and who were undergoing Ponseti treatment. Parents were interviewed, and data were collected on socio-demographic factors, and their satisfaction level was assessed using a modified orthotics prosthetics user survey. Data were analysed using SPSS version 23. **Results:** The median age of the parents was 39 years, and most were female (54%). 59.3% of the parents were satisfied with the Ponseti clubfoot treatment, and 40.7% were unsatisfied. The multivariate analysis revealed female gender (AOR=17.90, 95% CI=6.05-53.29), duration of treatment ≥ 8 months (AOR=8.30, 95% CI: 2.88-23.93), being employed (AOR=8.76, 95% CI=2.65-29), primary education (AOR=5.69, 1.49-21.62), intermediate education (AOR=7.35, 1.84-29.35) and graduate level education (AOR=10.80, 95% CI=2.52-46.19) were identified as major factors for parental satisfaction for ponseti treatment in children with clubfoot. **Conclusions:** It was concluded that factors such as being a father, children with short duration of treatment, having no job and education are significantly associated with parental dissatisfaction. Therefore, appropriate educational interventions should be devised to improve treatment results and adherence rates.

INTRODUCTION

Clubfoot, also known as congenital talipes equinovarus (CTEV), is a common lower-limb developmental disorder [1, 2]. It is usually detected at the time of birth; however, although it may also be detected at an early stage of pregnancy (from the 12th week) using a transvaginal ultrasound exam or in late stages of pregnancy (from the 3rd trimester) using an abdominal ultrasound [3]. Midfoot cavus, hindfoot equinus and varus, and forefoot adduction are all characteristics of clubfoot [2]. Every year, around 174,000 babies are born with clubfoot worldwide, with

nearly 90% of them from developing countries [4]. In developing countries like Pakistan, the incidence of CTEV was reported as 6,000 to 7,000 on average per year [5]. In nearly half of all cases of clubfoot, both feet are affected, and the incidence of clubfoot is greater in boys than girls (2/3 of children with clubfoot) [6]. Clubfoot disorder is 30 times more likely among siblings of afflicted children. The probability of CTEV associated with monozygotic siblings is 33%, whereas among dizygotic twins it is just 3% [7]. The causes of clubfoot are a combination of environmental and



genetic factors [8]. If clubfoot is not treated, then it has a potentially negative impact on the quality of life of the children. It makes a child disabled with the inability to perform daily activities. This also results in familial dependence and social stigma [9]. Before 2006, there were a variety of conservative therapy options for CTEV, including surgical intervention and the Kite approach [10]. Ponseti therapy, on the other hand, has lately gained popularity in Pakistan [10]. It is an effective, conservative, and now regarded gold-standard therapy for CTEV, consisting of weeks of strict manipulation and casting. An Achilles tenotomy is done when there is inflexible equinus and all other foot abnormalities have been corrected. After that, the child has to wear a brace for 4 to 5 years [9]. The process from diagnosis to treatment is simple, but it takes a long time [11]. Parents have to bring their child to the hospital for the casting process for weeks. Then parents have to go through an intensive bracing phase until their child is four years old. This process has a potential psychological impact on the child and their parents [11]. As a result, parents should be counselled by clinic assistants or parent educators as soon as possible after being diagnosed, so that they can understand each phase of Ponseti therapy and any obstacles they may face [9]. So, it is important to assess the factors associated with the satisfaction level of parents regarding treatment so that targeted interventions may be devised. These interventions can assist parents in sticking to their treatment plans, especially during the bracing period. Although the Ponseti method is the gold standard for treating clubfoot, parental satisfaction and adherence remain critical for successful outcomes. However, there is limited local evidence exploring the factors influencing parental satisfaction with Ponseti therapy, particularly in developing country settings like Pakistan. This study aims to determine how satisfied parents are with Ponseti therapy and the factors that influence it.

METHODS

It was a cross-sectional study carried out in the Department of Orthopaedics, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan, from January 2024 to December 2024. This research was approved by the ethical review committee of JPMC with IRB reference No. F.2-82/2023-GENL/20/JPMC, and written informed consent was taken from the parents of the children before initiating data collection. The sample size of 150 subjects was estimated by taking the frequency of favourable psychological outcome as 74.5% among parents [12], absolute precision as 7% and a 95% confidence level. The study enrolled the parents (either mother or father of age more than 18 years) of children diagnosed with clubfoot and who were undergoing Ponseti treatment. The research

excluded single parents, parents with mental illness or receiving psychiatric treatment, and parents of children who had previously failed therapy. Subjects were selected using a non-probability consecutive sampling technique. Parents were interviewed and data were collected on socio-demographic factors like age, gender, duration of treatment, ethnicity, income status, employment status and education. Parents' satisfaction with either the Mitchell brace or the Steenbeek brace was assessed using the modified orthotics prosthetics user survey (OPUS) [12]. Eleven items were included in the survey. The responses to each item were reported as "yes" or "no". A score of "1" was given to the "yes" response, and a score of "0" was given to the "no" response. An overall score of ≥ 8 out of 11 was deemed satisfactory, whereas a score < 8 was considered unsatisfactory. The researcher acquired all of the data himself, and the identities of the participants were coded to ensure confidentiality. Data were analyzed using SPSS version 23.0. Distribution of numeric data like age and duration of treatment was checked using the Shapiro-Wilk test, and median along with inter-quartile range were reported. Whereas, frequency and percentage were reported for categorical variables like gender, ethnicity, income status, employment status, education, survey items and overall satisfaction. Univariate logistic regression analysis was performed by taking parents' satisfaction as the dependent variable and other factors like age, duration of treatment, gender, ethnicity, income status, employment status and education as independent variables. All the independent factors which were significant in univariate analysis were moved into a single multivariate model. Multivariate logistic regression was applied. $A p < 0.050$ was considered statistically significant.

RESULTS

In a total of 150 participants, the median age was 39.00 (29.00-51.25) years. There were 81 (54.0%) participants who were female. The median duration of Ponseti treatment of children was 9 (9-10) months. The monthly income of 74 (49.3%) participants was $< 20,000$ PKR. The employment status of 53 (35.3%) participants was unemployed. The educational status of 9 (6.0%) participants was illiterate. Details about the baseline characteristics of study participants are shown in table 1.

Table 1: Baseline Characteristics of Parents (n=150)

Variables		Frequency (%)
Age of Parents (Years)	<40	76 (50.7%)
	≥ 40	74 (49.3%)
Gender	Male	69 (46.0%)
	Female	81 (54.0%)
Ethnicity	Urdu Speaking	16 (10.7%)
	Sindhi	31 (20.7%)

	Punjabi	44 (29.3%)
	Pathan	43 (28.7%)
	Baloch	16 (10.7%)
Monthly Income	<20,000 PKR	74 (49.3%)
	20,000-50,000 PKR	57 (38.0%)
	>50,000 PKR	19 (12.7%)
Employment Status	Employed	97 (64.7%)
	Unemployed	53 (35.3%)
Education	Primary	29 (19.3%)
	Matric	46 (30.7%)
	Intermediate	27 (18.0%)
	Graduate	29 (19.3%)
	Post Graduate	10 (6.7%)
	Illiterate	9 (6.0%)

There were 140 (93.3%) parents who agreed that braces were easy to put on, 127 (84.7%) agreed that the braces were durable, and 119 (79.3%) agreed that the skin was free of abrasions and irritations. The response to the questions agreed upon by the parents is shown in figure 1.

Overall, there were 89 (59.3%) parents who were satisfied with the Ponseti treatment of clubfoot. In univariate logistic regression, factors associated with parental satisfaction were tested. Factors such as age<40 years (OR=2.16, 95% CI: 1.12-4.21), female gender (OR=11.95, 95% CI=5.45-26.19), duration of treatment≥8 months (OR=5.319, 95% CI: 2.60-10.87), family monthly income of 20,000-50,000 (OR=2.85, 95% CI=1.36-5.69), being employed (OR=2.77, 95% CI: 1.39-5.54), being graduate (OR=11.47, 95% CI=0.57-228.53) were significantly associated with satisfaction of parents. In multivariate analysis, female gender (AOR=15.99, 95% CI=5.32-48.08), duration of treatment≥8 months (AOR=7.10, 95% CI: 2.51-20.13), and being employed (AOR=8.51, 95% CI: 1.71-33.09, p=0.008) were identified as major factors for parental satisfaction for ponseti treatment in children with clubfoot, as shown in table 2.

Table 2: Univariate and Multivariate Analysis for Parental Satisfaction of Children with Clubfoot

Variables	Satisfaction		Univariate Analysis			Multivariate Analysis		
	No (%)	Yes (%)	OR	95% CI	p-Value	AOR	95% CI	p-Value
Age in Years								
<40 Years	24 (39.3%)	52 (58.4%)	2.16	1.12-4.21	0.023	1.64	0.56-4.86	0.366
≥40 Years	37 (60.7%)	37 (41.6%)	Reference					
Gender								
Male	48 (78.7%)	21 (23.6%)	Reference					
Female	13 (21.3%)	68 (76.4%)	11.95	5.45-26.19	0.001	15.99	5.32-48.08	<0.001
Duration of Treatment (Months)								
<8	37 (60.7%)	20 (22.5%)	Reference					
≥8	24 (39.3%)	69 (77.5%)	5.319	2.60-10.87	0.001	7.10	2.51-20.13	<0.001
Ethnicity								
Urdu Speaking	9 (14.8%)	7 (7.9%)	Reference					
Sindhi	11 (18.0%)	20 (22.5%)	2.34	0.68-8.01	0.177	-	-	-
Punjabi	15 (24.6%)	29 (32.6%)	2.49	0.77-7.99	0.127	-	-	-
Pathan	18 (29.5%)	25 (28.1%)	1.79	0.56-5.68	0.327	-	-	-
Baloch	8 (13.1%)	8 (9.0%)	1.29	0.32-5.16	0.723	-	-	-
Monthly Income (PKR)								
<20,000	39 (63.9%)	35 (39.3%)	Reference					
20,000-50,000	16 (26.2%)	41 (46.1%)	2.85	1.36-5.96	0.005	1.53	0.43-5.50	0.511
>50,000	6 (9.8%)	13 (14.6%)	2.41	0.82-7.03	0.106	0.76	0.14-4.09	0.749
Employment status								
Unemployed	30 (49.2%)	23 (25.8%)	Reference					
Employed	31 (50.8%)	66 (74.2%)	2.77	1.39-5.54	0.004	8.51	1.71-33.09	0.008



Figure 1: Frequency Distribution of Satisfaction Level of Parents

Education								
Illiterate	7(11.5%)	2(2.2%)	1					
Primary	7(11.5%)	22(24.7%)	11	1.842-65.67	0.009	10.03	0.52-191.78	0.126
Matric	31(50.8%)	15(16.9%)	1.69	0.31-9.16	0.541	1.76	0.10-31.12	0.699
Intermediate	8(13.1%)	19(21.3)	8.31	1.41-49.06	0.019	10.48	0.52-211.39	0.125
Graduate	5(8.2%)	24(27.0%)	16.8	2.65-106.13	0.003	11.47	0.58-228.53	0.110
Post Graduate	3(4.9%)	7(7.9%)	8.17	1.03-64.94	0.047	3.10	0.08-124.80	0.549

DISCUSSION

CTEV is a congenital condition which, if not treated, raises the likelihood of impairment and misery as the patients grow older [10, 13]. Ponseti treatment is a conservative technique for treating CTEV, which was previously managed by physiotherapy, strapping and invasive surgical procedures [14]. Ponseti treatment is a very effective initial treatment for idiopathic clubfoot, however, good post-corrective management is essential for its success [15]. However, during treatment, parents of the affected child are likely to experience a variety of challenges, anxiety and ambiguities [12, 16]. If the treating doctor fails to identify and address these problems and concerns, the parents may quit therapy at any time [17]. Therefore, it is crucial that parents of the affected child should be satisfied with Ponseti treatment because it has been claimed that the actual challenge of this treatment is not the manipulation and casting, but rather the long-term abduction bracing that is agreeable to both the child and the family [16, 17]. Hence, this research highlights the important factors associated with parental satisfaction regarding Ponseti treatment. In our study, 59.3% of the parents were satisfied with the Ponseti treatment. Wherein, the highest satisfaction was observed for easiness of braces (93%) and the durability of the braces (85%), respectively. In the study by Mazelan *et al.*, about 44% of the parents were completely satisfied and 37% were fairly satisfied with the treatment. [18] Evans *et al.*, found that even with the family issues, problems with foot abduction brace and other problems associated with Ponseti treatment, 93% of the parents were satisfied with the treatment [19]. Rasheed *et al.*, found that 83% of the parents did not want to quit the treatment at any point in time because they were satisfied with the Ponseti treatment. He also discovered that parents were satisfied with the time of treatment completion, but had difficulty with the casting phase [11]. Hence, to improve outcomes, good physician-patient communication is required, in which they can exchange information and clarify problems so that caregivers become more confident, knowledgeable, and satisfied, and have a positive belief in their treatment and are more likely to adhere to it. The median age of the parents was 39 years, with the majority of them being under 40 years old. This indicates that the bulk of the parents were in their productive age. In a study by Esan *et al.*, about 62% of the parents were in their productive age, with a mean age of 31 years [20]. This suggests that the role of parents as

caregivers, particularly mothers, may interfere with efficiency at work, which leads to a reduction in productivity with a significant impact on the economic status of the family. The unique aspect of our study was determining parental satisfaction factors. The results showed that younger parents aged <40 years were 2.16 times more likely to be satisfied with club foot treatment. It could be because young parents might have fewer treatment expectations than older parents. The results also showed that females had higher satisfaction levels in terms of treatment. The higher female satisfaction can be associated with direct contact with the doctor, more knowledge about the disease, and managing the children solely. The duration of treatment >8 months was a significant factor for parental satisfaction. It might be because of treatment adherence, getting effective results from the management, and understanding the disease. This study showed that socioeconomic status played a significant role. Parents employed and earning between 25 to 50000 rupees were more satisfied. It might be because of trusting the doctor, having less knowledge about the treatment, and getting the treatment done as soon as possible. However, some other researchers have shown contradictory results where high socioeconomic status parents were more satisfied with the treatment [21]. On the other hand, a study found that socio-economic status did not alter the satisfaction of parents [22].

This study relied on self-reported parental satisfaction, which may introduce response bias and limit objective assessment of treatment outcomes. Additionally, being a single-center study with a relatively limited sample size, the findings may not be generalizable to broader populations. Future multicenter longitudinal studies should incorporate objective clinical outcomes alongside parental perceptions to better evaluate long-term effectiveness of Ponseti treatment.

CONCLUSIONS

It was concluded that factors such as being a father, children with short duration of treatment, having no job and education are significantly associated with parental dissatisfaction. Therefore, appropriate educational interventions should be devised to improve treatment results and adherence rates.

Authors' Contribution

Conceptualization: SS, WB

Methodology: PA, MAM, AG, SK, MA

Formal analysis: MAM

Writing and Drafting: MAM, SS, WB

Review and Editing: PA, MAM, AG, SK, MA, SS, WB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency of Osteoporosis in Patients Presenting with Chronic Liver Disease at Tertiary Care Hospital Karachi

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ABSTRACT

Osteoporosis is a disease of low bone mass and micro-architectural deterioration of bone tissue, resulting in bone fragility and an increased risk of fractures. Because osteoporosis suddenly manifests with fractures at multiple skeletal sites, most often at the spine, hip, or wrist, it is termed "silent disease". This becomes even important in CLD patients. **Objective:** To determine the frequency of osteoporosis in patients presenting with chronic liver disease (CLD) at Al Tibri Medical College and Hospital, Karachi. **Methods:** A Total of 120 CLD patients of either gender were included. Data like age, gender, residence, and duration of CLD were recorded and followed by a study of bone mineral density (BMD) in the distal forearm of the non-dominant hand using dual-energy X-ray absorptiometry (DEXA). If BMD <-2.5 SD, then osteoporosis was positive. SPSS version 23.0 was used for analysis. Descriptive statistics were calculated. Effect modification was controlled through Chi-square. p -value <0.050 was considered significant. **Results:** The mean age was 39.49 ± 8.12 years. Mean CLD duration was 5.93 ± 2.29 years. Male were 68.3%. A total of 31.7% of patients with CLD had a BMD score <-2.5 SD and were observed as osteoporosis. The frequency of osteoporosis decreased with increasing age, but not statistically significant. Numerically, male was more affected than female, however, with an insignificant association. The duration of CLD was an effect modifier insignificantly. **Conclusion:** Almost every third patient of CLD has osteoporosis. The current study recommends screening of all such patients.

INTRODUCTION

The process involving both destruction and/or regeneration of hepatic parenchyma that often leads to cirrhosis or fibrosis is known as CLD (Chronic Liver Disease) [1]. Compensated CLD often goes undetected for prolonged periods; thus, the incumbent complications, like skeletal problems, are also often detected [2]. Reduced bone mineral density, as an extrahepatic complication, reported in CLD cases, is well established [3]. In cases with advanced CLD, the bony destruction is called HO (hepatic osteodystrophy), which involves osteoporosis and

osteomalacia [4]. Among the two features, in osteoporosis, reduced levels and quality of bone mass are observed, which raises the risk for fragile bones leading to fractures [5]. Low mass of bone is associated with osteoporosis in addition to malformed micro-architecture and weakened structure of bone. Since the liver's involvement in various metabolic pathways is central, any disease of the liver leads to secondary osteoporosis. Nearly 30% of cases having CLD are reported to experience osteoporosis [6]. Nonetheless, the exact cause of loss of



bone in CLD is multifactorial and not yet fully understood [7]. The link between CLD and osteoporosis is thought to be due to resorption of bone and reduction in the formation of bone [8]. The decreased mass of bone, coupled with loss of strength, causes a fragile fracture resulting in substantial effects on quality of life and morbidity [9]. Osteoporosis is diagnosed by assessing the bone mineral density via T-score below -2.5 [10]. In cases with more than one fracture and those meeting densitometry criteria are termed as established or severe osteoporosis [11]. CLD's prevalence varies in-between 12% and 70% [12]. The causative agent behind CLD leading to osteoporosis is estimated to be viral hepatitis B in 10 % of cases, hepatitis C in 50 % of cases, alcoholic liver steatosis in about 30% of cases, while self-immune disease in around 12 to 55% of cases [13]. In cases with chronic cholestasis, around 37% of females were reported to have a T-score below -2.5 for osteoporosis, coupled with an incidence of fractures around 20.8 % in a research [14]. Osteoporosis is more common in female (30 to 50%) than in male (15 to 30%). The main reason behind this inclination is post-menopause and age >70 years, CLD and chronic therapy with glucocorticoids are known to be the most common causes of osteoporosis [15]. Post-liver transplant, osteoporosis is regarded to be the only remaining complication, persisting for years [16]. Since CLD and osteoporosis are linked together, osteoporosis is often overlooked in cases without cirrhosis [17]. In osteoporosis, the bones become porous, resulting in an increased risk of fractures. These fractures were associated with bone loss due to low osteocalcin levels in patients with chronic liver diseases [18]. Bone loss in liver disease causes vitamin D deficiency. Because osteoporosis suddenly manifests with fractures at multiple skeletal sites, most often at the spine, hip, or wrist, it is termed "silent disease" [19]. This becomes even important in CLD patients, most of whom are nutritionally deficient on hand and have decreased mobility on the other hand [20]. CLD is a quite common chronic disorder in which people have to live with it till it takes their lives. But living a good quality of life is their basic right. This right is deteriorating due to complications like osteoporosis. It is mandatory to identify these complications at the earliest and properly manage them using specific therapies. Limited availability of literature in the local context in Pakistan provided a strong rationale for this study. This study aims to assess the magnitude of the burden of hepatic osteodystrophic changes in CLD.

METHODS

An observational cross-sectional analytical study was carried out on the outpatients in the Department of Medicine, Al Tibri Medical College and Hospital, Karachi, from June to December 2024. Ethical Approval Letter was

taken with reference No: IERC/ATMC/14(01-2024)/49. The sample size was calculated with the help of the WHO sample size calculator. Keeping the following parameters, the sample size came out to be 120: Expected Proportion (p): 32% (based on prior studies of osteoporosis in CLD patients), Confidence Level: 95% ($Z=1.96$), Margin of Error (d): $\pm 8.5\%$ and Calculated Sample Size: 116 $\rightarrow$ rounded to 120. A total of 120 patients of both genders aged 25 to 50 years diagnosed with Chronic liver disease were included. The reason behind including patients between 25 to 50 years of age was to reduce confounding variables, as post-menopausal bone loss in females and age-related hypogonadism in males are independent risk factors for osteoporosis. Moreover, the period of ages included represents young to middle-aged patients, where peak bone mass is observed. Therefore, any reduction in BMD in this age range might reflect a pathological process. Patients with malabsorption syndrome, on vitamin D supplements, less sun exposure due to chronic use of veils by housewives, postmenopausal women, patients with child pugh score <5/15, chronic myeloid leukemia or multiple myeloma and liver transplantation, history of metabolic bone disorder prior diagnosis of CLD, hyperparathyroidism, hypoparathyroidism, chronic renal failure and patient taking steroids therapy >3 months for other chronic diseases, anorexia nervosa were excluded. Informed consent was obtained from all patients. For the selection of the sample, non-probability consecutive sampling was used. Patients were considered to have CLD if they had widespread fibrosis and regenerating nodules on liver biopsy, and based on laboratory, clinical and radiological testing. For Osteoporosis, all patients were assessed with dual-energy X-ray absorptiometry (DEXA scan of the distal forearm of the non-dominant hand) for bone mineral density. Osteoporosis was defined based on Bone Mineral Density (BMD) measurements obtained through a dual-energy X-ray absorptiometry (DEXA) scan. According to the World Health Organization (WHO), a person is considered to have normal BMD if the T-score is greater than or equal to -1.0. A T-score between -1.0 and -2.5 is classified as osteopenia, indicating low bone mass. Osteoporosis is diagnosed when the T-score is equal to or less than -2.5. If the T-score be re is -2.5 or lower and the individual has experienced one or more fragility fractures, the condition is classified as severe or established osteoporosis. Data collection was started with permission from the Ethical Committee of Dow University of Health Sciences and the Civil Hospital Karachi. Data were taken on a pre-determined and approved proforma. This included demographic variables like name, age, gender, residence (rural or urban), and duration of CLD. It was followed by a study of bone mineral density (BMD) in the distal forearm of the non-dominant hand using dual-energy X-ray

absorptiometry (DEXA). The presence of osteoporosis was recorded. The current study used SPSS version 23.0 for data analysis. Descriptive statistics were computed. Mean $\pm$ SD was calculated for quantitative variables like age, duration of CLD and bone mineral density (BMD). Frequency and percentage were calculated for qualitative variables, i.e. gender, residence (rural or urban), and osteoporosis (outcome variable). Stratification of age, gender, and duration of CLD was done to evaluate the effect of these modifiers on the outcome variable. It was followed by the application of the chi-Square test to see the association of outcomes with effect modifiers. A p-value ≤ 0.050 was taken as significant. Selection criteria were strictly followed to control for the confounders.

RESULTS

Average age of patients was 39.49 ± 8.12 years, with range of 25–50 years. Mean duration of CLD was 5.93 ± 2.29 years. Age and duration of disease were stratified in groups. The overall descriptive statistics of age and duration and also according to stratified groups are presented table 1.

Table 1: Descriptive Statistics of Age and Duration of Disease (n=120)

Variables		Mean $\pm$ SD	Median	Minimum	Maximum	Range
Age	Overall	39.49 $\pm$ 8.12	42.0	25.0	50.0	25.0
	25-35 Years	29.62 $\pm$ 2.70	30.0	25.0	34.0	9.0
	36-45 Years	41.92 $\pm$ 2.50	42.0	37.0	45.0	8.0
	46-50 Years	48.00 $\pm$ 1.41	48.0	46.0	50.0	4.0
Duration of Disease	Overall	5.93 $\pm$ 2.29	6.0	3.0	11.0	8.0
	$\leq$ 4 Years	3.29 $\pm$ 0.46	3.0	3.0	4.0	1.0
	5-8 Years	6.22 $\pm$ 0.85	6.0	5.0	8.0	3.0
	9-12 Years	9.71 $\pm$ 0.71	10.0	9.0	11.0	2.0

It was observed that 68.3% of patients were male, and female were 31.7%. The results showed that 35.8% of patients were between 25–35 years, 31.7% of patients were of age 36–45 years, while patients of age 46–50 years were 32.5%. The stratified groups of chronic liver disease showed that less than one third of patients (i.e. 30.8%) had CLD since last 4 years, half of all patients (51.7%) had been diagnosed their CLD between 5–8 years while 17.5% were such patients whose CLD history was between 9–12 years. The results are also presented in table 2.

Table 2: Frequency Distribution of Gender, Age Groups, and Duration of Disease Groups (n=120)

Variables	Frequency (%)
Gender	Male 82 (68.3 %)
	Female 38 (31.7 %)
Age Group	25–35 Years 43 (35.8 %)
	36–45 Years 38 (31.7 %)
	46–50 Years 39 (32.5 %)
Duration of Disease	≤ 4 Years 37 (30.8 %)
	5–8 Years 62 (51.7 %)

	9–12 Years	21 (17.5 %)

As far as living area is concerned, it was found that more than three fourths (i.e. 78%) patients were belonged to urban areas while only 22% of patients were belonged to rural areas, as in figure 1.

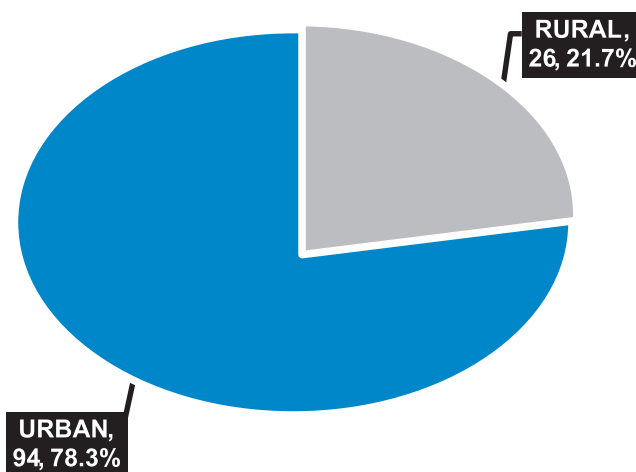


Figure 1: Percentage of Patients Belonged to the Living Area

The study observed that on DEXA scanning method of diagnosis, 31.7% patients had Bone Mineral Density (BMD) Score < -2.5 SD. Remaining 68.3% patients did not have had BMD Score < -2.5 SD, as presented in figure 2.

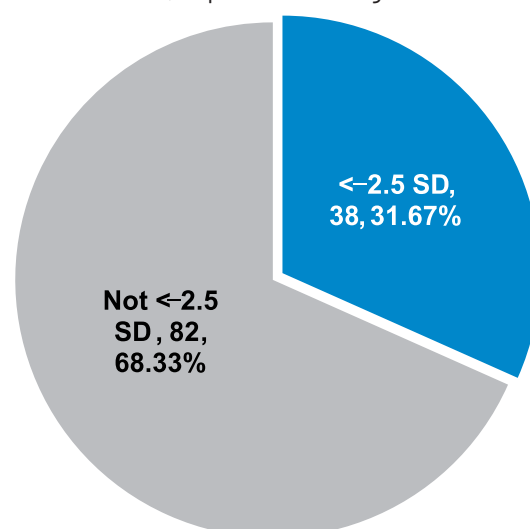


Figure 2: Percentage of Patients According to BMD Score

Thus, as per operational definition criteria used in this study, 31.7% of patients with Chronic Liver Disease had osteoporosis, as presented in figure 3.

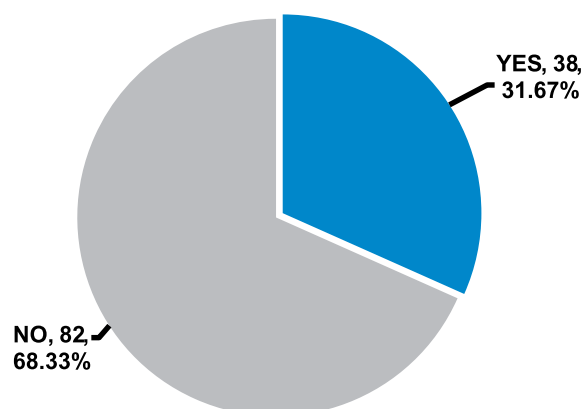


Figure 3: Percentage of Osteoporosis

Stratified analysis of gender showed that it was not significantly associated with gender (p -value=0.391); however, male group of CLD patients was more affected by osteoporosis (34.1%) than the female group (26.3%). The other stratified variable was age, and it showed that the frequency of osteoporosis slightly increased and then decreased with increasing age of CLD patients, but the result of osteoporosis was statistically insignificant (p -value=0.190). The duration of CLD was also a non-significant effect modifier, and it was noted that with increasing disease duration from up to 4 years to 9-12 years, there was more than a two-fold increase in the frequency of osteoporosis (21.6% in the former compared to 47.6% in latter category (p -value=0.122). And lastly, the residence was also insignificantly associated with CLD (p -value=0.911). The results are also presented in table 3.

Table 3: Association of Osteoporosis with Age, Gender, and Duration of Disease(n=120)

Variables		Osteoporosis		Total	p-Value	Confidence Intervals
		Yes (n=38)	No (n=82)			
Gender	Male	28 (34.1%)	54 (65.9%)	82	0.391	23.8% – 44.4%
	Female	10 (26.3%)	28 (73.7%)	38		11.8% – 41.8%
Age Group	25-35 Years	16 (37.2%)	27 (62.8%)	43	0.190	22.6% – 51.8%
	36-45 Years	14 (36.8%)	24 (63.2%)	38		21.4% – 52.2%
	46-50 Years	8 (20.5%)	31 (79.5%)	39		7.8% – 33.2%
Duration of Disease	≤4 Years	8 (21.6%)	29 (78.4%)	37	0.122	8.4% – 34.8%
	5-8 Years	20 (32.3%)	42 (67.7%)	62		20.7% – 44.0%
	9-12 Years	10 (47.6%)	11 (52.4%)	21		25.7% – 69.5%
Residence	Rural	8 (30.8%)	18 (69.2%)	26	0.911	13.1% – 48.5%
	Urban	30 (31.9%)	64 (68.1%)	94		22.4% – 41.4%

DISCUSSION

Chronic liver disease which itself is a syndrome like condition, had many direct and indirect implications and complications. One of such complications is abnormal bone metabolism caused by chronic liver disease. Due to disruption of bone metabolism, the CLD leads to very significant & detrimental effect on bone calcium deposition and remodeling. This eventually appears as brittleness of bone- the osteoporosis [21]. It was observed in the current study that the mean age of patients was

39.49 ± 8.12 years, with a range of 25-50 years. Compared to our findings, one international study reported a much higher mean age, i.e. 52.55 ± 12.34 years, of CLD patients who had osteoporosis [22]. This difference was due to the selection criteria which these studies used regarding the age of enrolled patients. This difference may also be based on the fact that in our country, chronic hepatic infections are more common even at younger ages due to contamination of syringes, blades at barber shops, vertical transmission and above all, contaminated blood transfusions [23]. The current study also noted that males were in the majority, which was more than two-thirds of all participants and also three-fourths of the total sample belonged to urban areas. This was because the study was conducted in an urban setting. But it is a fact that Hepatitis C and CLD are equally prevalent in rural areas of Pakistan, or even more than in the urban population in some areas. Then, it can be expected that these areas may be equally affected by osteoporosis [24, 25]. The main outcome variable of the study, i.e. the osteoporosis, was found to be much common. Almost one third of CLD patients, 31.7%, were diagnosed to have osteoporosis. This rate is quite high and is in line with the results of other studies. The pool of evidence suggests that the frequency of osteoporosis among CLD patients ranges from 11% to 40% [25]. Our results thus highlight the importance of the subject by replicating the available research data. The wide range of frequency of osteoporosis is thought to be due to the regional differences. The study evaluated osteoporosis in CLD patients. The DEXA scanning of the distal forearm of the non-dominant hand was done to evaluate the bone mineral density of enrolled patients. There were two categories: one having BMD below -2.5 SD, while the others did not have BMD below -2.5 SD as per operational definitions.

This study was conducted in a single urban center with a restricted age range, which may limit the generalizability of findings to rural populations and older age groups. Additionally, bone mineral density was assessed only at the distal forearm, which may not fully represent overall skeletal involvement. Future studies should include multicenter populations and assess BMD at multiple skeletal sites to better understand the burden of osteoporosis in chronic liver disease.

CONCLUSIONS

Osteoporosis is highly common among patients with chronic liver disease, as reported in this study. Many of the patients affected by this were young to middle-aged. Apart from those who are diagnosed with osteoporosis, many are at risk of developing it if not treated prophylactically. Therefore, the current study recommends screening of all such patients. Their Bone mineral density should be evaluated thoroughly, and to treated for those found to have overt osteoporosis in addition to those who have osteopenia.

Authors' Contribution

Conceptualization: HZ

Methodology: HZ, BN, HA

Formal analysis: HK

Writing and Drafting: WM, AM, AK

Review and Editing: WM, AM, AK

All authors approved the final manuscript and take responsibility for the integrity of the work

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Original Article


Comparing the Learning Experience of Student LED CBL (S-CBL) and Instructor Led CBL (I-CBL) in BDS Clinical Years

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ABSTRACT

Literature suggests that in instructor led CBL, where clinical cases are delivered by the facilitators, student's ability to view the authentic context of oral diseases from multiple sources of real world is hampered. **Objective:** To compare the level of satisfaction regarding instructor led CBL (I-CBL) and student led CBL (S-CBL) of dental students in their clinical years and the test exam score of dental students gone through instructor led CBL (I-CBL) and student led CBL (S-CBL). **Methods:** Comparative cross-sectional study was carried out at Bahria Dental College Karachi for 1 year after approval of synopsis. Non-probability Sampling Technique was used for sample collection. Inclusion criteria included dental students in five clinical rotations for two months and students who provided consent to participate in study. Data were analyzed using SPSS version 25.0 and chi square test was applied. **Results:** Among total subjects 22% were females and 78% were males. Both S-CBL and I-CBL received high ratings for satisfactory sessions, but S-CBL participants (69%) experience was slightly higher, that indicated a preference for the student-led approach. Prioritized teaching method using it was recommended by 65% of the students, especially in clinical years of dentistry. **Conclusions:** It also brought students and faculty together to create a healthy communication flow. A strong preference for CBL as a better learning strategy especially for clinical knowledge was found among many dental institutions by dental undergraduates. PBL was also recommended by many students in problem solving, communication skills and sharpening critical thinking.

INTRODUCTION

Small Group Teaching (SGT) is an educational session for students with a facilitator to guide. It is well established in higher education as commonly used teaching method for undergraduate medical and dental students [1]. SGT is characterized by student involvement in the discussion, sharing of ideas and reflects upon their practice. However, it is one of the most challenging and highly skilled teaching technique which needs to be planned and organized carefully [2]. Looking at literature, small group teaching approaches were developed, evaluated and modified to use

in health profession education curricula considering the needs of students and handy resources. The chart topping pure SGT methods that are based on active learning and authentic clinical scenarios evidence were problem based learning (PBL) and Case Based Learning (CBL) [3, 4]. However, researchers revealed numerous drawbacks and issues related to PBL [5-7]. Wang et al., evaluated the effectiveness of integrating problem-based learning with a flipped classroom model to enhance ophthalmic clinical skill training. [8]. Owing to the above mentioned fact, CBL is

one of the most commonly used vigorous learning approaches in recent times. Introduced as a student centered and ground breaking strategy, it works on the principles of constructivism theory as it helps the learners to actively participate in learning using their background knowledge to resolve the problems and challenges. It also prompt students to formulate their own questions, allow multiple interpretations and expressions of learning and encourage group work and the use of peers as resources that results in collaborative learning [9]. Keeping in view the above stated principles of constructivism theory, CBL approaches usually focus on using varieties of medical and clinical cases to teach students regarding real patient care circumstances. In this approach, the teachers play role as a guide to the students to instrument their acquired information based in making conclusions on real life cases that they may face in practice [10, 11]. Studies also suggest that CBL involves students in research and investigation, collaboration, creativity, communication, critical thinking, and team work [12]. Students absorb and remember material better and for longer when they are energetically involved in their own learning in an environment that is designed to inspire them [13]. There is no doubt that CBL has a lot of benefits mentioned above, but in spite of that there is multiple potential challenges which cannot be understood [14]. The first and the foremost one is the time required to develop authentic cases by teachers leading them to put in a lot of efforts for making clinical cases bank to conduct CBL [15]. On that account to avoid this arduous and time consuming activity, teachers mostly use old clinical cases without reviewing them [16]. Furthermore, students are dependent on the facilitators to develop the cases and objectives or questions to solve the cases which are developed from their own knowledge but not from the recent clinical experience [17, 18]. This hampers the ability of the students to think critically out of the box and they may not be able to relate the cases with the real clinical patients that they experience meeting at present which culminates the students, willingness and the concern to involve in energetic case debates [19]. CBL is based, in part, on vital argument and debate of the case issues and the array of the possible resolutions for the vocal students [20]. It is occasional that all the students in a case conversation will be enthusiastic to contribute and state their opinions without reluctance specifically when it comes to undergraduate students. Some of these students may contribute after a few sitting when encouraged to do so by their peers or instructor. Nevertheless, minimal or nonparticipation stays to be problematic issue that prevents fellow students from benefitting from each other's insight and instructors will be unable to evaluate progress unbiasedly [21]. In view of the above mentioned challenges of case based learning, the aim of this study is to develop an innovative approach of teaching and learning

called "student led case based learning (S-CBL)". Unlike CBL that is led by the instructors, this approach was led by and for dental students where they were asked to develop and present a clinical case in a small group of 10 students. This was foster their learning as student led CBL was perceived as more effective way of learning when delivered by a peer educator. S-CBL stimulates students need learning independently and presenters were gained confidence in leading the case based discussions and so were more engaged in their dental education. Students were exposed to real life clinical cases in OPD helped them to had a clearer picture of single disease.

Although case-based learning (CBL) is widely used in medical education, challenges such as limited student participation and reliance on instructor-led cases persist. There is short literature found on this study to foster student's active contribution, improved thinking process and helped in better retention of knowledge. This study aims to evaluate the effectiveness of student-led case-based learning (S-CBL) in improving student engagement, critical thinking, and learning outcomes among undergraduate dental students.

METHODS

Comparative cross-sectional study was carried out at Bahria Dental College Karachi for 1 year (i.e from 1-03-2023 to 28-2-2024), after getting approval from research ethics committee of BUHS Karachi (ERC-18/2023). Sample size was calculated by the following equation The following formula is used to compute the sample size for this research:

$$n = Z^2 \times p \times q / e^2$$

Where z represents the confidence interval, e is the margin of error, p is the estimated prevalence (6.6%), and q is 100 - p (93.4%). The calculated sample size was 94; however, it was increased to 100 to enhance the strength and reliability of the study [13]. Clinical posting of third and final year BDS having age range of 21 to 24 years. Non-probability Sampling Technique was used for sample collection. Inclusion criteria included dental students in five clinical rotations for two months each and students who provided consent to participate in study, While, the exclusion criteria included students who had attendance percentage less than 75% in the S-CBL sessions. Dependent variables were scores of satisfaction on I-CBL and S-CBL, and having test exams scores of each clinical rotation. Independent variables were instructor led CBL sessions and student led CBL sessions. Data collection procedure was as third year BDS 2022 (50 students) were asked to fill I-CBL questionnaire and their scores were recorded. The third year BDS students were promoted to final year BDS in January 2023 (50 students) and S-CBL sessions were conducted throughout the year. Distribution of students for S-CBL was as; in S-CBL sessions, these students were

further divided into five groups according to their roll numbers and each group was posted in its respective dental OPD's i.e. (Oral surgery, Prosthodontics, Orthodontics, Periodontology, and Operative Dentistry) for the clinical rotations of two months each. Each group comprising of 10 students in their clinical rotations were further divided into 2 groups (Group A and B) of 5 students each. According to their clinical rotations a topic from their subject was allocated to both the groups and were given a task to prepare a clinical case within 2 weeks. Once the clinical case was prepared, group A lead the case based learning session with group B in the presence of facilitator and vice versa. Training for implementation of S-CBL was guidance and support provided to the students and the faculty involved in S-CBL via training sessions, workshops and a mock conducted by the subject experts and medical educationists in the campus with principal's permission. Students satisfaction level for I-CBL and S-CBL was by the end of their professional exams in year 2023, all the students of final year BDS who has experienced S-CBL sessions were asked to fill the S-CBL questionnaire and their scores were recorded and compared with the scores obtained from I-CBL questionnaire of the same cohort in year 2022. Inal year BDS 2022 test scores were compared with test scores of final year BDS 2023, after each S-CBL session an assessment consisting of 15 one best MCQ's were conducted. Data were analyzed using excel and SPSS version 25.0. Descriptive data like age and gender of the students were presented as frequencies and percentages. The chi-square test was applied to determine association between variables. A p-value of ≤ 0.050 was taken as significant.

RESULTS

Out 100 students 22 (22%) were females and 78 (78%) were males.

Table 1: Gender of Students

Gender	Frequency (%)
Male	78 (78)
Female	22 (22)

There were 50 students from third year and then 50 were those who were promoted to final year.

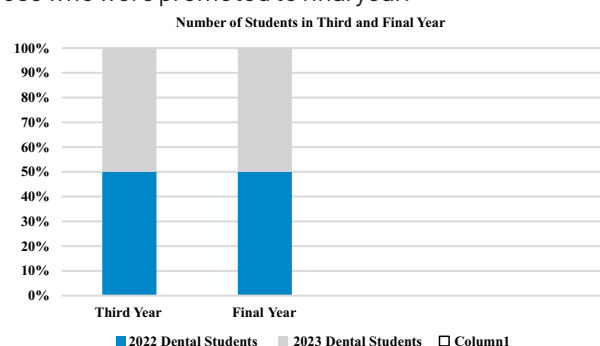


Figure 1: Number of Students in Third and Final Year

In a survey of 100 dental students, among which majority of the students 69 (69%) found out that student led CBL (S-CBL) was more interesting teaching strategy as compared to the instructor led CBL (I-CBL), and 65 (65%), were satisfied with CBL teaching strategy. Thus, CBL was recommended to include more in the curriculum. On further research, many 35% of the students suggested that PBL should be included in the pre-clinical curriculum of dentistry, while 65% of the students recommended and suggested that CBL should be included in the clinical years of the dental education. As CBL was found more efficient when used in teaching strategy in achievement of maximum levels of knowledge 52%, encouraged learning about the practical cases and scenarios 58%, reduce the amount of time needed for self-study 59%, helped in understanding the course objectives 56%, accelerated decision making potential 50%. It also helped students to manage their time accurately. On the other hand, I-CBL was found more effective in problem solving skills 62%, improving critical thinking 55%, in a way that they can achieve best learning outcomes and on improving their communication skills, as compared to S-CBL. However, I-CBL has to require more learning terms as compared to the S-CBL. While, the learning attitudes shows maximum level of knowledge (0.05) students for S-CBL as compared to I-CBL, encouraged learning for practical cases ($p=0.010$), helps in understanding course objectives (0.010) and decision potentials (p -value 0.060) that indicates non-significant association.

Table 2: Percentage Learning Terms for S-CBL and I-CBL

Learning Terms	S-CBL (%)	I-CBL (%)	p-Value
Maximum level of knowledge	52%	62%	0.050
Encouraged learning about the practical cases and scenarios	58%	55%	0.010
Reduce the amount of time needed for self-study	59%	54%	0.040
Helped in understanding the course objectives	56%	51%	0.010
Accelerated decision making potential	50%	47%	0.060

DISCUSSION

Teaching methods which were inquiry based increased the ability of learning. To enable to define their goals, set learning objectives, and actively seeking resources students direct learning puts students in driver seat. Theoretical knowledge seems connecting less likely to the practical world as CBL and PBL acts as bridges, enhancing understandings and make students ready for the real world challenges [15, 16]. As indicated in this research CBL was found more efficient in teaching strategy in achievement of maximum levels of knowledge 52%, encouraged learning about the practical cases and scenarios 58%, reduce the

amount of time needed for self-study 59%, helped in understanding the course objectives 56%, accelerated decision making potential 50%. It also helped students to manage their time accurately. CBL was preferred as more effective learning strategy shown by the results explored by the students. S-CBL was considered more beneficial than I-CBL, so CBL was recommended to incorporate into the study than in the traditional methods shown. Conceptual understanding, real world application, knowledge acquisition and discipline learning objectives were considered more significant by students with CBL than by PBL. Student's perception on comparison across many teaching institutions provided similar results for the investigated aspects. However, an interesting exception was demonstrated by Ranabir Pal et al., assessed the impact of small group teaching on student learning outcomes in community medicine [3]. Significant variations were seen in a study which showed both teaching methods in the institutions [3]. An overwhelming majority of the faculty and students shown in another work which represented proclivity for CBL over PBL as 89% and 84% respectively. For both faculty and learner, it was consistent [4]. Doctoring courses from PBL to CBL were converted in another study conducted in a medical school. A 24 items questionnaire was prepared by the students and faculty after ten months as they gained experience in both modes of instructional methods. Learning inter-professional curriculum through CBL as compared to PBL was considered more effective. Student's satisfaction was also improved in this learning style [5]. Another study was done for prosthodontics education among dental interns check the efficacy of CBL. 45 dental interns purposive sample was taken for the study. CBL effectiveness was found in the overall findings that were demonstrated [6]. Three instructional strategies as lectures, PBL, CBL were compared in a study, where CBL shown great result as traditional learning modes in interns, to enhance their performance, while its effectiveness showed a short problem based learning [3]. Study finding parallel to the traits of mentioned findings were similar with the exceptions of problem solving skills and critical thinking which makes PBL more efficient. A fact that CBL has ability to improve the diagnostic interpretations, student's critical thinking and logical thinking skills, it was all found out by Aldabbus [7]. Singh P argued in a case based learning of proponents where he mentioned that learning outcomes enhanced, attendance in class increased, positive attitude among students and faculty inculcates, ethical issues awareness, multiple perspectives recognition, relevant issues identity, objective judgement making ability, problem solving and reasoning skills, cognitive skills and positive learning environment through knowledge retention all are boosted and is superior strategy than problem based learning [8]. Aldabbus discussed the

implementation of project-based learning and highlighted the key challenges faced during its application in educational settings [7]. Perna et al., conducted a comprehensive literature survey on challenge-based learning, exploring its principles, implementation strategies, and educational impact [9]. Compared to CBL, PBL demands independent approach to learning, and has unguided inquiry approach. Developing communication skills and guided learning approach to facilitate the additional influence on learner CBL is much more supported by some studies [6, 10]. Revealed in present study that CBL is an interesting learning strategy with higher knowledge, to make understand the coarse objective much easier than PBL. Where a study done by Perna et al., where students said that PBL is more engaging technique of learning and is more stimulating as it created situational interest, and heightened more motivation in learning the objectives of the study as compared to the CBL [9]. A strong preference for PBL was also shown by the Nigerian participants. In learning process they perceived it as more reliable in fostering a deeper understanding and effective in accomplishing learning objectives [11]. Ribeiro examined the advantages and disadvantages of problem-based learning (PBL) from the teacher's perspective, highlighting both its educational value and instructional challenges [6]. Tang et al., explored the preliminary effects of challenge-based learning in enhancing multidisciplinary collaboration among nursing students in community health care settings [12]. Pu et al., investigated how critical thinking disposition influences the learning efficiency of problem-based learning in undergraduate medical education [13]. Das et al., analyzed faculty perspectives on case-based learning as a modern teaching approach aligned with current curriculum needs [14]. While in this study, training for implementation of S-CBL was guidance and support provided to the students and the faculty involved in S-CBL via training sessions, workshops and a mock conducted by the subject experts and medical educationists in the campus with principal's permission. Student's satisfaction level for I-CBL and S-CBL was by the end of their professional exams in year 2023, all the students of final year BDS who has experienced S-CBL sessions were asked to fill the S-CBL questionnaire and their scores were recorded and compared with the scores obtained from I-CBL questionnaire of the same cohort in year 2022. In this study, students led CBL for the first time was improved on developing critical thinking and increase confidence. It also brought students and faculty together to create a healthy communication flow.

This study is limited by its single-institution setting and reliance on self-reported student perceptions, which may introduce response bias. Additionally, the absence of objective academic performance measures limits the ability to fully compare the effectiveness of CBL and PBL.

Future studies incorporating multicenter designs and objective learning outcomes are recommended to validate the effectiveness of CBL and its long-term impact on clinical competence.

CONCLUSIONS

A strong preference for CBL as a better learning strategy especially for clinical knowledge was found among many dental institutions by dental undergraduates. PBL was also recommended by many students in problem solving, communication skills and sharpening critical thinking. Furthermore, future research for cross-disciplinary comparisons recommended.

Authors' Contribution

Conceptualization: FK

Methodology: FK

Formal analysis: FK, RZ

Writing and Drafting: FK, RZ, AN, TB, AZ, AK

Review and Editing: FK, RZ, AN, TB, AZ, AK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Unveiling Pelvic Organ Pathologies: A Laparoscopic Exploration of Female Infertility at a Tertiary Care Hospital

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ABSTRACT

The World Health Organization (WHO) estimates the global prevalence of infertility at 17.5% with little discrimination among regions, lifetime prevalence coming to 17.8% in high-income countries and 16.5% in low- and middle-income countries. In Pakistan, no large-scale multicenter studies have been conducted to assess the prevalence of infertility. The United Nations Population Fund (UNFPA) estimated it to be around 22% in 2003. No studies other than small-scale cross-sectional studies have been done. **Objective:** To investigate the causes of unexplained infertility in Pakistani women undergoing diagnostic laparoscopy. **Methods:** A cross-sectional study was conducted at Shalamar Medical College and Teaching Hospital from October 2023 to June 2024. All patients >18 years of age, who had a complete infertility workup (ultrasonography (USG), endocrine markers and male partner semen analysis negative or equivocal, resulting in no diagnosis, were included in this study. **Results:** Primary infertility (73%) was more frequent than secondary infertility (27%). The most common diagnoses for primary infertility were polycystic ovaries (22%) and endometriosis (16.4%). Tubal blockages (52.5%) were the most frequent tubal pathology. Laparoscopy confirmed the diagnosis of unexplained infertility and provided valuable information for treatment planning. **Conclusions:** This study suggests a high prevalence of primary infertility with delayed diagnosis in Pakistan. Traditional delays in seeking treatment and limited access to laparoscopy highlight the need for improvement in infertility care. Laparoscopy provides a panoramic and magnified view of the pelvic organs. It is a reliable tool to identify the causes of infertility that are usually missed on a non-invasive work-up.

INTRODUCTION

According to The International Glossary on Infertility and Fertility Care, 2017, infertility is a condition characterized by the failure to establish clinical pregnancy following 12 months of regular unprotected sexual intercourse or due to an impairment of a person's capacity to reproduce either as an individual or with his/her partner [1, 2]. World Health Organization (WHO) estimates the global prevalence of infertility at 17.5% with little discrimination among regions, lifetime prevalence coming to 17.8% in high-income countries and 16.5% in low- and middle-income countries [3]. In Pakistan no large-scale multicenter studies have been conducted to assess the prevalence of infertility,

United Nations Population Fund (UNFPA) estimated it around 22% in 2003, no studies other than small-scale cross-sectional studies have been done, which show that in Islamabad and Lahore prevalence of infertility is around 7% [4-6]. The causes of infertility are multi-fold; it can be because of male factor, female factor, or both [7]. Common conditions affecting the male component include azoospermia, oligozoospermia, asthenozoospermia, teratospermia and mixed pathology [7,8]. Similarly, conditions affecting the female component include anovulation, tubal factors, uterine factors, mixed pathology, polycystic ovarian syndrome, endocrine



disorders, and premature ovarian failure [7, 8]. Furthermore, unexplained infertility was identified with no apparent cause [8]. Unexplained infertility, with an incidence of 10-30%, is diagnosed when all standard infertility testing does not reveal any abnormality [9]. Standard infertility testing includes hysterosalpingography (HSG), endocrine testing including LH, FSH, progesterone, and prolactin level, and semen analysis [10]. To determine the cause of infertility in such cases, laparoscopic evaluation of pelvic organs to visualize the pathologies is considered the gold standard [11, 12]. In two studies done in India, HSG was compared with the gold standard, i.e., laparoscopy, the sensitivity came around to be 64-91% and the specificity around 81-88.9%, to diagnose tubal pathologies [13, 14]. However, laparoscopy is a far superior technique than others in diagnosing pelvic floor adhesions, endometriosis, and tubal obstruction, including peri-tubal pathologies [15]. Furthermore, laparoscopy has allowed for the development of concomitant accessory therapeutic procedures, allowing it to be the best treatment and diagnostic intervention in an infertile couple [16]. Laparoscopy is an essential step for the assessment of the pelvic region. It acts as a prelude before future surgery, providing evidence for the nature and extent of surgery [15]. Laparoscopy is a minimally invasive investigation, not routinely performed in the assessment of infertility, only advised later once primary non-invasive, directed workup has been conducted [17]. But the use of laparoscopy in the assessment of pelvic pathologies is limited in the local setting, and data for the local populace is lacking. Although the Ponseti method is the gold standard for treating clubfoot, parental satisfaction and adherence remain critical for successful outcomes. However, there is limited local evidence exploring the factors influencing parental satisfaction with Ponseti therapy, particularly in developing country settings like Pakistan. This study aims to warrant the assessment of the causes of unexplained infertility in Pakistani women undergoing diagnostic laparoscopy.

METHODS

A cross-sectional study was conducted at the Department of Bacteriology and Gynaecology of Shalamar Hospital, Lahore, after approval from the institutional review board of Shalamar Medical College and Teaching Hospital with vide # SMDC-IRB/AL/29/2023. The data of the patients who underwent laparoscopic evaluation for primary or secondary infertility from October 2023 to June 2024 were analyzed. All patients >18 years of age, who had a complete infertility workup (ultrasonography (USG), endocrine markers and male partner semen analysis negative or equivocal (having lab values within normal range), resulting in no diagnosis, were included. Informed consent was taken. All the ultra-sonographies were performed by the

same consultant to avoid personal bias, and decisions for negative scans were made on normal scans with no pelvic organic pathology and for ambiguous results, where further investigations were required, were defined as equivocal, and where pathologies were noted were declared as affected individuals and were excluded. Moreover, exclusion criteria included abnormal semen analysis of the male partner or a positive preliminary infertility workup. Patients with missing or incomplete data were also excluded. A sample size of 101 was calculated by using the World Health Organization sample size calculator with the prevalence of primary infertility at 7% (5) with a confidence interval of 95% and margin of error of 5%. After approval from the Institutional Review Board, the data were retrieved from the hospital database and registers. A structured proforma was used to collect the data, which included age, partner's age, duration of infertility, treatment taken for infertility, laboratory, hysterosalpingography (HSG), ultra-sonographic findings, and laparoscopic findings. Laboratory findings included a hormonal profile, including LH, FSH, serum prolactin and TSH levels. On laparoscopy, the size of the uterus, fibroids and adhesions were recorded. Similarly, for the ovary and tubes, normality, cysts, adhesions and masses were looked at and recorded. The data were analyzed using Statistical Package for Social Sciences (SPSS) version 25.0 and were duly compared for errors and omissions. Quantitative data as age of study participants, age of husband and duration of infertility were presented in the form of mean and standard deviations and independent sample t test was employed for the comparison, while qualitative data regarding pelvic disease like findings of the uterus, fallopian tubes, ovaries, and dye test on laparoscopy was presented as frequencies and percentages chi-square test was employed. A p-value less than 0.050 was regarded as significant.

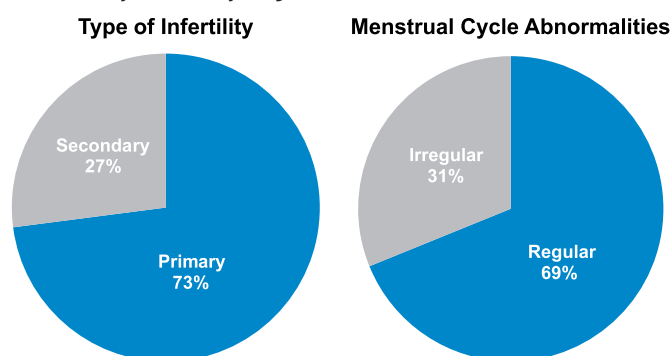
RESULTS

A total of 122 patients had diagnostic laparoscopy with a mean age of 32 ± 5.3 years. The patients were further divided into two groups based on the cause of infertility over diagnostic laparotomy findings, i.e. primary ($n=89$) and secondary ($n=33$), with no significant mean age difference (p -value 0.342) on application of the independent sample t test. Mean duration for the infertility was also compared, which was 7.13 ± 3.87 v/s 6.11 ± 2.90 years with a p -value of 0.052. Husbands' age in both study groups was compared, and it was observed that the secondary infertility group had a higher age of husbands, with a p -value of 0.027.

Table 1: Assessment of Age, Duration of Infertility and Husband's Age in Patients of Primary and Secondary Infertility Employing Independent Sample T Test

Study Parameters	Type of Infertility		p-Value
	Primary (n=89)	Secondary (n=27)	
Age	31.26 ± 5.33	34.24 ± 5.26	0.342
Duration of Infertility	7.13 ± 3.87	6.11 ± 2.90	0.052
Husband's Age	35.90 ± 4.78	39.89 ± 4.35	0.027*

Out of the patients reviewed, 84 (69%) had a regular menstrual cycle, while the remaining 38 (31%) had an irregular menstrual cycle. One hundred and twenty-two patients had undergone diagnostic laparoscopy as a part of infertility testing, and out of these patients, 89 (73%) had been diagnosed with primary infertility and 33 (27%) with secondary infertility (Figure 1).

**Figure 1:** Primary and Secondary Infertility, and Irregular Menstrual Cycles

Laparoscopic findings of the uterus revealed a bulky uterus in 18 (20.2%) and 6 (18.2%) of cases with primary infertility and secondary infertility, respectively. Adhesions were more common in patients with primary infertility, 16 (17.9%), as compared to only 4 (12.1%) in the secondary infertility group, with a p-value of 0.003. Conversely, fibroids were more common in secondary infertility cases, 9 (27.3%), compared with primary 5 (5.6%). Normal uterine findings were seen in the rest of the 64 (52.5%) cases. In terms of ovarian findings, only half, 56 (45.9%), were normal. PCOS was the most common finding, 24 (19.7%), particularly in primary infertility, 20 (22.5%). Endometriotic findings were present in 20 (16.4%) of women, more frequently in patients diagnosed with primary infertility. Most identified abnormalities in these patients were chocolate cysts 6 (6.7%) and endometriotic spots 10 (11.2%). Normal fallopian tubes were observed in 54 (44.3%) of women. Tubal adhesions were the most frequent abnormality in 24 (26.9%), exclusively seen in women with primary infertility. Other tubal pathologies included hydrosalpinx 18 (14.8%), parafimbrial cysts 6 (4.6%), and convoluted tubes 16 (13.1%). Notably, a small number of women had complete tubal blockage due to tubercles 4 (3.3%). Tubal patency testing revealed blockages in 64 (52.5%) of women. Unilateral 12

(9.8%) and bilateral blockages 52 (42.6%) were identified, with a higher prevalence of bilateral blockages 43 (48.3%) in the primary infertility group. Among the 36 patients who underwent HSG before laparoscopy, 20 (55.6%) had bilateral tubal blockages, and 4 (11.1%) had unilateral obstruction. Fisher's exact tests indicated a significant association between HSG findings and laparoscopic dye test results ($p < 0.001$) (Table 2).

Table 2: Comparison of Findings of the Uterus, Fallopian Tubes, Ovaries, and Dye Test on Laparoscopy on Application of Chi-Square Test

Study Parameters		Type of Infertility		p-Value
		Primary (n=89)	Secondary (n=27)	
Uterus on Laparoscopy	Normal	50 (56.2%)	14 (42.4%)	0.003*
	Bulky	18 (20.2%)	6 (18.2%)	
	Fibroid	5 (5.6%)	9 (27.3%)	
	Adhesions	16 (17.9%)	4 (12.1%)	
Ovaries on Laparoscopy	Normal	35 (39.3%)	21 (63.6%)	0.001
	Chocolate Cyst	6 (6.7%)	0 (0.0%)	
	PCOS	20 (22.5%)	4 (12.1%)	
	Endometriotic Spots	10 (11.2%)	4 (12.1%)	
	Tubo-Ovarian Mass	12 (13.4%)	2 (6.0%)	
	Complex Cyst	6 (6.7%)	2 (6.0%)	
Tubes on Laparoscopy	Normal	34 (38.2%)	20 (60.6%)	0.002
	Adhesions	24 (26.9%)	0 (0.0%)	
	Hydrosalpinx	12 (13.5%)	6 (18.2%)	
	Parafimbrial Cyst	4 (4.5%)	2 (33.3%)	
	Convoluted Tubes	11 (12.4%)	5 (6.1%)	
	Tubercles	4 (4.5%)	0 (0.0%)	
Dye test	Negative Spill	43 (48.3%)	9 (27.3%)	0.001
	Unilateral Positive	10 (11.2%)	2 (6.1%)	
	Bilateral Positive	36 (40.4%)	22 (66.7%)	

DISCUSSION

Infertility is becoming ever so common in the lower- and middle-income countries (LMICs), with estimates suggesting 1 in 6 women suffer from this condition [3]. Studies have further estimated that the prevalence of infertility in LMICs may be double (9–30%) that of those in the high-income countries (15%) [18]. Primary infertility in our study was almost 3 times (73%) more frequent as compared to secondary infertility (27%). This is in line with other cohorts of patients, undergoing laparoscopic evaluation for infertility in Pakistan, where the ratio of primary to secondary infertility was 2:1, with a predominance of primary infertility [19, 20]. This is in contrast to the global prevalence of primary (0.6–3.4%) and secondary infertility (8.7%–32.6%) [21]. The median age of participants with primary infertility was 31, and with secondary infertility was 35 years. Which is higher compared to other studies showing mean ages of 26–28 and 31–32 years amongst primary and secondary infertility

subgroups [19, 20]. It may be attributed to changing societal norms in regards to marriage and child rearing in the region [22]. The duration of primary and secondary infertility was 6-10 years and >10 years, respectively, before these patients underwent laparoscopy to find out a definitive cause for their infertility. The mean duration before patients underwent laparoscopy varied among different regions. In Pakistan, a study showed mean duration to be 1.95-3.7 and 2.70-7.3 years for primary and secondary infertility, respectively [19, 21]. In Egypt and India, this duration was between 4 and 6 years [23, 24]. The difference amongst the regions exists due to varying cultural factors as partial access to healthcare facilities and societal taboos, the type and the duration during which the respective studies were conducted. Diagnostic laparoscopy (DL) has been hailed as the gold standard investigation to evaluate unexplained infertility (UEI) and visualize pelvic anatomy to diagnose tuboperitoneal disease. To visualize the uterine and tubal pathologies, hysterosalpingography (HSG) has also been employed. However, it has a sensitivity of only 65%. Furthermore, a study also showed that 25% of patients with unexplained infertility, with normal HSG, had stage 3 or 4 endometriosis, mandating a laparoscopic evaluation for confirmation [25]. Amongst our findings, the most common diagnoses for primary infertility were polycystic ovaries (20) and endometriotic findings including chocolate cysts (6), endometriotic spots (10) and uterine adhesions (16). These findings are in line with the findings from another study that revealed PCO and endometriosis as the most common diagnoses amongst those undergoing DL for UEI [19, 21]. Uterine fibroids (9) were the most common diagnosis amongst those with secondary infertility. Tubal pathologies were most common amongst those with primary infertility, ranging from adhesions (27%), hydrosalpinx (13%), convoluted tubes (12%) to parafimbrial cysts (4%). Pelvic adhesions are the leading cause of tubal factor infertility. The European Society for Gynaecological Endoscopy (ESGE) has found a clear correlation between adhesions and infertility [26]. Furthermore, diagnostic laparoscopy can offer a therapeutic approach as lysis surgery can be performed simultaneously to improve chances of conception [26]. Care must be taken to perform this surgery in select cases to prevent further exacerbation of disease through iatrogenic adhesion formation. Hydrosalpinx is a pathological abnormality shape of the tubes; laparoscopic salpingotomy can be utilized in mild cases to improve fertility. Convoluted and distorted tubes are another factor for infertility, with minimal data on recommendations. Lastly, fimbrial pathologies, including cysts, resulted in the highest rate of ectopic pregnancy (22.5%) in a study done in China [26]. Our study also

revealed a positive association between the dye test performed during laparoscopy and HSG findings on tubal patency ($p < 0.001$). However, to identify the type and nature of pelvic pathology, DL is preferred to confirm the diagnosis and start definitive treatment. In Pakistan, there is a traditional delay in accessing infertility treatment, and further escalation of treatment to DL. These factors need to be addressed to improve access and compliance for diagnostic laparoscopy.

This was a single-center study with a relatively small sample size, which may limit the generalizability of findings to the wider infertile population. Additionally, selection bias may be present as only patients undergoing diagnostic laparoscopy were included, excluding those managed conservatively. Future multicenter studies with larger, more diverse populations are needed to validate these findings and optimize early diagnostic pathways for infertility.

CONCLUSIONS

It was concluded that primary infertility was more frequent, with a delayed diagnosis. Polycystic ovaries, endometriosis, and tubal blockages (adhesions, hydrosalpinx and convoluted tubes) were the most common diagnoses. Laparoscopy proved a valuable tool for diagnosis and treatment, which provides a detailed, magnified and panoramic view of the pelvic organs. It is a reliable tool to identify the causes of infertility that are usually missed on a non-invasive work-up.

Authors' Contribution

Conceptualization: SJ, ST, FUQ

Methodology: SJ, ST, FUQ, HH, IN, TNA, MZS

Formal analysis: SJ, ST, FUQ, MZS

Writing and Drafting: ST, FUQ, HH, IN, TNA, MZS

Review and Editing: SJ, ST, FUQ, HH, IN, TNA, MZS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

Antibiotic Resistance: Investigating the Prevalence of Antibiotic Resistance in *E. Coli* Infections among Patients Treated with Ciprofloxacin versus AmoxicillinSuhail Marfani¹, Nadiya Khan², Muhammad Ali Zubair³, Syed Liaquat Ali⁴, Khawar Anwar^{4*} and Ayesha Islam⁵¹Department of Medicine, Prime Health Care Group, Al-Qasimia, United Arab Emirates²Department of Pharmacology, Ameer Ud Din Medical College, Lahore, Pakistan³Department of Pharmacology, Shahida Islam Medical and Dental College, Lodhran, Pakistan⁴Department of Biochemistry, Shahida Islam Medical and Dental College, Lodhran, Pakistan⁵Department of Family Medicine, Shahida Islam Medical and Dental College, Lodhran, Pakistan

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ABSTRACT

Among all gram-negative organisms that cause bacteremia, the most frequent one is *Escherichia coli*. **Objectives:** To determine the prevalence of antibiotic resistance towards *E. coli* infections in patients treated with ciprofloxacin and amoxicillin. **Methods:** This cross-sectional descriptive study was carried out at the Shahida Islam Medical College and Hospital for six months from July 2024 to December 2024. Isolates of specimens from various samples, such as blood, urine, stool, pus of the ear and skin were included. Isolates positive for *Escherichia coli* were included, while isolates from other organisms were excluded. Antibiotic sensitivity towards Ciprofloxacin and Amoxicillin was tested. SPSS version 25.0 was used for data analysis. Chi-square test was applied for statistical analysis, keeping $p < 0.05$ as statistically significant. **Results:** The study analyzed 208 *E. coli* isolates, mostly from patients over 55 years and presenting with outpatient infections. Antibiotic resistance was significantly higher to amoxicillin (68.75%) compared to ciprofloxacin (41.35%) ($p < 0.001$). Only 9.62% of isolates were sensitive to amoxicillin, while 44.71% were sensitive to ciprofloxacin. These findings highlight a concerning prevalence of resistance, particularly against amoxicillin, among *E. coli* infections. **Conclusions:** The results of this study reported a higher prevalence of antibiotic resistance to Amoxicillin when compared with the resistance towards Ciprofloxacin. Further, multicenter studies with a greater sample size would be better able to authenticate the findings observed in this research.

INTRODUCTION

Among all gram-negative organisms that cause bacteremia, the most frequent one is *Escherichia coli* [1]. Even then, published literature regarding the prognostic factors of *E. coli* associated bloodstream infections is limited, especially the local data. In the past couple of decades, a significant increase in antibiotic resistance towards *E. coli* infections has been observed, altering the patients' outcomes having bacteremia [2]. Multi and extended drug-resistant *E. coli* are becoming increasingly challenging as their incidence is rising, and so resistance to

a broad range of Beta-lactams and other groups of anti-microbial agents as well [3]. Due to increased incidences, treatment options are becoming limited day by day, affecting *E. coli* linked infections to have a limited prognosis [4]. Adequate and prompt antibiotic therapy can affect the outcome of *E. coli* bacteremia. Due to the rising antibiotic resistance, an increase in the misuse of empirical antimicrobials can lead to a delay in the initiation of the appropriate therapy [5]. Having information about the *E. coli* bacteremia, whether empirical therapy is



adequate, and the outcomes (prognosis) is vital for establishing strategies which might improve patient prognosis of patients with *E. coli* associated bacteremia [6]. The frequency of *E. coli* urinary tract infections (UTIs) is around 75-90 % worldwide. Studies have demonstrated escalating antibiotic resistance towards *E. coli* associated bacterial infections [7]. A study from Turkey reported 17 % *E. coli* strains showing uncomplicated infections, while 38 % showed complicated *E. coli* infections towards ciprofloxacin [8]. Ciprofloxacin resistance to *E. coli* has been reported to increase from 1.8 % to 15.9 % within the last decade in research from Switzerland [9]. Local data regarding resistance to antimicrobials is limited. *E. coli* is observed to be the most frequent source of infection (86.4 %), with resistance rising to as high as 27.4 % among outpatients while 72 % amongst admitted patients [10]. Factors associated with antibiotic resistance include senility, gender, immune-compromised patients, diabetes mellitus, recurrent infections, previous therapy with quinolones, hospital-acquired infections etc [11]. Only a handful of studies have been carried out in the local populations as well as in the developed populations, which have analyzed and compared the demographic data for determining prevalence and risk factors of antibiotic resistance using ciprofloxacin and/or amoxicillin [12]. Similarly, resistance to amoxicillin has also been reported in studies. However, data regarding it is scarce. Since the most commonly used antibiotics in both outpatients and admitted patients are ciprofloxacin and amoxicillin [13]. Antimicrobial resistance (AMR) is an ongoing worldwide issue that affects both developing and developed populations. For microorganisms' survival, AMR is regarded as a natural phenomenon. It is vital to slow down the development of AMR to maintain anti-microbial usefulness [14]. As AMR decreases the efficacy of treatment, it is pivotal to consider susceptibility testing in routine care for guiding individualized patient care as well as for surveillance of AMR [15].

Despite increasing antibiotic resistance in *E. coli* infections, there is limited local data comparing resistance patterns to commonly used antibiotics like ciprofloxacin and amoxicillin. Moreover, the impact of this resistance on treatment outcomes and empirical therapy decisions remains underexplored in the local population. This study aims to determine the prevalence of antibiotic resistance towards *E. coli* infections in patients treated with ciprofloxacin and amoxicillin.

METHODS

This cross-sectional descriptive study was carried out at the Shahida Islam Medical College and Hospital for six months from July 2024 to December 2024 after ethical approval from the institutional review board committee, IRB certificate no: SIMC/ET.C/00023/24. Isolates of

specimens from various samples, such as blood, urine, stool, pus of the ear and skin were included. Isolates positive for *Escherichia coli* were included, while isolates from other organisms, such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Klebsiella pneumoniae*, etc., were excluded from the study. Prior informed consent was taken. Antibiotic sensitivity towards Ciprofloxacin and Amoxicillin of 6 mm disks (5 µg) was obtained commercial market (Oxoid Limited, Basingstoke, Hampshire, England). Sensitivity towards antibiotics on the clinical isolates was tested through Muller-Hinton medium (Oxoid Limited, Basingstoke, Hampshire, England). The incidence of AMR to *E. coli* as reported in the local study was 16%; therefore, the sample size was calculated using the open EPI online software for sample size calculation. Keeping the following values, the sample size came out to be 207 [16]. Therefore, a total of 208 specimen isolates were included in the study. Sample size (n) = $[(DEFF * Np(1-p)) / ((d^2 / Z^2 * \alpha / 2 * (N-1) + p * (1-p)))]$ (Table 1).

Table 1: Sample Size and Confidence Levels for Frequency in a Population

Variables	Percentage
Population size (for finite population correction factor or fpc) (N):	1000000
Hypothesized % frequency of outcome factor in the population (p):	16% +/- 5
Confidence limits as % of 100 (absolute +/- %) (d):	5%
Design effect (for cluster surveys- DEFF):	1
Confidence Levels	Sample Size (n)
95%	207
80%	89
90%	146
97%	254
99%	357
99.9%	582
99.99%	814

Isolated colonies of *E. coli* from agar plates were included. The broth was incubated at 37°C for 8 to 24 hours. Broth incubation was carried out according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) in preparing Mueller-Hinton broth as well as agar medium. Using a 0.5 McFarland standard for reference, bacterial culture suspension was prepared having appropriate turbidity. A sterile cotton swab was dipped and streaked in 3 directions over Mueller-Hinton agar for obtaining uniformity in growth, according to the specifications of the manufacturer. For 5 minutes, plates were dried. Disks of Ciprofloxacin and Amoxicillin 5µg were prepared using sterile forceps. Discs were then placed 15 mm from the plate's edge and less than 25 mm from each other. Incubation of plates was carried out within 15 minutes after application of disks for 24 hours at 37°C. According to standard values of NCCLS, reference ranges

used were >21 mm as sensitive, between 16 to 20 mm as intermediate resistant and 15 mm as resistant. Intermediate resistance (IR) was not termed as susceptible or sensitive organism against Ciprofloxacin and Amoxicillin. SPSS version 25.0 was used for data analysis. Numerical data (qualitative) was reported as frequency and percentages. Categorical (quantitative) data were recorded as mean and standard deviation. Chi-square test was applied for statistical analysis, keeping $p < 0.050$ as statistically significant.

RESULTS

Out of the 208 *E. coli* isolates included in the study, 98 (47.12%) were from male patients and 110 (52.88%) from female patients. The majority of the patients, 160 (76.9%), were aged over 55 years. In terms of infection type, 167 (80.29%) cases were outpatient, followed by 22 (10.58%) post-surgical infections and 19 (9.13%) nosocomial infections. Regarding co-morbidities, 108 (51.92%) patients had diabetes, 93 (44.7%) had hypertension, 32 (15.38%) had COPD, and 26 (12.5%) reported other comorbid conditions (Table 2).

Table 2: Baseline Demographics and Clinical Characteristics of Isolates Included in the Study (n=208)

Variables		Frequency (%)
Gender	Male	98 (47.12 %)
	Female	110 (52.88 %)
Age >55 Years		160 (76.9 %)
Type of Infection	Out-patient	167 (80.29 %)
	Nosocomial	19 (9.13 %)
	Post-surgical	22 (10.58 %)
Co-morbidity	Hypertension	93 (44.7 %)
	Diabetes	108 (51.92 %)
	COPD	32 (15.38 %)
	Other	26 (12.5 %)

Findings show the sources of *E. coli* isolates varied among clinical specimens, with the most common being urine samples, followed by blood, stool and pus from ear and skin specimens. This distribution reflects the high prevalence of urinary tract infections among the specimen population included in the study (Figure 1).

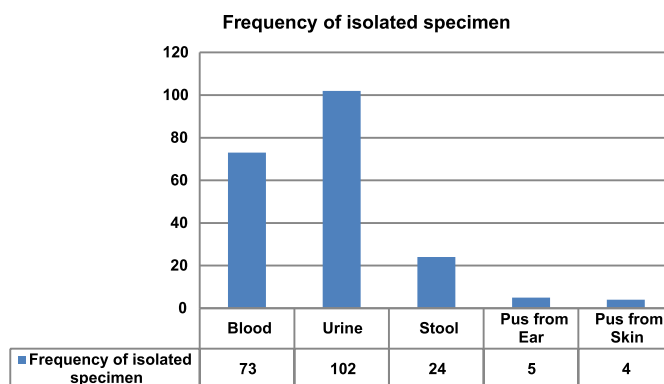


Figure 1: Route of *E. Coli* Isolated from Specimen (n=208)

Among the 208 clinical isolates tested, resistance to ciprofloxacin was observed in 86 (41.35%) isolates, while amoxicillin resistance was considerably higher at 143 (68.75%). Intermediate resistance was found in 29 (13.94%) isolates for ciprofloxacin and 45 (21.63%) for amoxicillin. Only 93 (44.71%) of the isolates were sensitive to ciprofloxacin compared to just 20 (9.62%) for amoxicillin. The difference in resistance patterns between the two antibiotics was statistically significant ($p < 0.001$), indicating a markedly higher resistance of *E. coli* to amoxicillin than ciprofloxacin (Table 3).

Table 3: Antibiotic Resistance Ratio of Various Isolates Against Ciprofloxacin versus Amoxicillin (n=208)

Clinical Isolates of <i>E. Coli</i>	Ciprofloxacin (5 ug)	Amoxicillin (5 ug)	p-Value
Resistant (R): <15 mm	86 (41.35 %)	143 (68.75 %)	<0.001
Intermediate Resistance (IR): 16-20 mm	29 (13.94 %)	45 (21.63 %)	
Sensitive (S): >21 mm	93 (44.71 %)	20 (9.62 %)	

DISCUSSION

Among the 208 specimen isolates included in the study, the prevalence of resistance to Ciprofloxacin was 86 (41.35%), while that of Amoxicillin was 143 (68.75%). Higher rates of resistance were observed in isolates to Amoxicillin as compared with Ciprofloxacin. Likewise, among the specimen isolates, sensitivity with Ciprofloxacin was reported to be higher, 93 (44.71%) in comparison to Amoxicillin, 20 (9.62%). A significant difference of < 0.001 was observed between the two antibiotics. Literature also reports similar results to the findings of this study. AMR, as reported in other research as well, shows that failure of treatment because of resistance by *E. coli* leads to higher mortality rates [17, 18]. Routine analysis of resistance development using *E. coli*, one of the most common gram-negative pathogens, was isolated in urine specimens [19]. This is in line with the published literature, where urinary tract infections have been observed as the major source of infection. Similar to the findings of our study, Ciprofloxacin has been reported to show good activity against *E. coli*,

27.02 % as compared to 44.71 % in our study [20]. In other studies, the range of Ciprofloxacin resistance by *E. coli* infections is between 10% and 40% [21]. Likewise, rising *E. coli* related infections to amoxicillin are also reported to be a major challenge to health care, with the highest reported incidence being resistant bloodstream infections [22]. However, in our study, the most common isolated specimens were urine samples, followed by blood. Since Amoxicillin is known to be the most commonly used first-line empirical antibiotic for commonly observed infections, many clinicians are in consideration of broadening the use of second and third-line antibiotics to counter resistance [23]. In line with the reported resistance to Amoxicillin (68.75%), a study reported 76 % resistance to *E. coli* associated infections [24]. In contrast, resistance to Ciprofloxacin in our study was at 41.35 % while in another research it was 54.2% [25].

This study had a relatively short follow-up period, limiting evaluation of long-term outcomes such as post-traumatic arthritis and implant-related complications. Additionally, absence of detailed radiological parameters and potential observer bias in functional scoring may affect the accuracy of outcome assessment. Future randomized controlled trials with longer follow-up and inclusion of standardized radiological and functional assessments are recommended to validate these findings.

CONCLUSIONS

The results of this study reported a higher prevalence of antibiotic resistance to Amoxicillin when compared with the resistance towards Ciprofloxacin. Further, multicenter studies with a greater sample size would be better able to authenticate the findings observed in this research.

Authors' Contribution

Conceptualization: SM

Methodology: NK

Formal analysis: MAZ, SLA

Writing and Drafting: NK, MAZ, SLA, KA, AI

Review and Editing: NK, MAZ, SLA, KA, AI

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Prevalence of Leg Ulcers in Sickle Cell Disease and Their Association with Disease Severity, Inflammatory, and Oxidative Stress Markers

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ABSTRACT

Leg ulcers are a devastating problem of sickle cell disease (SCD) and are associated with elevated inflammation and oxidative stress. Understanding their prevalence, severity, and biochemical associations is essential for improved management. **Objective:** To determine the prevalence and severity of leg ulcers in sickle cell disease and evaluate their association with oxidative and inflammatory stress markers, addressing the gap in the literature regarding biochemical correlates of ulcer development in SCD patients. **Methods:** This cross-sectional study was carried out at Gujranwala Teaching Hospital, Gujranwala Medical College. A total of 323 genetically confirmed SCD patients were enrolled. Clinical data, including leg ulcer characteristics and SCD severity, were documented. Serum levels of Tumor Necrosis Factor Alpha (TNF- α), Interleukin-6 (IL-6), Total Antioxidant Capacity (TAC), and Total Oxidative Stress (TOS) were quantified using ELISA. Statistical analysis was completed using SPSS-25. **Results:** The prevalence of leg ulcers was 30.0% (97/323; 95% CI: 25.1%–35.3%), increasing with SCD severity ($p < 0.001$). Ulcerated patients had significantly higher TNF- α (28.5 ± 5.3 vs. 19.6 ± 4.8 pg/mL; 95% CI for difference: 7.3–10.2, $p < 0.001$) and IL-6 (21.2 ± 4.7 vs. 12.9 ± 3.6 pg/mL; 95% CI: 6.9–9.6, $p < 0.001$). TOS was elevated (48.7 ± 9.5 vs. 32.3 ± 7.1 $\mu\text{mol H}_2\text{O}_2$ equiv./L; 95% CI: 13.5–18.2, $p < 0.001$), while TAC was lower (0.82 ± 0.14 vs. 1.27 ± 0.21 mmol Trolox equiv./L; 95% CI: -0.54 to -0.38 , $p < 0.001$). **Conclusions:** Leg ulcers are prevalent in SCD, particularly in patients with severe disease. SCD severity showed significant associations with inflammatory and oxidative stress markers.

INTRODUCTION

Sickle cell disease (SCD) is a collection of hemoglobinopathies categorized by existence of sickle hemoglobin (HbS). Sickle cell anemia (SCA) is the homozygous form (HbSS) of SCD [1, 2]. Hemoglobin C (HbC) inheritance alongside HbS results in hemoglobinopathy SC (HbSC) [3]. SCD manifests with systemic complications, including vaso-occlusion, stroke, pulmonary hypertension, and chronic leg ulcers (CLUs) [4]. Sickle leg ulcers (SLUs) are chronic, non-healing skin lesions. These commonly

affect the lower extremities, particularly the malleolar regions [5, 6]. SLUs typically present with superficial wounds with raised borders. Sometimes these are accompanied by serous, purulent, or bloody discharge [7]. Wound characteristics include necrotic tissue due to poor vascularization, granulation tissue associated with angiogenesis, and epithelized areas indicating partial healing [8]. The size, recurrence, and duration of ulceration vary significantly, with unclear contributing factors [9].



The pathophysiology of SLUs is multifactorial. This involves oxidative stress, vaso-occlusion, endothelial dysfunction, and chronic inflammation [10]. Neutrophils play a vital role in SCD pathology by initiating and propagating inflammatory responses and vaso-occlusive crises (VOCs) [11]. Increased neutrophil adhesion to endothelial cells leads to vascular obstruction, ischemia, and tissue damage [12]. These cells exhibit heightened activation, producing inflammatory mediators and reactive oxygen species (ROS), exacerbating oxidative stress and endothelial dysfunction [13, 14]. Excessive ROS contribute to oxidative damage in SCD, including superoxide, hydrogen peroxide, and malondialdehyde. This leads to reduced nitric oxide (NO) bioavailability, endothelial injury, and impaired wound healing [15, 16]. Imbalances between antioxidant defenses, like catalase, superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px), and ROS production create a persistent oxidative environment [17]. Dysregulated cytokine production, including elevated interleukin-10 (IL-10), myeloperoxidase (MPO), and tumor necrosis factor- α (TNF- α), further perpetuates inflammation plus tissue damage [18]. Oxidative stress has been quantified by Total Antioxidant Capacity (TAC) and Total Oxidative Status (TOS) levels. By assessing cumulative oxidant and antioxidant activity in biological fluids [19]. The oxidative stress index (OSI) and the TOS/TAC ratio provide a comprehensive measure of oxidative burden [20]. While previous studies have examined oxidative stress markers of VOCs and hemolysis, their role in SLU pathogenesis remains underexplored [18]. Despite the significant morbidity associated with SLUs, their prevalence and severity in SCD patients remain poorly characterized. Particularly with inflammatory and oxidative stress markers.

This study aims to examine the occurrence and sternness of SLUs in patients of SCD. This also assess the impact of inflammatory and oxidative stress markers on disease progression. Current study is aimed to appraise the occurrence and severity of leg ulcers in SCD patients. The study also analyze their association with inflammatory markers (MPO, IL-10, TNF- α) and oxidative stress markers (TOS, TAC, OSI).

METHODS

A cross-sectional study was designed to measure the occurrence and leg ulcers in patients having sickle cell disease (SCD). The study investigates the impact of inflammatory and oxidative stress markers. The study was conducted at Gujranwala Teaching Hospital, Gujranwala Medical College (a constituent college of UHS, Lahore) over one year from January 8, 2024, to January 7, 2025. Ethical approval was acquired from the Institutional Review Board (IRB) of Gujranwala Medical College (Approval No IRB. 23/GMC). Informed consent, in writing, was obtained from the participants or their legal guardians before enrollment.

The sample size was designed by incorporating the Open Epi software. A confidence interval of 95% was set with 80% statistical power, based on an estimated 21% occurrence of leg ulcers in SCD patients as reported in previous studies [21]. With a 5% margin of error, the final calculated sample size was 323 patients. Patients with genetically confirmed SCD were included, and time since diagnosis was recorded for all patients to assess its association with leg ulcer severity. Only patients aged 12 years and above were included, considering the increased likelihood of ulcer development in older age groups. Patients with other causes of leg ulcers (such as venous insufficiency, diabetes, or trauma) or those receiving immunosuppressive therapy were excluded. A well-structured proforma was created to gather sociodemographic and clinical data from participants of the study and from their parents/guardians, including age, gender, time since SCD diagnosis, history of blood transfusion, hospitalization, frequency of vaso-occlusive crises, and lifetime complications. These data were verified using medical records. Socioeconomic status was classified using the Oyediji method, which assesses parental education and occupation. The original five socioeconomic classes were merged into three categories: one is high (I and II), the second is middle (III), and the third is low (IV and V). The prevalence and severity of leg ulcers were assessed through clinical examination and patient history. The presence of active or healed ulcers was recorded, including location, number, size (in cm^2), depth, and presence of infection. Severity classification was based on ulcer size and healing status, with mild ulcers being $<2 \text{ cm}^2$, moderate ulcers between $2\text{--}6 \text{ cm}^2$, and severe ulcers $>6 \text{ cm}^2$ or with evidence of infection. The Helvacı *et al.*, method was used to evaluate SCD severity, incorporating acute chest syndrome (ACS), avascular necrosis (AVN), splenomegaly, hepatomegaly, hematocrit levels, total white cell count, and lifetime cumulative frequency of complications such as gallstones, meningitis, cerebrovascular disease, osteomyelitis, chronic leg ulcers, and priapism. Based on these scores, patients were categorized as having mild (score <8), moderate (8–17), or severe (>18) disease [22]. The number of inflammatory markers, including Tumor Necrosis Factor Alpha (TNF- α) and Interleukin-6 (IL-6), was determined employing enzyme-linked immunosorbent assay kits (Elabscience, Cat. No. E-EL-H0109 for TNF- α and Cat. No. E-EL-H6156 for IL-6). Every blood sample was taken at the initial presentation to the clinic and before starting any different treatments. The Total Antioxidant Capacity (TAC) and Total Oxidative Stress (TOS) were determined in serum samples. To determine TAC levels, orthodiansidine was bleached and detected at 660 and 870 nm with the Biolab[®] 310 analyzer, the results being spoken of as mmol Trolox equivalents/L. TOS levels were found from a hydrogen peroxide reference curve and reported as $\mu\text{mol H}_2\text{O}_2$ equivalents/L/L. The statistical analysis was done with SPSS version 25.0. Performances were analyzed with percentages, standard deviation and mean. An

independent t-test was performed to look for differences in continuous variables (e.g., inflammation and oxidative stress markers) between patients with and without ulcers. Pearson's correlation coefficient was chosen to assess the way ulcer severity relates to the markers found in biological fluids. A p-value<0.050 was recognized as statistically significant.

RESULTS

The incidences of leg ulcers increased with disease severity, with 48.5% of patients with severe SCD having

Table 1: Prevalence of Leg Ulcers among SCD Patients

SCD Severity	Total Patients (n=323)	Patients with Leg Ulcers (n=97)	Mild Ulcers	Moderate Ulcers	Severe Ulcers	p-value
Mild SCD (Score <8)	114 (35.3%)	18 (15.8%)	12 (66.7%)	5 (27.8%)	1 (5.5%)	<0.001
Moderate SCD (Score 8-17)	141 (43.7%)	44 (31.2%)	20 (45.5%)	15 (34.1%)	9 (20.4%)	
Severe SCD (Score >18)	68 (21%)	35 (48.5%)	9 (25.7%)	16 (45.7%)	10 (28.6%)	

Patients with leg ulcers were older, predominantly male, and had more frequent vaso-occlusive crises compared to those without ulcers. The patient's mean age with ulcers was 27.8 ± 6.5 years, significantly higher than non-ulcerated patients (22.3 ± 5.9 years, $p=0.002$). Male had an elevated prevalence of ulcers (68.0%) compared to females (32.0%, $p=0.04$). The frequency of vaso-occlusive crises (VOC) was significantly elevated in the ulcerated group (5.2 ± 1.4 episodes/year) compared to non-ulcerated patients (3.1 ± 1.2 episodes/year, $p<0.001$). Additionally, patients having leg ulcers had a high history of blood transfusions (76.3% vs. 49.6%, $p<0.001$) and more frequent hospitalizations in the past year (2.8 ± 1.1 vs. 1.5 ± 0.7 , $p<0.001$) (Table 2).

Table 2: Sociodemographic and Clinical Features of SCD Patients with and without Leg Ulcers

Patient Characteristics	Ulcerated (n=97)	Non-Ulcerated (n=226)	p-value
Vaso-Occlusive Crises (Episodes/Year)	5.2 ± 1.4	3.1 ± 1.2	<0.001#
Blood Transfusion History, n (%)	74 (76.3%)	112 (49.6%)	<0.001*
Hospitalization (Last Year)	2.8 ± 1.1	1.5 ± 0.7	<0.001#

#Data are presented as mean $\pm$ standard deviation (SD) for continuous variables (independent t-test was applied); *Data are presented as number (percentage) for categorical variables (chi-square test was applied). A statistically significant p-value was considered <0.050

Higher TNF- α and IL-6 levels indicate increased inflammation in ulcerated patients. Lower TAC and higher TOS levels suggest greater oxidative stress in patients with leg ulcers. Levels of serum of TNF- α and IL-6 were significantly elevated in ulcerated patients compared to ones who were without ulcers ($p<0.001$). In the same manner, TOS levels were significantly elevated in the ulcerated cluster, while TAC levels were lower ($p<0.001$) (Table 3).

Table 3: Inflammatory and Oxidative Stress Markers in SCD Patients with and without Leg Ulcers

Biomarkers	Ulcerated (n=97)	Non-Ulcerated (n=226)	p-value
TNF- α (pg/mL)	28.5 ± 5.3	19.6 ± 4.8	<0.001
IL-6 (pg/mL)	21.2 ± 4.7	12.9 ± 3.6	<0.001

ulcers compared to 31.2% in moderate SCD and 15.8% in mild SCD. Out of 323 enrolled SCD patients, 97 (30.0%) had active or healed leg ulcers at the time of the study. Among these, 41 (42.3%) had mild ulcers, 36 (37.1%) had moderate ulcers, and 20 (20.6%) had severe ulcers. The incidences of leg ulcers were significantly elevated in patients with severe SCD (48.5%) in comparison to those with moderate (31.2%) or mild disease (15.8%) ($p<0.001$) (Table 1).

TAC (mmol Trolox equiv./L)	0.82 ± 0.14	1.27 ± 0.21	<0.001
TOS (μ mol H ₂ O ₂ equiv./L)	48.7 ± 9.5	32.3 ± 7.1	<0.001

Data are presented as mean $\pm$ SD, and an independent t-test was applied. A p-value<0.05 was considered statistically significant.

Higher inflammatory (TNF- α , IL-6) and oxidative stress (TOS) markers correlated with increased ulcer severity, while TAC levels showed an inverse relationship. Pearson's correlation analysis depicted a strong positive correlation amongst ulcer severity and TNF- α ($r=0.72$), IL-6 ($r=0.69$), and TOS ($r=0.74$). Conversely, TAC levels correlated negatively with ulcer severity ($r=-0.67$) (Table 4).

Table 4: Correlation of Leg Ulcer Severity with Inflammatory and Oxidative Stress Markers

Parameters	r-value
TNF- α (pg/mL)	0.72
IL-6 (pg/mL)	0.69
TAC (mmol Trolox equiv./L)	-0.67
TOS (μ mol H ₂ O ₂ equiv./L)	0.74

The r-value (Pearson correlation coefficient) ranges from -1 to +1, where values nearer to +1 or -1 show stronger positive or negative correlations, respectively. A negative r-value indicates an inverse relationship.

DISCUSSION

Leg ulcers are a common yet severe complication of sickle cell disease (SCD), often connected to increased oxidative stress and inflammation. The study highlights the high occurrence of leg ulcers amongst SCD patients, particularly in those with severe disease. The overall prevalence was 30.0%, with significantly higher rates

observed in patients with severe SCD compared to moderate and mild cases. Such conclusions are in accordance with earlier research. Ultimately, representing a direct relationship between disease severity and ulcer occurrence [21-23]. Oxidative stress has been incriminated in the pathophysiology of SCD and its complications, including leg ulcers. Our findings revealed significantly elevated total TOS levels in patients with leg ulcers. These levels are presented as compared to those without ulcers. Additionally, total antioxidant capacity TAC levels were markedly lower in patients having ulcers than non-ulcerated ones. As a result, endothelial cells do not work properly and wounds take longer to heal in people with SCD [13, 24]. Inflammation is another critical factor in the pathogenesis of leg ulcers in SCD. Patients having ulcers exhibited significantly higher points of pro-inflammatory cytokines, as well as tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6), compared to non-ulcerated patients. These elevated inflammatory markers may contribute to chronic vascular inflammation, delayed healing, and ulcer recurrence, as previously reported in similar cohorts [25, 26]. The correlation analysis further reinforced these associations. Ulcer severity displayed a strong positive correlation with TNF- α , IL-6, and TOS, while TAC levels correlated negatively with ulcer severity. These results propose that systemic inflammation and oxidative stress have a crucial part in ulcer progression, necessitating targeted interventions to mitigate their effects [27-29]. Apart from biochemical markers, demographic and clinical factors also influenced ulcer prevalence. Ulcerated patients were significantly older, mostly male, and experienced more frequent vaso-occlusive crises. Additionally, history of blood transfusion and hospitalizations in the past year were significantly higher among ulcerated patients, suggesting that these clinical parameters may serve as risk factors for ulcer development [30, 31]. Given the significant role of oxidative stress and inflammation in leg ulcer pathogenesis, therapeutic strategies aimed at restoring antioxidant balance and reducing inflammatory burden should be explored. Antioxidants, such as N-acetyl cysteine and omega-3 fatty acids, have shown promise in reducing oxidative stress in SCD, but further randomized controlled trials are needed to evaluate their efficacy in ulcer prevention and treatment [32, 33].

This study had a relatively small sample size and cross-sectional design, limiting the ability to establish causal relationships between oxidative stress, inflammation, and leg ulcer development. Additionally, being conducted at a single center, the findings may not be generalizable to all SCD populations. Future research should explore interventional strategies aimed at reducing inflammation and oxidative burden to prevent or mitigate severe leg ulcers in SCD.

CONCLUSIONS

It was concluded that leg ulcers are a prevalent complication among patients with sickle cell disease (SCD), with their severity significantly associated with the underlying progression/ complication of SCD. Additionally,

oxidative stress and inflammation play a pivotal role in the development and progression of these ulcers. Elevated levels of TNF- α , IL-6, and TOS, alongside reduced TAC levels, were significantly correlated with greater ulcer severity. These findings highlight the need for routine screening of oxidative stress markers in SCD patients with leg ulcers. Patients should be advised to follow antioxidant-rich diets and avoid factors that may trigger oxidative stress.

Authors' Contribution

Conceptualization: RS

Methodology: FM, SA, FAF, RMAK

Formal analysis: MTJ

Writing and Drafting: RMAK

Review and Editing: MTJ, FM, RS, SA, FAF, RMAK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Efficacy of Suprachoroidal Triamcinolone Acetonide Injections in Resistant Diabetic Macular Edema

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ABSTRACT

Localized drug delivery through the suprachoroidal space can be used for more targeted therapies whilst minimize exposure to the healthy tissues. **Objectives:** To determine the efficacy of suprachoroidal triamcinolone injection given by the suprachoroidal route in patients with resistant diabetic macular edema. **Methods:** A quasi-experimental study was done at Al Ibrahim Eye Hospital, Karachi's Vitreo-retina Department. Duration of research was 6 months (July to December 2024)(ATMC/ERC/13(01/2023/22). Adult patients attending the vitreo-retinal OPD with resistant diabetic macular edema were included. Data were analyzed using SPSS version 22.0. Discrete variables were reported as mean and standard deviation, and continuous variables as frequencies and percentages. BCVA and CST readings at 4, 8 and 12 weeks were compared with baseline using a paired t-test, with p-value <0.050 statistically significant. **Results:** Before injection. The pre- and post SCTA BCVA and CST with baseline mean BCVA were 1.1 ± 0.30 , which progressively improved at subsequent follow-ups, reaching 0.33 ± 0.18 by the third month post-injection. **Conclusions:** SCTA injections significantly improve visual acuity and reduce central subfield thickness in patients over a three-month follow-up period. The progressive enhancement in Best Corrected Visual Acuity and consistent reduction in Central Subfield Thickness highlight the efficacy of SCTA.

INTRODUCTION

Treating diabetic macular edema involves localized or systemic immune-modulatory drugs. Localized therapies rely on corticosteroids, which are administered as topical eye drops, peri-ocular injections, intraocular or as an implant technology [1]. Using anti-VEGF (vascular endothelial growth factors) is less common because of limited efficacy and the requirement of multiple and frequent administrations as opposed to corticosteroids [2]. There are multiple ways for administering corticosteroids in the eye. Diffusion from peri-ocular sites,

direct injection into the vitreous or re-distribution via the vascular system after systemic absorption [3]. Nonetheless, some adverse events are linked with such local treatments as glaucoma and cataract [4]. The challenging task to achieve drug localization effectively when systematically administered underscores the requirement for improved local treatments having better safety profiles in the management of non-infectious uveitis, leading to secondary macular edema [5]. The space in between the sclera and the choroid, known as the



suprachoroidal space, is vital to maintain the intraocular pressure via uveoscleral outflow [6]. Under normal circumstances, the space remains collapsed; however, it can expand and so be used as a drug delivery system for targeted therapy since it is in close approximation to choroid, retina and retinal pigment epithelium [7]. Normally, this space is accessed during surgical procedures such as for drug delivery or sclerotomy, but poses a challenge for safe and consistent procedure performance [8]. Therefore, the intravitreal injection is the most common drug delivery method used [9]. Presently, micro-needles are increasingly being used for drug administration via the suprachoroidal space. Right after injecting, the drug tends to disperse around the eye, which allows gradual diffusion to the retina and retinal pigment epithelium [10]. Research has demonstrated the use of suprachoroidal space injections for administering high concentrations of drugs into the chorioretinal tissues [11]. In addition, faster clearance is observed in comparison to intra-vitreous injection when used in animals [12]. Results show triamcinolone acetonide in rabbits caused minimal drug expansion into the anterior segment and lens, only remaining confined to the choroid and retina [13]. Researchers suggest that drug delivery localization to the suprachoroidal space can be used for more targeted therapies whilst minimize exposure to the healthy tissues. Further studies are required to confirm the amount of drug required to maintain desired drug efficacy for as much as three months, highlighting the potential for the treatment of retinal or choroid diseases effectively [14].

Although corticosteroids are widely used for diabetic macular edema, conventional delivery methods are associated with limited targeting and significant adverse effects. There is limited clinical evidence on the efficacy and safety of suprachoroidal triamcinolone injections, particularly in resistant cases, highlighting the need for further evaluation. This study aims to determine the efficacy of suprachoroidal triamcinolone injection given by the suprachoroidal route in patients with resistant diabetic macular edema.

METHODS

This interventional quasi-experimental research was done at the Department of Vitreo-Retina of Al Ibrahim Eye Hospital, part of the ISRA University in Karachi (Ethical approval number- ATMC/ERC/13 (01/2023/22)). The study spanned six months (July to December 2024), utilizing a consecutive sampling. The calculation of sample size was done by the Open Epi online tool, assuming a baseline BCVA and 80% power. A total of 45 patients were included in the study. Keeping the frequency of macular edema at 7% as reported in literature, at a 95% confidence level and 5 % margin of error, the sample size came out to be 101%. This

research included adults visiting vitreo-retinal OPD who had resistant diabetic macular edema, despite having received three intra-vitreous anti-VEGF injections at one-month intervals. Exclusion criteria were set for patients with an IOP >20 mmHg, macular ischemia (as confirmed by fluorescein angiography), cataract, renal disease or ocular hypertension. Additionally, patients who had received posterior sub-Tenon triamcinolone acetonide or intravitreal triamcinolone injections within the last three months were also excluded. Informed consent was taken from each patient. Resistant diabetic macular edema was defined as macular edema in diabetic patients that did not respond effectively to a loading dose of three anti-VEGF injections given one month apart. No improvement in CMT (measured with OCT) or BCVA (measured using the Snellen chart) was considered a lack of improvement. Eligible participants were given an SCTA injection. Using an applanation tonometer, measurement of IOP at pre-injection was done. The injection process involved using a 1 cc insulin syringe using a 30-gauge needle. Triamcinolone acetonide (TA) was injected at 40 mg/ml (Kenakort A). The injection was administered via a 24-gauge IV catheter. After all aseptic measures, 0.1 ml of TA (equivalent to 4 mg) was injected into the supra-choroidal space, 3.5 mm from limbus, in either the infra-temporal or supra-temporal region. The needle was gradually withdrawn, and a cotton-tip applicator was applied to minimize reflux at the injection site. Moxifloxacin eye drops were applied to the cornea following the procedure. Patients were closely monitored for three months, with follow-up visits scheduled at 4, 8, and 12 weeks. BCVA and CST were measured and documented at each follow-up visit. Using SPSS version 22.0 for data analysis, discrete variables were tabulated as mean and standard deviation, while continuous as frequencies (%). Paired t-test was applied to test between pre-operative BCVA and CST and post-operative injections at one, two and three months, with a p-value of <0.050 statistically significant.

RESULTS

The pre- and post-SCTA BCVA and CST with baseline mean BCVA were 1.1 ± 0.30 , which progressively improved at subsequent follow-ups, reaching 0.33 ± 0.18 by the third month post-injection. Similarly, the Central Subfield Thickness (CST) showed significant reductions from a pre-injection mean of $638.78 \pm 242.62 \mu\text{m}$ to $309.65 \pm 80.14 \mu\text{m}$ at the third-month follow-up. These findings suggest marked improvements in both BCVA and CST over the observation period (Table 1).

Table 1: Pre and Post-SCTA BCVA and CST in Patients Included in the Study (n=45)

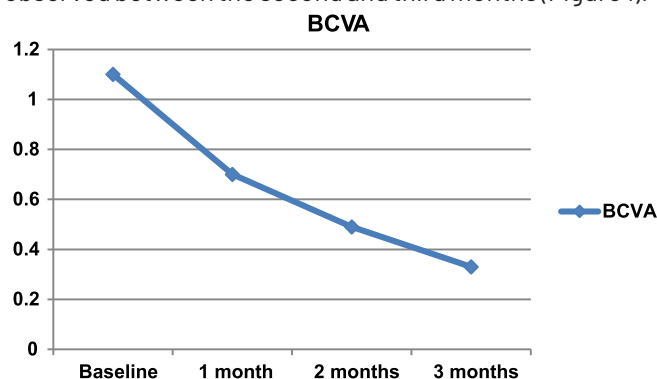
Injection Durations	Mean $\pm$ SD	
	Best Corrected Visual Acuity (95 % CI)	Central Subfield Thickness (um) (95 % CI)
Pre-Injection	1.1 $\pm$ 0.30 (0.99-1.21)	638.78 $\pm$ 242.62 (548.18-729.38)
One Month	0.7 $\pm$ 0.21 (0.62-0.78)	463.29 $\pm$ 168.22 (400.48-526.10)
Two Months	0.49 $\pm$ 0.19 (0.42-0.56)	395.88 $\pm$ 122.61 (350.10-441.66)
Three Months	0.33 $\pm$ 0.18 (0.26-0.40)	309.65 $\pm$ 80.14 (279.73-339.57)

The mean difference between BCVA and CST at Various Time Frames Pre- and Post-operatively are analyzed. There were statistically significant improvements in BCVA and CST at all post-injection time points compared to the baseline. Mean BCVA improved consistently from 1.1 $\pm$ 0.30 to 0.7 $\pm$ 0.21 at one month, 0.49 $\pm$ 0.19 at two months, and 0.33 $\pm$ 0.18 at three months ($p < 0.001$). Correspondingly, the mean CST decreased from 638.78 $\pm$ 242.62 μ m pre-operatively to 463.29 $\pm$ 168.22 μ m, 395.88 $\pm$ 122.61 μ m, and 309.65 $\pm$ 80.14 μ m at one, two, and three months, respectively ($p < 0.001$). These results confirm sustained structural and functional improvements (Table 2).

Table 2: Mean Difference between BCVA and CST at Various Time Frames Pre and Post-Operatively (n=45)

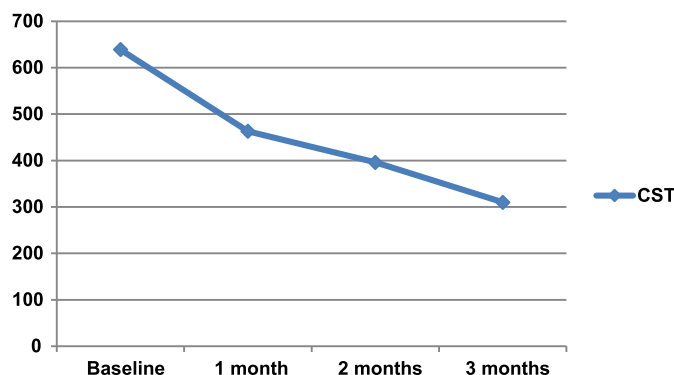
Duration of Injection	Pre-operative	Pre-operative vs. One Month	Pre-operative vs. Two Months	Pre-operative vs. Three Months	p-Value
Best Corrected Visual Acuity	1.1 $\pm$ 0.30 (0.99-1.21)	0.7 $\pm$ 0.21 (0.62-0.78)	0.49 $\pm$ 0.19 (0.42-0.56)	0.33 $\pm$ 0.18 (0.26-0.40)	<0.001
Central Subfield Thickness (um)	638.78 $\pm$ 242.62 (548.18-729.38)	463.29 $\pm$ 168.22 (400.48-526.10)	395.88 $\pm$ 122.61 (350.10-441.66)	309.65 $\pm$ 80.14 (279.73-339.57)	<0.001

The progressive improvement in BCVA following SCTA injection is depicted. The trend indicates significant functional recovery, with the most notable improvement observed between the second and third months (Figure 1).

**Figure 1:** Graphical Representation of BCVA at Baseline, One Month, Two Months and Three Months Post SCTA Injection

The CST reduction across the observation periods is observed. The marked decline in CST reflects effective control of edema, with the most substantial changes occurring within the first two months' post-injection (Figure 2).

CST

**Figure 2:** Graphical Representation of CST at Baseline, One Month, Two Months and Three-Month Post SCTA Injection

DISCUSSION

This study demonstrated that suprachoroidal injection of triamcinolone acetonide was safely evaluated for its effects on BCVA and CST over both short-term and long-term periods. Similarly, published literature has also reported findings in line with our study [15-17]. Immediately post-suprachoroidal triamcinolone acetonide injection (SCTA), a decrease in both BCVA and CST was observed. Likewise, another study by Jamil et al reported that the mean change in CST after a month of SCTA was 593.62 $\pm$ 116.87 μ m (baseline) and 303.55 $\pm$ 31.29 μ m, respectively ($p < 0.001$). Similarly, BCVA before and after one month was significantly lower, i.e. 0.81 $\pm$ 0.16 and 0.45 $\pm$ 0.03, respectively ($p < 0.001$). The study concluded that SCTA is useful in the management of CST and BCVA [18]. Similar to the findings of our study, another study by Nawar, reported that CST reduced significantly from 478.7 $\pm$ 170.2 μ m pre-injection to 230.2 $\pm$ 47 μ m 12 months after SCTA ($p < 0.001$). BCVA improved from 1.193 $\pm$ 0.2 to 0.76 $\pm$ 0.3 after 12 months of SCTA ($p < 0.001$) [19]. Akhlaq et al., in yet another research carried out to determine the efficacy of SCTA in patients of refractory diabetic macular edema reported it to be a safe and effective treatment modality as it decreased CST and improved BCVA [20]. However, research has reported that the risk of significant IOP, CST and BCVA elevation can be substantial in patients receiving suprachoroidal triamcinolone acetonide, especially in those with pre-existing risk factors such as a history of glaucoma or steroid-induced elevation. The timing of this elevation can vary, but it is generally observed within the first few months after injection [21]. Overall, the evidence suggests that while there is a notable short-term increase in IOP following suprachoroidal triamcinolone acetonide injection, this effect is generally transient, with IOP stabilizing back to baseline levels within a few months. This pattern highlights the importance of monitoring IOP in patients receiving this treatment, particularly in the short term.

This study was limited by a relatively small sample size and lack of a control group, which may affect the strength and comparability of the findings. Additionally, longer-term safety outcomes, particularly regarding intraocular pressure changes, were not extensively evaluated. Future large-scale randomized controlled trials with extended follow-up are needed to better assess long-term efficacy and safety of suprachoroidal triamcinolone acetonide.

CONCLUSIONS

The study findings demonstrate that SCTA injections significantly improve visual acuity and reduce CST over a three-month follow-up period. The progressive enhancement in BCVA and consistent reduction in CST highlight the efficacy of SCTA as a therapeutic intervention for the management of retinal conditions associated with edema. More studies are recommended to evaluate long-term outcomes and optimize treatment protocols.

Authors' Contribution

Conceptualization: VK

Methodology: VK, UH

Formal analysis: VK

Writing and Drafting: NAM, UK, SHS, AQ

Review and Editing: VK, NAM, UH, UK, SHS, AQ

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Determination of Mean Blood Loss with Tranexamic Acid in Patients Undergoing Total Knee Arthroplasty

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ABSTRACT

Orthopedic surgeons routinely perform total knee arthroplasty (TKA). The use of antifibrinolytic therapy is one of the strategies to manage perioperative bleeding. TXA works by occupying the lysine-binding sites on plasminogen, thereby hindering its attachment to fibrin and ultimately halting the fibrinolysis process. Blood loss during gynaecological, cardiac, and orthopedic surgeries can be effectively managed with tranexamic acid. **Objectives:** To determine the average reduction in blood loss achieved with tranexamic acid in patients undergoing total knee arthroplasty. **Methods:** This interventional study was conducted over six months, from 25-08-2020 to 25-02-2021. A total of 60 patients from the OPD of the Orthopedic Department at Mayo Hospital, Lahore, were included in the study based on selected criteria. All participants signed informed consent forms. Demographic data were recorded, and TXA was administered after the surgery. All procedures were performed under general anesthesia. **Results:** The analysis showed that the average blood loss during surgery was 255.14 ml with the use of tranexamic acid. Excessive blood loss can have detrimental effects on a patient's health. **Conclusions:** It was concluded that tranexamic acid is effective in reducing bleeding during total knee replacement. Its use may also be more cost-effective compared to managing the consequences of significant blood loss.

INTRODUCTION

In joint reforming surgery, the damaged part of the joint is surgically removed or reshaped using osteotomy or the same process is done with various surgical techniques [1]. Usually, arthroplasty is carried out by choice to relieve pain and bring back movement in a joint that was damaged by arthritis or injury [2]. For most of the past 45 years, surgeons have most commonly and successfully repaired damaged joints by replacing the joint's surface with a prosthesis [3]. An illustration is when someone has

osteoarthritis of the hip, in which the surgeon may replace both the socket of the hip (acetabulum) and the upper part of the femur (the head and neck) with prosthetics [4]. During the operation, the objectives are to remove the pain, get the patient moving again, help walking and strengthen their muscles [5]. The loss of blood in this surgery is usually between 1,000 and 1,800 mL, so a transfusion is often necessary [6, 7]. Some studies have shown that after uncomplicated total knee arthroplasty, about 10% to 38%



of patients need allogeneic transfusions [8, 9]. Blood transfusion may cause problems with breathing and heart function, disease transmission, an immune reaction and postoperative infection [10]. Administration of tranexamic acid can be given locally or intravenously at the start of surgery, and it has been found to lower the amount of blood loss and the requirement for blood transfusion in this setting [11]. The total blood loss was reduced, and blood transfusion was not required. This painless and safe use of tranexamic acid means it controls the discharge of surplus blood efficiently after knee arthroplasty [12, 13]. Using tranexamic acid can help reduce bleeding after big surgical procedures. It is usually given to patients through a vein during total joint replacement. Even though there have been studies on how safe tranexamic acid is for its antifibrinolytic effect, it still should not be used systemically [14]. During a total knee arthroplasty, it is possible to inject tranexamic acid into the joint [15]. But, not many studies have been done on how much chemo to give, its effects, and what side effects it might cause [16]. Research by Bidolegui et al., 363.4 ± 141 milliliters of drain loss was found at 24 hours when using tranexamic acid [17]. Results found by Yen et al., suggested that the menstrual blood loss was 921 milliliters after tranexamic acid use, and this statistic was significant ($p < 0.05$) [18]. Literature reports that tranexamic acid may help lessen blood loss that results from a knee replacement. Sometimes, losing lots of blood can be harmful to both health and cost to the patient. Giving tranexamic acid is generally more economical than facing the expensive results of major blood loss. Furthermore, nothing local shows proof of this happening. That's why we needed to do this study, so in the future we can add tranexamic acid to the surgical procedure to help reduce blood loss. By doing this, our care will be better, and we will make sure to update local instructions for managing total knee replacement by including tranexamic acid.

Total knee arthroplasty (TKA) is frequently associated with substantial perioperative blood loss, which may increase the need for blood transfusion and lead to postoperative complications. Although tranexamic acid (TXA) has been reported to reduce blood loss in orthopedic procedures, evidence regarding its effectiveness in the local Pakistani population remains limited. Furthermore, variations in patient characteristics and healthcare settings may affect the generalizability of international findings. Therefore, this study aimed to determine the mean blood loss in patients receiving tranexamic acid during total knee arthroplasty and to provide local evidence regarding its effectiveness in reducing perioperative bleeding.

METHODS

From August 25, 2020, to February 25, 2021, which is six months, this interventional study took place in Unit I of the

Department of Orthopedic Surgery at Mayo Hospital in Lahore. The study focused on understanding the results of total knee replacement surgery for patients. A total of sixty cases were chosen to keep the error within 1%, achieve a 95% confidence level, and show that tranexamic acid reduced bleeding by an average of 921 ± 252 milliliters. The sampling method used was non-probability consecutive sampling. The inclusion criteria were patients who were 50 to 70 years old, of either gender, having a unilateral total knee replacement as outlined by the surgery description. Among the exclusion criteria were patients who had taken part in prior unsuccessful treatments or repeatedly fractured, patients with fractures that involved the entire bone (open fractures), those with severe double fractures of the knees (comminuted fractures), and those who required bilateral knee replacements. The ethical approval letter was taken from Green International University with registration No: IRC-GIU-155-04-2025. Informed consent was signed. Basic information about patients (name, age, gender, BMI, affected anatomical site, and duration of osteoarthritis) was collected before surgery, and 10 mg/kg of TXA was administered at the end of the procedure. All patients were placed under general anesthesia during surgery, which was carried out by a single surgical team with the researcher's assistance. An area of the wound was fitted with a suction drain to help remove excess blood. Post-surgery, patients remained in the post-surgical area to be carefully monitored for the next 24 hours. The suction drain was removed within a day, and the amount of blood drained was measured as defined by the operation. All the information about the study was recorded in a preform that had been prepared beforehand. The collected data were analyzed using SPSS version 23.0 to perform statistical analysis. The average values and standard deviation (SD) for age, BMI, and duration of osteoarthritis were reported as mean ± SD. The results for the qualitative variables (such as gender and the side of the body) were presented as frequencies and percentages. The groups were categorized based on age, gender, BMI, side of the affected joint, and the duration of osteoarthritis. The results from the post-stratification independent sample t-test were considered significant if the p-value was less than or equal to 0.050.

RESULTS

Studying the age of the patients, we found that 32 individuals (53.3% of the total sample), were 50-60 years old and 28 individuals (46.7%) were aged 61-70 years and had a calculated mean age of 60.18 ± 5.52 years. Also, examining the gender of the patients showed 38 (63.3%) were male and 22 (36.7%) were female (Table 1).

Table 1: Distribution of Age, Gender, and Anatomical Side (n=60)

Gender	Frequency (%)
Age	
50-60 Years	32 (53.3%)
61-70 Years	28 (46.7%)
Total	60 (100%)
Gender	
Male	38 (63.3%)
Female	22 (36.7%)
Total	60 (100.0%)
Anatomical Side	
Right	20 (33.3%)
Left	40 (66.7%)
Total	60 (100.0%)

During total knee arthroplasty, patients receiving tranexamic acid had a mean blood loss of 255.14 ± 81.68 ml (Table 2).

Table 2: Distribution of BMI, Duration of Osteoarthritis, and Blood Loss (n=60)

Variables	Mean $\pm$ SD
BMI (kg/m ²)	25.66 ± 2.16
Duration of Osteoarthritis (months)	9.00 ± 4.23
Blood loss (ml)	255.14 ± 81.68

The data were arranged by age, gender, body mass index, affected side and disease duration (Table 3).

Table 3: Stratification for Blood Loss Concerning Age, Gender, Anatomical Side, BMI and Duration of Osteoarthritis Using Independent Sample t-test (n=60)

Blood Loss	n	Mean ± SD	SD Error Mean	p-Value
Age				
50-60 Years	32	243.22 ± 74.286	13.132	0.230
61-70 Years	28	268.76 ± 88.793	16.780	
Gender				
Male	38	254.01 ± 87.722	14.230	0.336
Female	22	257.09 ± 71.989	15.348	
Anatomical side				
Right	20	250.10 ± 66.404	14.848	0.632
Left	40	257.66 ± 89.032	14.077	
BMI				
17-25 kg/m ²	25	240.25 ± 65.768	13.154	0.236
>25 kg/m ²	35	265.77 ± 90.809	15.350	
Duration of Osteoarthritis				
<=12 Months	49	263.84 ± 85.754	12.251	0.081
>12 Months	11	216.36 ± 45.227	13.636	

DISCUSSION

Knee replacement surgery, which is also called knee arthroplasty or total knee replacement, replaces the surface of the damaged knee joint. While the procedure is being done, plastic and metal are positioned along the bone surfaces that make up the knee joint, such as the kneecap.

It's offered to someone who has serious arthritis or a major knee injury. Many forms of arthritis may cause problems in the knee. Usually, osteoarthritis occurs in adults over 40 due to losing the joint cushion, which worsens with time [19]. Synovial membrane inflammation caused by rheumatoid arthritis leads to excess fluid, pain and stiffness. A history of injury can lead to traumatic arthritis, which can damage the knee's cartilage. The objective of knee replacement surgery is to replace and cover up the parts of the knee that are damaged, and this helps relieve severe pain that other methods have not helped. Total knee replacement (TKR) is widely recognized as an effective and accepted way to treat knee osteoarthritis. It was found in the research that the age distribution of the patients put 53.3% of the patients (n=32) aged 50-60 years and 46.7% of them (n=28) aged 61-70 years. The average age was 60.18 ± 5.52 years. A greater number of males, 63.3%, were in the sample (38 participants), and fewer females, 36.7%, were in the sample (22 participants) [20]. Mean blood loss in those patients who received tranexamic acid was seen to be 255.14 ± 81.68 . Bidolegui et al., showed that the drain loss within 24 hours averaged 363.4 ± 141 ml in patients given tranexamic acid [17], while Yen et al., found it to be 921 ± 252 ml (p=0.014) [18]. In orthopedic surgeries, blood loss is commonly managed with TXA, because studies show it to help prevent and treat complications that occur while the patient is in the hospital. Numerous studies have been done to check if TXA is safe and effective for patients needing orthopedic surgery. When TXA was given peri-operatively to patients undergoing total hip arthroplasty (n=57), there was a 30% decrease in the need for transfusion when compared to a group receiving the placebo [21]. Many differences exist between developing countries and Western developed countries. In terms of age, physical appearance, how severe their condition is and their habits, patients in these two areas are different [22]. Also, when used in patients who do not do much physical activity, modern joint replacements with strong bearing surfaces may result in prolonged durability of the arthroplasty in developing countries [22]. Among a nationwide group of over 870,000 people who had elective total knee or hip arthroplasties in 510 U.S. hospitals, intravenous TXA used before or during surgery was not linked to a higher chance of any complication. Acute renal failure, dying in the hospital, heart attack, stroke and thromboembolic problems were the investigated issues. This is important because, besides demonstrating that TXA is safe in adults undergoing major orthopedic surgery, the authors also grouped patients by how much TXA was given (none, $\leq 1,000$ mg, 2,000 mg and $\geq 3,000$ mg). Studies found that TXA administration was closely linked to a significant decrease in blood transfusions, and odds ratios for this effect ranged from 0.31 to 0.38. The overall risk of

transfusion-related reactions (OR) for allogeneic transfusions was 0.29 to 0.37. Important to note, these patients had no important rise in the risk of different complications like combined complications, renal failure, admission to intensive care or the risk of thromboembolic events [23]. In the research, giving people a 2,000 mg dose of TXA was found to offer the best combination of results and safety. Nevertheless, some experts worry about the constant use of TXA in elderly patients who have surgery [24].

This study has several limitations, including a relatively small sample size, single-center setting, and the absence of a comparison or control group not receiving tranexamic acid. In addition, only short-term perioperative outcomes were assessed, limiting evaluation of long-term safety and effectiveness. Future studies should employ larger multicenter randomized controlled designs with appropriate control groups and longer follow-up periods to comprehensively assess the efficacy, safety, and cost-effectiveness of tranexamic acid in total knee arthroplasty patients.

CONCLUSIONS

It was concluded that for this study, researchers looked at how much blood the patients lost when tranexamic acid was used during total knee arthroplasty. Mean blood loss among the group using tranexamic was 255.14 ± 81.68 ml. Suffering from excessive bleeding can be very harmful to your health. Thus, we understood that tranexamic acid lessens bleeding after total knee replacement and may be more cost-effective than the problems of excessive bleeding.

Authors' Contribution

Conceptualization: MAA, SA

Methodology: MAA, HAS, SH

Formal analysis: MAA, SSS, SH

Writing and Drafting: MAA, SA, SSS, MI, HMAA

Review and Editing: MAA, SA, SSS, MI, HMAA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Volar Locking Plate and Percutaneous Pinning Using the Faisal Technique for Volar Barton Fractures

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ABSTRACT

Volar plates are employed for buttressing volar fragments in most situations, and even dorsal fragments are stabilized by this technique. K-wires are often preferred. **Objective:** To compare the frequency of excellent outcomes in volar Barton fractures of the distal radius managed with open reduction and internal fixation using volar plates versus percutaneous pinning by the Faisal technique. **Methods:** A total of 60 patients with volar Barton fractures, aged 20 to 70 years of both genders, were included. Patients with bilateral fractures, recurrent fractures on the same side, open fractures, wrist dislocations, arthritic wrists, neurovascular injury, and Chauffeur's fractures were excluded. In Group A, a volar plate was implanted. In Group B, percutaneous pinning using K-wires was performed. After 3 months, patients were evaluated for functional outcomes using the Green O'Brien Scoring System. **Results:** The mean age of patients in Group B was 42.37 ± 15.23 years, and in Group A was 42.33 ± 14.04 years. The majority of patients, 31 (51.67%), were between 20 to 45 years of age. Of the 60 patients, 47 (78.33%) were male and 13 (21.67%) were female, with a male-to-female ratio of 3.6:1. An excellent outcome was observed in 24 (80.0%) patients in Group B and 11 (36.67%) patients in Group A, with a p-value of 0.001. **Conclusion:** This study concluded that the frequency of excellent outcomes in volar Barton fractures of the distal radius was significantly higher with percutaneous pinning by the Faisal technique compared to volar plate fixation.

INTRODUCTION

Distal radius fractures are the most prevalent fractures of the forearm and account for about 16% of all skeletal fractures. They most often occur from falling onto an outstretched hand but also result from direct trauma or axially loaded forces. These fractures are classified based on the direction of radial angulation and displacement, the involvement of the joint surface (intra-articular or extra-articular), and the presence or absence of associated ulnar

or carpal bone injuries [1, 2]. Displaced fractures involving the articular surface of the distal radius generally have a worse prognosis than extra-articular fractures. This is due to the potential for incongruity and arthrosis of the radiocarpal and distal radioulnar joints, carpal subluxation, and associated intercarpal ligament injuries [3]. Among the specific types of distal radius fractures are Colles' fracture, Smith's fracture, Barton's fracture, and Chauffeur's



fracture. The latter received its name because the crank used to start early automobiles would sometimes kick back and break the chauffeur's wrist in a specific pattern. While these eponyms are still used to describe fracture patterns, there remains some confusion, particularly since "Colles' fracture" is often used as a generic term for distal radius fractures [2]. Intra-articular fractures of the distal radius represent a greater therapeutic challenge when compared with unstable extra-articular fractures [1, 2]. Most distal radius fractures, including 89.6% of AO C3-type fractures, can be successfully treated with volar locking plates [3]. Volar locking plates have recently gained widespread acceptance as the primary treatment option for this trauma. However, dorsally displaced fractures accompanied by certain conditions remain difficult to manage using a single volar locking plate [4, 5]. Although dorsal plating offers an advantage in the reduction and fixation of dorsally displaced fractures, it has fallen out of favor due to a historically higher complication rate, including extensor tendon injuries [4, 6]. Nevertheless, volar plating remains an appropriate treatment option for highly selected cases of dorsally displaced, comminuted intra-articular distal radius fractures particularly when soft tissue coverage is intact [7]. Overall, volar locking plates continue to be widely used for the osteosynthesis of distal radius fractures [8]. Clinical studies have demonstrated variable outcomes between fixation techniques. One trial reported excellent outcomes (Green and O'Brien score >90-100) in 86.67% of patients treated with percutaneous K-wires compared to 53.33% treated with volar plates for volar Barton fractures ($p = 0.0463$) [9]. Another study provided further support for Faisal's technique defined as closed reduction by dorsiflexing the wrist, reducing the fragment through ligament taxis, and applying percutaneous pinning in an anti-glide fashion showing promising results that merit further investigation through randomized controlled trials [10]. Conversely, some evidence still favors volar plating through open reduction and internal fixation as the preferred method for managing unstable distal radius fractures [11]. The rationale for this interventional study was to compare the excellent outcomes of volar Barton fractures of the distal radius managed with open reduction and internal fixation using volar plates versus percutaneous pinning by Faisal's technique.

Although the volar plate method is generally preferred for volar fractures, conflicting results in the literature have raised uncertainty about its superiority over the percutaneous approach. Limited research, especially at the local level, has been conducted to address this controversy. Therefore, this study aims to confirm the beneficial role of volar plates in managing these fractures. The findings will potentially improve clinical practice and

inform future updates to local guidelines for the management of volar Barton fractures.

METHODS

The study was an interventional study conducted in Unit I, Department of Orthopedic Surgery, Mayo Hospital, Lahore from 31st July 2019 to 30th January 2021. The ethical approval was obtained from Green International University (Ref. No: IRC-GIU-156-04-2025). The sample size was 60 cases, with 30 cases in each group, calculated with 80% power of study, 5% level of significance, and taking the expected percentage of excellent outcome (on Green and O'Brien Score >90-100 points) i.e., 86.67% with percutaneous K-wires and 53.33% with volar plate for volar Barton fracture [9]. Non-probability consecutive sampling technique was applied. Inclusion criterion was patients of age 20-70 years of either gender, presenting with volar Barton fracture (as per operational definition) within 15 days of fracture. Excluded were the patients with bilateral fracture, recurrent fracture of the same side (on medical record), patients with open fractures, with dislocation of wrist, arthritic wrists, neurovascular injury and Chauffeur's fracture. After taking approval from the Green International University ethical committee, 60 patients fulfilling the selection criteria were included in this study from emergency of Department of Orthopedic Surgery, Mayo Hospital, Lahore. An informed consent was obtained. Demographic profile (name, age, gender, anatomical side, cause of fracture and duration of volar Barton fracture) were noted. Patients were randomly divided into two interventional groups by using lottery method. In Group A, volar plate fixation was performed. In Group B, percutaneous pinning using K-wires was done. It was reduced closed by dorsiflexing the wrist and by ligamentotaxis, followed by percutaneous pinning in anti-glide mode from the dorsal proximal fragment of the distal radius into the volar fragment and along the subchondral cortex under image intensifier. In some cases, additional cross K-wires were added for increased stability. A short arm cast in volar flexion was used to support fixation stability. Less than 2 mm of articular step-off was acceptable (Annexure I). All surgeries were performed under general anesthesia by a single surgical team with assistance of the researcher. Patients were followed up for 3 months. After 3 months, patients were evaluated for functional outcome using Green O'Brien Scoring system. A total score of 90-100 points was recorded as excellent outcome (as per operational definitions). Data were entered and analyzed in SPSS version 21.0. The quantitative variables like age and duration of fracture were presented as mean & standard deviation. The qualitative variable like gender, anatomical side, cause of fracture and excellent outcome were presented as frequency and percentage. Chi-square test was used to compare excellent outcome in both groups. P -value < 0.050 was considered as significant. Data were stratified for age, gender, anatomical side, BMI,

cause of fracture and duration of fracture. Post-stratification, Chi-square test was used to compare excellent outcome in both groups. P-value<0.050 was considered as significant.

RESULTS

Age range in this study was from 20 to 70 years with mean age of 42.34 ± 14.56 years. The mean age of patients in group B was 42.37 ± 15.23 years and in group A was 42.33 ± 14.04 years. Majority of the patients, 31 (51.67%), were between 20 to 45 years of age. Out of these 60 patients, 47 (78.33%) were male and 13 (21.67%) were females with ratio of 3.6:1. The mean duration of injury in group B was 5.40 ± 2.39 days and in group A was 5.40 ± 2.16 days. Mean BMI was 28.83 ± 2.91 kg/m². Distribution of patients according to anatomical side (Table 1).

Table 1: Distribution of Patients According to Duration of Fracture, BMI, and Anatomical Side Fractured (n=120)

Variables	Group A Frequency (%) / Mean $\pm$ SD	Group B Frequency (%) / Mean $\pm$ SD	Total Frequency (%) / Mean $\pm$ SD
Duration (Days)			
≤ 7 Days	28 (93.33)	26 (86.67)	54 (90.0)
8–15 Days	02 (6.67)	04 (13.33)	06 (10.0)
Mean	5.40 ± 2.16	5.40 ± 2.39	5.40 ± 2.21

BMI (Kg/m²)			
≤ 27	10 (33.33)	10 (33.33)	20 (33.33)
> 27	20 (66.67)	20 (66.67)	40 (66.67)
Mean	28.93 ± 3.03	28.77 ± 2.84	28.83 ± 2.91
Anatomical Side			
Right	14 (53.33)	16 (53.33)	30 (50.0)
Left	16 (46.67)	14 (46.67)	30 (50.0)

Excellent outcome was seen in 24 (80.0%) patients in group B (percutaneous pinning by Faisal technique) and 11 (36.67%) patients in group A (volar plate) with p-value of 0.001. Comparison the frequency of excellent outcome of volar Barton fracture of distal radius with open reduction and internal fixation with volar plate versus percutaneous pinning by Faisal technique (n=60) were Analyzed (Table 2).

Table 2: Volar Barton fraction of distal radius with reduction and internal fixation with volar versus percutaneous pinning

Outcome	Group A Yes (%)	Group B Yes (%)
Excellent	11 (36.67%)	24 (80.0%)
Not Excellent	19 (63.33%)	6 (20.0%)

*P value is 0.001 which is statistically significant.

Stratification of excellent outcome with respect to age, gender, and BMI of patients is shown in Table 3.

Table 3: Stratification of Excellent Outcome with Respect to Age, Gender, and BMI of Patients (n=60)

Variables	Category	Group A (Excellent)	Group A (Not Excellent)	Group B (Excellent)	Group B (Not Excellent)	p-Value
Age	20–35	3	12	13	3	0.001
	36–50	8	7	11	3	0.153
Gender	Male	6	18	19	4	0.001
	Female	5	1	5	2	0.612
BMI	≤ 27	5	5	8	2	0.160
	> 27	6	14	16	4	0.001

Stratification of excellent outcome with respect to duration of fracture, cause of fracture, and anatomical side is shown in Table 4.

Table 4: Stratification of Excellent Outcome with Respect to Duration of Fracture, Cause of Fracture, and Anatomical Side (n=60)

Variable	Category	Group A (Excellent)	Group A (Not Excellent)	Group B (Excellent)	Group B (Not Excellent)	p-Value
Duration (days)	≤ 7	11	17	21	5	0.002
	> 7	0	2	3	1	0.083
Cause	Trauma	2	5	5	3	0.189
	RTA	9	14	19	3	0.001
Anatomical Side	Right	5	9	13	3	0.011
	Left	6	10	11	3	0.024

DISCUSSION

Distal radius fractures constitute a high percentage of presentations in accident and emergency departments [12, 13]. They are most frequently the result of road traffic accidents, falls from height, industrial injuries, and sporting injuries [12]. Traditionally the treatment for intra-articular distal radius fractures consisted of the application of plaster casts. Conservative treatment in this fashion resulted in collapse of the fracture fragments and

radial shortening, angulation, and irregularities in the joint surface that would lead to permanent deformity. Loss of alignment also results in ulnar overlengthening and subsequent medial wrist pain. Traditional terms like Colles', Smith's, and Barton's fractures have now been consolidated into the general term Distal Radius Fractures (DRF) that encompasses both intra- and extra-articular fractures. While several classification systems have been

created, the Fernandez Classification remains one of the most widely accepted [13]. Plate fixation, in particular locking plates, has gained prominence due to the stability that it provides, the shorter period of immobilization, and the simplicity of early return to normal activities. It offers precise anatomical restoration of the articular surface and the alignment of the fragments and produces better functional outcomes and less likelihood of early-onset osteoarthritis [14, 15]. Nevertheless, Open Reduction and Internal Fixation (ORIF) possesses several drawbacks including the potential for skin scarring, tendon injury, the need for further surgery for hardware removal, higher cost, and the requirement for higher surgical skills than percutaneous fixation by K-wires. Volar plates are usually utilized for volar fragments and also stabilize dorsal fragments by the same method. K-wires are still the preferred choice in most situations because they are easy to insert, cause little disruption to the soft tissue, and are applied traumatically, minimizing swelling and stiffness [16, 17]. They also have the added advantages of less risk of infection and good fracture healing [17, 18]. I have conducted this study to compare the frequency of excellent outcome of volar Barton fracture of distal radius with open reduction and internal fixation with volar plate versus percutaneous pinning by Faisal technique. The mean age of patients in group B was 42.37 ± 15.23 years and in group A was 42.33 ± 14.04 years. Majority of the patients 31 (51.67%) were between 20 to 45 years of age. Out of these 60 patients, 47 (78.33%) were male and 13 (21.67%) were females with ratio of 3.6:1. Excellent outcome was seen in 24 (80.0%) patients in group B (percutaneous pinning by Faisal technique) and 11 (36.67%) patients in group A (volar plate) with p-value of 0.001. One trial found that excellent outcome (Green and O'Brien score $>90 - 100$) was achieved in 86.67% with percutaneous K-wires and 53.33% with volar plate for volar Barton fracture ($p=0.046$) [9]. Another study reaffirmed the evidence and documented successful outcomes using Faisal's Technique—closed reduction by wrist dorsiflexion, fragment reduction by ligamentotaxis, and percutaneous anti-glide pinning—in the management of volar Barton's fractures. The outcome suggests the need for further randomized controlled trials in order to establish the efficacy of the technique in such circumstances [10]. But another trial suggested that volar plating through open reduction and internal fixation is the preferred method of managing unstable distal radius fractures [19, 20]. Beharrie et al., in 2004 published a study comparing these two methods [21]. Radwan conducted a randomized trial comparing two treatments for late-presenting displaced distal radius fractures, while Hull et al., evaluated functional outcomes of volar locking plates versus K-wire fixation in acute distal radius fractures [22, 23]. Gartland and Werley proposed a widely used scoring system for evaluating functional outcomes of healed Colles' fractures [24]. Their results are contrary to this but the outcome measured at the end of their work was

radiological restoration of articular surface unlike this. A satisfactory result in 68.3% was obtained by Gartland and Werley by the method of casting. Sarmiento et al., also obtained a higher 82% satisfaction by the same method [25]. Spira and Weigl [27] observed that there was an unsatisfactory result in 51.4% in the treatment of comminuted distal radius fractures involving the articular surface by the method of reduction and simple casting alone [28]. Closed percutaneous pinning either by intra-focal manipulation and pinning or by manual traction and subsequent pinning and anatomical reduction has been described by many authors. Clancey achieved satisfactory outcome in 96.4% in 30 patients who were percutaneously pinned if the radial articular surface wasn't fractured into more than two fragments [29, 30]. McMurtry et al., described techniques and outcomes of distal radial osteotomy for correcting deformities following malunited distal radius fractures [31]. While external fixators were found superior in the restoration of radial length than percutaneous pinning and casting, they were typically insufficient in the restoration of normal volar tilt [32]. Green reported an 86% satisfactory result with this technique used in the treatment of 75 patients with severely comminuted intra-articular fractures [33]. The technique is so easy that most surgeons become familiarized with this procedure in a relatively short time. The wires usually can be withdrawn in the outpatient clinic with relative ease when healing is sufficient. All three authors Shukla et al., Kreder et al., and Saving reported that external fixation performed better than internal fixation for the treatment of distal radius fractures [33-35]. Kreder et al., in the Randomized Controlled Trial (RCT) of displaced intra-articular distal radius fractures, reported that patients who underwent indirect reduction and external fixation regained function more quickly and overall results were improved provided that the articular gap and the step-off were adequately minimized [34]. Similarly, Shukla et al., in one Level 4 prospective RCT involving 110 patients with Cooney's Type 4 displaced intra-articular distal radius fractures, reported that patients who underwent external fixation had superior wrist range of motion, grip strength, and overall results than patients who underwent volar locking plates. Pain scores and activity scores were the same between the two groups, leading the authors to conclude that external fixation yielded superior results than Open Reduction and Internal Fixation (ORIF) by volar locking plates at one year [33]. In another RCT, 118 patients compared who were either treated by volar locking plates or external fixators for unstable distal radius fractures. They found that the functional outcomes were the same between the two treatment groups, yet the volar plate group developed more post-traumatic arthrosis and more reoperations. However, Kapoor et al., reported in their RCT that internal fixation proved to have less associated articular complication secondary to better anatomical restoration. They further included that functional results

were worse in severely comminuted fractures secondary to the difficulty in achieving stable fixation using locking plates [36]. The Faisal technique may be superior due to its minimally invasive nature, preservation of soft tissue integrity, and reduced surgical trauma. Early stabilization with K-wires under image guidance could facilitate quicker functional recovery and lower complication rates compared to volar plating.

This study has limitations including a relatively short follow-up duration, which limits the assessment of long-term outcomes such as arthritis. We also did not include radiological parameters like volar tilt or radial height, and potential observer bias may have influenced functional scoring. Future randomized controlled trials with longer follow-up and inclusion of standardized radiological and functional assessments are recommended to validate these findings.

CONCLUSIONS

This study concluded that frequency of excellent outcome of volar barton fracture surgery of distal radius with open reduction and internal fixation was higher in percutaneous pin by Faisal technique than volar plates. Health care systems should prefer percutaneous pinning for catering fracture cases.

Authors' Contribution

Conceptualization: SA

Methodology: HSA, SH

Formal analysis: SSS, HMAA, SH

Writing and Drafting: SA, MAA, SSS, HAS, HMAA, MI

Review and Editing: SA, MAA, SSS, HAS, HMAA, MI

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Case Study



Abdominal Ectopic Pregnancy: Surgical Management in Low-Resource Settings

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ABSTRACT

Abdominal ectopic pregnancy (AEP) is a rare and potentially life-threatening condition in which a fertilized ovum implants within the peritoneal cavity outside the uterine structures. It accounts for approximately 1% of all ectopic pregnancies and poses significant diagnostic and management challenges. AEP is a rare but serious obstetric emergency requiring high clinical suspicion for early diagnosis. Prompt imaging and appropriate surgical intervention are crucial in preventing maternal morbidity and mortality. We hereby report a case of a 42-year-old Gravida5 Para4 Alive1, a 17-week pregnant woman from a remote rural area presented with shock and sudden lower abdominal pain for 5 hours. Abdominal ultrasound revealed an abdominal ectopic pregnancy with the fetus in the right iliac fossa. Due to hemodynamic instability, an emergency laparotomy was performed, revealing a 17-week male fetus in the peritoneal cavity with 1500 mL of hemoperitoneum. The placenta was attached to the right fallopian tube, necessitating a salpingectomy. Postoperative recovery was uneventful without complications. This case highlights the importance of considering AEP in differential diagnoses of atypical abdominal pain in pregnancy and underscores the role of multidisciplinary management for optimal patient outcomes.

INTRODUCTION

Abdominal Ectopic pregnancy (AEP) is an extremely rare condition, accounting for approximately 0.6–4% of all ectopic pregnancies [1]. The most frequent locations for ectopic implantation are the ampullary (70%), isthmic (12%), fimbrial (11%), and ovarian (3.2%) regions [2, 3]. AEP is a potentially life-threatening condition where a pregnancy develops outside the uterus, either primarily or secondarily, in the abdominal cavity [4]. A primary AEP occurs when the fertilized ovum is directly implanted in the abdominal cavity. The fallopian tubes and ovaries are unharmed in these situations. On the other hand, when an extra-uterine tubal pregnancy ruptures or aborts and is re-implanted inside the abdomen, this is known as a secondary AEP [5]. Before 20 weeks of amenorrhea, abdominal ectopic pregnancy is considered to be early;

after 20 weeks, it is considered late. The patient is constantly at risk for both maternal and fetal problems [6]. Maternal complications can occur in the antepartum, peripartum or postpartum periods. These complications include spontaneous separation of the placenta leading to massive hemorrhage, shock, disseminated intravascular coagulation, organ failure, and death [7]. Due to inadequate prenatal care, low socioeconomic patient status, and a lack of sufficient medical resources, diagnoses can often go unnoticed in low-resource settings [8, 9].

Abdominal ectopic pregnancy is a rare and life-threatening condition with limited documented evidence, especially in low-resource settings like Pakistan. Moreover, due to its nonspecific presentation, delayed diagnosis remains a major challenge, and local data on its clinical outcomes are



scarce. This study aims to evaluate the clinical presentation, diagnostic approach, and maternal outcomes of abdominal ectopic pregnancy.

Case Report

A 42-year-old woman, Gravida5 Para4 A11, presented to the Emergency Department of Women and Children Hospital, Dera Ismail Khan, in hemorrhagic shock. Ethical approval for the publication of this case report was obtained from the Institutional Ethical Review Committee of Gomal Medical College, Dera Ismail Khan, under reference number 224/GJMS/JC. The report was prepared in accordance with the ethical standards and clinical research guidelines established by the Declaration of Helsinki. Written informed consent was obtained from the patient's family prior to the preparation and submission of this report. The family was fully informed about the nature and purpose of the case report, the inclusion of anonymized clinical data and surgical images, and the intended publication in a peer-reviewed medical journal. The consent process involved clear communication in a language they understood, and the family was given sufficient time to ask questions and make an informed decision. The patient's identity has been protected by ensuring that no personal details or facial features are disclosed. All images and data have been carefully anonymized to maintain confidentiality. The authors confirm that publication of the case report respects the patient's dignity and privacy and that all necessary approvals and written consents were obtained before submission. She had a 15-year history of consanguineous marriage and previous adverse obstetric outcomes, including three early neonatal deaths due to sustained birth trauma. Her medical history included chronic pelvic inflammatory disease and a family history of tubal pregnancy. She reported 17 weeks of gestational amenorrhea and presented with a sudden onset of severe lower abdominal pain lasting five hours. She had been referred from a remote rural tribal area, leading to a delay in seeking medical attention. During the history taking, the pregnancy remained undiagnosed due to the patient's history of irregular menstrual cycles over the last few years. Initially, she visited a local healthcare facility, where she was diagnosed with pregnancy; however, due to a lack of trained health personnel and adequate facilities at that time, she was quickly transferred to our facility. On examination, her vital signs were: BP 80/50 mmHg, HR 130 bpm, RR 26/min, with marked pallor (++). Chest and heart sounds were normal. Abdominal examination revealed a distended, tender abdomen with signs of peritonitis. Fetal parts were not palpable clinically, and fetal heart sounds were inaudible. Pelvic examination showed a uterus that was not separately palpable, a normal cervix with a closed Os, and cervical motion tenderness. Due to the patient's deteriorating condition, a detailed obstetric and Doppler ultrasound, MRI or CT scan could not be performed. However, an urgent obstetric ultrasound revealed a 17-

week extra-uterine male fetus in the right iliac fossa with significant free fluid in the abdomen. Laboratory investigations showed Hb: 8.5 g/dL and elevated β -hCG, consistent with a second-trimester pregnancy. Given her worsening hemodynamic instability, an emergency exploratory laparotomy was planned. During the initial resuscitation and stabilization of the patient before emergency laparotomy, the team first secured the airway, evaluated breathing, and made sure the patient had enough circulation throughout the initial resuscitation and stabilization. The insertion of two large-bore (18G) IV lines allowed for quick fluid resuscitation. Rapid administration of crystalloids, such as Ringer's lactate or normal saline, was initiated to address hemodynamic instability and blood loss. Additionally, as needed, blood products such as packed red blood cells (RBC), fresh frozen plasma (FFP), and Platelets were started. Vital indicators such as blood pressure, oxygen saturation, heart rate, and urine output were all regularly monitored by the team. Throughout this process, preparation for emergency laparotomy continues with ongoing fluid and blood product resuscitation during the transfer to the operating room. Communication with the surgical team and anesthesiologist was maintained to ensure coordinated care, with all interventions and observations carefully documented. She was transfused with three units of blood during surgery. Intraoperatively, around 1500 mL of hemoperitoneum was found, along with a 17-week male fetus floating freely in the peritoneal cavity. The placenta was densely adherent to the right fallopian tube, giving the clinical picture of secondary ectopic pregnancy, and was the source of active bleeding. A salpingectomy was performed, along with tubal ligation with consent of the family; hemostasis was secured, and the peritoneal cavity was thoroughly irrigated. The placenta was carefully detached from the tubal attachment to prevent excessive bleeding, as it was a clinically complete evacuation of the foetus, placental membrane and placenta, ensuring no residual tissue was left behind. The patient had an uneventful recovery, with gradual stabilization of vital signs. On follow-up visit on day 12 of the procedure, the urine pregnancy test was done and was found to be negative, with serial serum β -hCG levels for the next three weeks till stabilization of it to the baseline. Densely adherent placenta is shown in Figure 1.



Figure 1: Image of A Densely Adherent Placenta

Extra-uterine fetus lying in the right iliac fossa is given a full urinary bladder, as shown in Figure 2.



Figure 2: Extra-Uterine Fetus Lying in the Right Iliac Fossa in A View of Full Urinary Bladder

The surgical specimen consisted of a well-formed 17-week male fetus, placenta, and associated tissues, as shown in Figure 3.



Figure 3: The Surgical Specimen Consisting of a Well-Formed 17-Week Male Fetus, Placenta, And Associated Tissues

DISCUSSION

Abdominal Ectopic pregnancy (AEP) is unique among ectopic pregnancies in that it can potentially advance to full term [10]. AEP is a rare and high-risk form of ectopic pregnancy, associated with significantly increased complications and mortality for the mother [11]. Survival rates for fetuses in abdominal pregnancies are extremely low, and those who do survive often experience severe birth defects and high perinatal mortality, with fetal mortality rates ranging from 40% to 90% [12]. Maternal Age over 35, pelvic inflammatory disease, endometriosis, smoking, assisted reproduction, a history of fallopian tube inflammation or abnormal shape, a history of ectopic pregnancy, a history of getting pregnant while using an

intrauterine device, and scarring from pelvic surgery are risk factors for ectopic pregnancy. However, there are no known risk factors for half of the women with ectopic pregnancy diagnoses [13]. Early diagnosis is crucial for minimizing morbidity, enhancing the success of subsequent treatments, and reducing long-term complications. Unfortunately, even in the modern era, an ectopic pregnancy may remain undiagnosed or, worse, misdiagnosed, putting a woman's life at risk [14]. Early ultrasound is crucial in diagnosing cases with suspected EP or AEP [15]. Pelvic ultrasound remains the most effective diagnostic tool for detecting adnexal or peri-uterine pregnancies. The detection rate improves when combined with a quantitative serum β -hCG measurement. For locating abdominal pregnancies, MRI is the preferred method, though in emergencies, CT is the quickest option [16]. A recent comparative study by Khan et al., compared the results of surgical and medical treatment for ectopic pregnancy patients. According to the study, surgical management had a 95% success rate, while medical management with methotrexate had an 85% success rate. However, compared to medical management (10%), surgical interventions were linked to a marginally higher complication rate (12%) [17]. The surgical approach for abdominal pregnancy depends on several factors, including the pregnancy location, the patient's condition, surgical technique, the surgeon's experience, and available resources. Laparoscopy is preferred in stable patients with early diagnosis and experienced surgeons [18]. Comparing laparoscopy versus laparotomy, the former led to a shorter operating time, less blood loss, and fewer hospital days [19]. However, if the patient's condition is hemodynamically unstable with an ultrasound finding of fluid interpreted as hemoperitoneum, laparotomy is urgent to terminate the pregnancy and control the bleeding as found in this case [20].

Being a single case study, the findings have limited external validity and cannot be generalized to the broader population. Additionally, the lack of follow-up data restricts assessment of long-term outcomes. Further multicenter studies with larger sample sizes are recommended to validate the diagnostic utility of NLR in perforated appendicitis and to establish more reliable cut-off values for clinical practice.

CONCLUSIONS

Abdominal ectopic pregnancy (AEP) is a rare but serious obstetric emergency requiring high clinical suspicion for early diagnosis. Prompt and accurate diagnosis is crucial in minimizing the risks and complications associated with abdominal pregnancy, ultimately reducing mortality and morbidity rates. This case highlights the importance of considering AEP in differential diagnoses of atypical abdominal pain in pregnancy and underscores the role of multidisciplinary management for optimal patient outcomes. This case report highlights the critical

importance of timely intervention in resource-limited settings while managing abdominal pregnancy, providing valuable surgical insights that can enhance our understanding and inform our approach to caring for such patients in clinical practice.

Authors' Contribution

Conceptualization: RA, AA, MO

Methodology: RI

Formal analysis: RA

Writing and Drafting: RA, AA, UEAS, MO, RI, MW

Review and Editing: RA, AA, UEAS, MO, RI, MW

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Systematic Review


Trimester-Specific Hemodynamic and Blood Volume Adaptations in Pregnancy: A Systematic Review of Normal and High-Risk Populations

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ABSTRACT

Pregnancy involves significant cardiovascular adaptations, including increased blood volume, cardiac output (CO), and reduced systemic vascular resistance (SVR), which are essential to support fetal development. While these changes are well established, the timing, magnitude, and variability across maternal risk profiles remain inconsistently reported. **Objectives:** To synthesize original research from 2015 to 2025 examining trimester-specific changes in maternal hemodynamic and blood volume, with a focus on both normal and high-risk pregnancies. **Methods:** Systematic searches were conducted in PubMed, Science Direct, Scopus, and Wiley Online Library. Inclusion criteria encompassed original English-language studies involving human pregnancies that assessed maternal blood volume or cardiovascular parameters using validated methods. Extracted data were synthesized across four domains: study characteristics, trimester-wise trends, methodology, and quality. **Results:** Nine studies met the inclusion criteria. Most reported a rise in CO and plasma volume from early to mid-pregnancy, alongside a reduction in SVR. In contrast, high-risk groups, including those with fetal growth restriction (FGR), preeclampsia (PE), and obesity, demonstrated impaired adaptation, marked by persistently high SVR and reduced stroke volume. **Conclusions:** It was concluded that trimester-specific hemodynamic adaptation is essential for healthy pregnancy progression. Deviations in high-risk populations may serve as early markers of complications. Incorporating non-invasive cardiovascular monitoring into routine prenatal care may improve risk stratification and outcomes.

INTRODUCTION

Pregnancy induces a series of profound physiological changes to support fetal growth and maternal adaptation [1]. Among the most critical are cardiovascular adjustments, including increased cardiac output (CO), plasma volume expansion, and reduced systemic vascular resistance (SVR), which ensure adequate uteroplacental perfusion. These changes begin as early as the first trimester and peak during mid-pregnancy, allowing for

enhanced nutrient and oxygen delivery to the fetus [2, 3]. Normal gestation is typically characterized by a 40–50% increase in maternal blood volume and up to a 50% rise in CO by the second trimester, accompanied by a drop in SVR and arterial blood pressure [4, 5]. These adaptations are not only vital for fetal development but also serve as indicators of maternal cardiovascular health. When these physiological shifts are impaired or absent, the risk of

pregnancy complications increases. Conditions such as preeclampsia (PE), fetal growth restriction (FGR), and maternal obesity are often associated with reduced CO, persistently elevated SVR, and abnormal vascular remodelling [6, 7]. Despite these established principles, there is inconsistency in the literature regarding the precise timing, magnitude, and clinical relevance of hemodynamic changes across trimesters. Many earlier studies focused predominantly on the second or third trimesters, often overlooking early cardiovascular markers detectable in the first trimester [8-10]. Furthermore, methodological variability in measurement tools ranging from Doppler ultrasound to NICOM (non-invasive cardiac output monitoring) and MRI complicates cross-study comparison. As a result, there is a lack of consolidated data detailing normative versus pathological trends in maternal hemodynamic across different risk groups and gestational stages [11]. In recent years, the use of advanced, non-invasive cardiovascular monitoring has become more widely available in both clinical and research settings. These tools have enabled earlier and more precise tracking of maternal cardiovascular function, highlighting the need to re-evaluate and synthesize current evidence. Clinical guidelines from the American College of Obstetricians and Gynaecologists (ACOG) and the World Health Organization (WHO) increasingly emphasize the importance of early maternal risk stratification and individualized antenatal care [12, 13]. Understanding how hemodynamic profiles differ by trimester and maternal risk status is central to this approach.

Pregnancy is associated with substantial cardiovascular and blood volume adaptations that are essential for maintaining maternal health and supporting fetal growth. However, the timing, magnitude, and progression of these hemodynamic changes across different trimesters remain inconsistently reported, particularly among high-risk pregnancies such as preeclampsia, fetal growth restriction, and obesity. Existing studies also vary considerably in methodology and measurement techniques, limiting direct comparison and clinical application. Therefore, this systematic review aimed to synthesize current evidence on trimester-specific maternal hemodynamic and blood volume adaptations in both normal and high-risk pregnancies and to identify patterns that may support early risk stratification and improved prenatal care.

METHODS

This systematic review followed the PRISMA 2020 guidelines. Its objective was to synthesize original research examining maternal hemodynamic and blood volume changes during pregnancy across different gestational stages and population risk profiles. Studies were included if they met the following criteria: Study Type:

Original, peer-reviewed research articles (cohort, cross-sectional, or observational studies). Population: Pregnant women at any gestational age, including both healthy and high-risk groups (with hypertension, FGR, or obesity). Outcomes: Reported maternal hemodynamic parameters such as CO, SV, SVR, blood pressure (BP), or plasma volume. Methods: Used validated measurement techniques (NICOM bioreactance, Doppler ultrasound, impedance cardiography, MRI, or tonometry). Language and Date: Published in English between January 1, 2015 and March 30, 2025. Exclusion criteria included: non-original articles (reviews, editorials, case reports), animal studies, studies not reporting maternal outcomes, or those lacking trimester-specific data. A comprehensive search was conducted in PubMed, Scopus, Science Direct, Wiley Online Library, Google Scholar, and reference lists. The final search was completed in March 2025 using Me-SH terms and keywords such as "maternal blood volume," "hemodynamic adaptation," and "cardiac output," with Boolean operators to refine results. Search results were imported into EndNote and duplicates removed. Two reviewers independently screened titles and abstracts, followed by full-text reviews for eligibility. Discrepancies were resolved through discussion or adjudicated by a third reviewer. Inter-rater agreement was achieved through consensus. Discrepancies in interpretation were reviewed and resolved by a third investigator. Study quality was evaluated using a modified version of the Joanna Briggs Institute (JBI) checklist for cohort and observational studies. Two reviewers independently assessed five key domains: (1) clear inclusion criteria, (2) validity of exposure measurement, (3) validity of outcome measurement, (4) confounder identification and control, and (5) adequacy of follow-up. "Partial" scores were assigned when criteria were only partly met for example, when studies had small pilot samples limiting generalizability, or when key confounders such as BMI or parity were not adjusted for. Final quality ratings (high, moderate) were reached through reviewer consensus. A total of 186 records were initially retrieved; after screening, nine studies met all inclusion criteria and were included in the final review. The selection process is illustrated in the PRISMA 2020 flow diagram. Extracted variables included: Author and publication year. Country and study design. Sample size and gestational window. Measurement methods. Maternal characteristics (age, BMI, comorbidities) and reported hemodynamic outcomes and key findings (Figure 1).

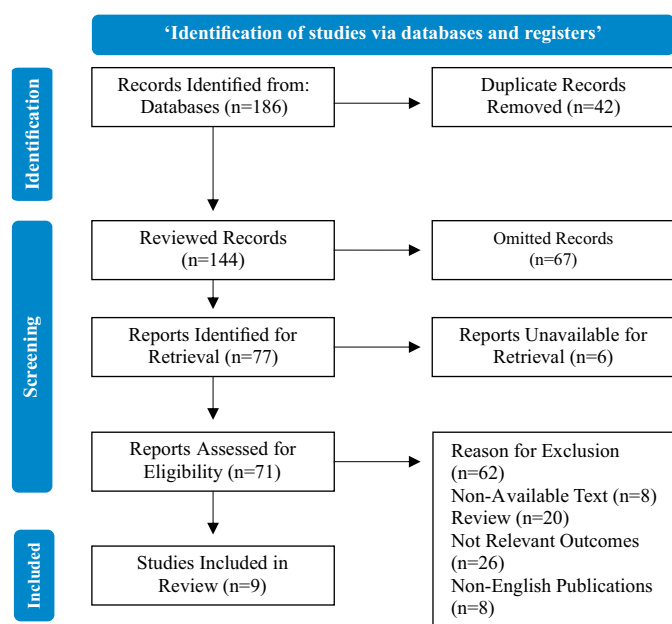


Figure 1: PRISMA 2020 Flow Diagram Illustrating the Process of Study Identification, Screening, and Inclusion

RESULTS

This systematic review included nine original studies published between 2015 and 2025 that examined maternal hemodynamic and blood volume changes during pregnancy. CO showed a consistent increase from the first to the second trimester across most studies, typically peaking mid-gestation. For example, Ling *et al.*, reported a rise in CO from approximately 5.2 L/min in early pregnancy to 6.4 L/min in the second trimester among younger

women, accompanied by a significant reduction in systemic vascular resistance (SVR) [14]. In women with fetal growth restriction (FGR), Stott *et al.*, observed persistently low CO and elevated SVR throughout the second and third trimesters, indicating poor cardiovascular adaptation [15]. Several studies, including those by O'Callaghan *et al.*, and Iacobaeus *et al.*, identified a biphasic adaptation pattern [16, 17]. During early pregnancy, vascular resistance declined, along with a drop in central blood pressure. By the third trimester, these trends began to reverse slightly, with some studies reporting a modest increase in SVR and a reduction in stroke volume (SV). Measurement methods varied but remained non-invasive and clinically validated. Bioreactance via NICOM was most frequently used, while others applied MRI, Doppler ultrasound, and pulse wave analysis. Despite differences in methodology, trends were largely consistent. Studies focusing on high-risk groups, such as Pisani *et al.*, on hypertensive pregnancies and Patel *et al.*, on obesity, showed altered hemodynamic characterized by higher SVR and reduced vascular compliance [18, 19]. Geographic representation spanned Europe, North America, and Scandinavia. However, early gestational data (first trimester) were underrepresented in some studies, with several initiating follow-ups only from the second trimester. Furthermore, only a few studies, such as Gragasin *et al.*, explored relationships between maternal hemodynamics and fetal or placental outcomes [11]. Findings summarize the design, population, gestational window, and key findings of these studies (Table 1).

Table 1: Summary of Included Studies on Maternal Hemodynamic and Blood Volume Adaptations (2015–2025)

Sr. No.	References	Country	Study Design	Sample Size	Gestational Window	Methods	Population	Key Hemodynamic Findings
1	[11]	Canada	Cross-sectional	182	Term only	HemoCue Hb201+	Healthy term pregnancies	Cord Hb ↑ with BW:PW ratio; maternal Hb not associated
2	[14]	UK	Prospective longitudinal	1,789	11–13, 20–22, 34–37 weeks	NICOM	Healthy, stratified by age/BMI	↑CO, ↓SVR in younger women; age influences adaptation
3	[15]	UK	Prospective longitudinal	140	20–36 weeks	NICOM	FGR vs. AGA pregnancies	FGR group had sustained ↓CO, ↑SVR
4	[16]	Ireland	Prospective longitudinal	100	14, 24, 36 weeks	Tonometry	Normotensive singleton pregnancies	↓Central BP mid-pregnancy; CO peak at 24 weeks
5	[17]	Sweden	Prospective longitudinal	55	10–40 weeks	US, FMD	Healthy singleton pregnancies	↑FMD early, ↓FMD near term; biphasic vascular function
6	[18]	Belgium	Prospective observational	120	12–40 weeks	Non-invasive monitor	Normotensive, GHTN, PE	↑SVR, ↓CO in PE; distinct hypertensive profiles
7	[19]	Denmark	Prospective observational	115 (65 obese, 50 controls)	14, 24, 36 weeks	NICOM	Obese vs. normal BMI	Obese group: ↑CO, ↑SVR, ↓vascular compliance
8	[20]	USA	Pilot study	14 pregnant, 14 non-pregnant, 9 postpartum	Mean 26 ± 7 weeks	Quantitative MRI	Healthy and PE	↓Vascular reactivity; more dysfunction in PE postpartum

9	[21]	Belgium	Data synthesis	Not stated	Late 1st to 3rd trimester	Impedance, Doppler	Aggregated prospective data	↑Venous capacity, redistribution essential for adaptation

↑ = Increase; ↓ = Decrease; CO = Cardiac Output; SV = Stroke Volume; SVR = Systemic Vascular Resistance; FGR = Fetal Growth Restriction; PE = Preeclampsia; GHTN = Gestational Hypertension; BMI = Body Mass Index; FMD = Flow-Mediated Dilation; BP = Blood Pressure; NICOM = Non-Invasive Cardiac Output Monitoring; US = Ultrasound; MRI = Magnetic Resonance Imaging; BW:PW = Birth Weight to Placental Weight Ratio

Findings present a critical appraisal of the included studies using a modified Joanna Briggs Institute (JBI) checklist for cohort and observational designs. Most studies demonstrated high methodological rigor, particularly in clear inclusion criteria, valid outcome measurements, and adequate follow-up protocols. Studies by Ling *et al.*, Stott *et al.*, and Pisani *et al.*, received “High” quality ratings due to longitudinal follow-up, well-defined populations, and effective control for confounders [14, 15, 18]. In contrast, Gragasin *et al.*, and Langham *et al.*, were rated Moderate [11, 20]. Langham *et al.*, was a small pilot study, which limited generalizability and statistical power, while Gragasin *et al.*, used a cross-sectional design and did not adjust for potential confounders such as body mass index (BMI) or parity [11]. Greenspan., although methodologically structured, synthesized data from earlier prospective studies rather than collecting new participant-level data [21]. Therefore, while the measurement tools used were valid, the absence of original data collection reduced their empirical strength and led to a “Moderate” rating. Partial ratings in the table indicate criteria that were only partially met. For example, a study may have used validated tools and defined outcomes well but lacked comprehensive control of confounders or had limitations in design (pilot nature, small sample size, or reliance on aggregated data). These nuances were considered when assigning overall quality scores (Table 2).

Table 2: Quality Assessment of Included Studies (Modified JBI Checklist)

Sr. No.	References	Inclusion Criteria Clear	Valid Exposure Measurement	Confounder Control	Adequate Follow-up	Overall Quality
1	[11]	Yes	Yes	Partial (no confounder control)	Not applicable	Moderate
2	[14]	Yes	Yes	Yes	Yes	High
3	[15]	Yes	Yes	Yes	Yes	High
4	[16]	Yes	Yes	Yes	Yes	High
5	[18]	Yes	Yes	Yes	Yes	High
6	[17]	Yes	Yes	Yes	Yes	High
7	[19]	Yes	Yes	Yes	Yes	High
8	[20]	Yes	Yes	Partial (pilot study, small N)	Yes	Moderate
9	[21]	Partial (synthesis data)	Yes	Yes	Not applicable	Moderate

“Partial” = Criteria partially met (pilot design, absence of confounder adjustment, or reliance on synthesized data). “Not applicable” = Study design (e.g., cross-sectional or secondary analysis) did not involve longitudinal follow-up. All studies used validated measurement tools, but external validity was limited in smaller or non-comparative studies.

Results highlight the trimester-specific cardiovascular adaptations during pregnancy across the included studies. A biphasic pattern is evident in most healthy pregnancies: the first trimester is marked by systemic vasodilation, reflected in reduced systemic vascular resistance (SVR) and blood pressure, while CO begins to rise. These changes intensify during the second trimester, when CO typically peaks, and vascular compliance improves further to meet the increasing metabolic demands of the developing fetus. This physiologic adaptation supports placental perfusion and fetal oxygenation. In the third trimester, some of these trends begin to reverse. Several studies reported a plateau or slight increase in SVR and a reduction or stabilization in CO and flow-mediated dilation (FMD), suggesting a compensatory phase as the cardiovascular system adjusts to late gestational load. For example, Ling *et al.*, documented a peak CO of approximately 6.4 L/min in the second trimester with a modest rise in SVR approaching term [14]. In contrast, pregnancies complicated by FGR, obesity, or PE exhibited abnormal hemodynamic patterns throughout gestation. Studies by Stott *et al.* and Pisani *et al.*, consistently reported reduced CO and persistently elevated SVR in these high-risk groups [15, 18]. Similarly, Patel *et al.*, noted that obese women maintained high SVR and impaired vascular compliance across all trimesters, indicating suboptimal adaptation [19]. Overall, the table underscores that healthy pregnancies exhibit dynamic, gestation-specific hemodynamic regulation, while deviations in high-risk pregnancies reflect underlying pathophysiology that may predispose to adverse outcomes (Table 3).

Table 3: Hemodynamic Trends by Trimester Across Included Studies

Sr. No.	Study	Early Pregnancy (1st Trimester)	Mid-Pregnancy (2nd Trimester)	Late Pregnancy (3rd Trimester)
1	[11]	-	-	Cord Hb ↑ with BW: PW ratio; maternal Hb uncorrelated
2	[14]	↑CO (~5.2 L/min), ↓SVR in younger women	↑↑CO (~6.4 L/min), SVR stable	CO maintained, slight ↑SVR
3	[15]	-	↓CO, ↑SVR in FGR	Sustained ↓CO, ↑SVR in FGR
4	[16]	↓cfPWV, ↓brachial BP	Peak CO (~6.0 L/min)	↑BP, CO returned to baseline
5	[17]	↑FMD, ↓central BP	BP plateaued	↓FMD, ↑central BP
6	[18]	-	Profiles varied by HTN type	PE: ↑SVR (~1800 dyn·s/cm ⁵), ↓CO
7	[19]	↑CO, ↑SVR in obese group	Persistent ↑SVR	↑SVR, ↓vascular compliance
8	[20]	-	↓Vascular reactivity in pregnancy group	Compared to the postpartum group
9	[21]	↑Venous capacity	Redistribution of blood volume	↑Uterine venous impedance

↑ = Increase; ↓ = Decrease; CO = Cardiac Output; SVR = Systemic Vascular Resistance; FMD = Flow-Mediated Dilation; BP = Blood Pressure; cfPWV = Carotid-Femoral Pulse Wave Velocity; PE = Preeclampsia; HTN = Hypertension; FGR = Fetal Growth

Restriction; Hb = Hemoglobin; BW:PW = Birth Weight to Placental Weight Ratio. “-” = Not reported in that trimester

The study summarises the methodological diversity among the included studies in terms of design, sample size, population type, measurement tools, and gestational coverage. Most studies employed prospective longitudinal designs, allowing repeated assessments across gestation and enhancing temporal validity. The inclusion of high-quality monitoring methods such as bioreactance-based NICOM, Doppler ultrasound, and pulse wave analysis ensured accurate, non-invasive evaluation of cardiovascular parameters. Sample sizes varied considerably, ranging from 37 participants in Langham *et al.*, MRI pilot study to over 1,700 in Ling *et al.*, population-based cohort. This heterogeneity impacted the generalizability and statistical power of findings [20, 14]. While most studies focused on healthy pregnancies, several included high-risk groups such as women with PE [18], FGR [15], or obesity [19], offering valuable comparisons. Gestational timing also varied. Some studies followed participants throughout pregnancy, while others Gragasin *et al.*, were limited to term-only assessments, missing temporal trends [11]. Studies beginning in the second trimester may have overlooked early hemodynamic changes critical for risk prediction. Overall, despite differences in design and timing, the inclusion of diverse populations and validated tools strengthens the review's clinical relevance, though it poses challenges for direct comparison (Table 4).

Table 4: Methodological and Population Characteristics of Included Studies

References	Study Design	Population	Sample Size	Measurement Method	Gestational Window
[11]	Cross-sectional	Healthy term pregnancies	182	Hemoglobin analyzer (HemoCue)	Term only (delivery)
[14]	Prospective longitudinal	Healthy, age-stratified pregnant women	1,789	NICOM (bioreactance)	11–37 weeks
[15]	Prospective longitudinal	FGR vs. AGA pregnancies	140	NICOM (bioreactance)	20–36 weeks
[16]	Prospective longitudinal	Normotensive pregnancies	100	Applanation tonometry, cfPWV	14, 24, 36 weeks
[18]	Prospective observational	Normotensive, GHTN, PE	120	Non-invasive CO monitor	12–40 weeks
[17]	Prospective longitudinal	Healthy singleton pregnancies	55	Flow-mediated dilation, pulse wave	10–40 weeks
[19]	Prospective observational	Obese vs. normal BMI	115 (65+50)	NICOM	14, 24, 36 weeks
[20]	Prospective pilot study	Pregnant, non-pregnant, postpartum	37 (14+14+9)	Quantitative MRI (vascular function)	~26 weeks (mean GA)
[21]	Synthesis of earlier studies	Aggregated from multiple sources	Not stated	Impedance cardiography, Doppler	1st–3rd trimester

DISCUSSION

This review synthesizes findings from nine studies on maternal hemodynamic and blood volume changes, highlighting normal adaptations and deviations in high-risk pregnancies. In healthy women, rising cardiac output and declining SVR in early to mid-pregnancy were consistently observed, supporting adequate placental perfusion and fetal growth [22–24]. A key trend observed was the

biphasic nature of adaptation. CO tends to rise early and peak mid-gestation, while SVR decreases and then stabilizes or slightly rebounds by the third trimester. This pattern was supported by Aguree S and A.D. Gernand [25], who reported plasma volume increases of up to 48% by the third trimester, and by Lopes van Balen *et al.*, who described two phases of endothelial remodelling: rapid

early expansion and later stabilization [26]. The discussion of high-risk pregnancies further underscores the importance of these adaptive processes. Studies focusing on women with fetal growth restriction (FGR), preeclampsia (PE), or obesity consistently reported persistently low CO and elevated SVR indicative of impaired cardiovascular remodelling [27, 28]. These findings were supported by previous research, including work by Ducas *et al.*, and Valensise *et al.*, which found that such deviations often precede clinical symptoms and may serve as early markers of poor placental function [29, 30]. These deviations also have clinical implications. The presence of abnormal maternal hemodynamics may be an early indicator of placental insufficiency and increased perinatal risk. Non-invasive methods like bioreactance monitoring and Doppler ultrasound, as suggested by Loreto *et al.*, and Ornaghi *et al.*, offer potential for earlier detection and more tailored prenatal care [27, 28]. Maternal characteristics, including age and obesity status, were also shown to influence cardiovascular adaptation. Ling *et al.*, found that younger women had more favourable CO and SVR profiles [14], while Patel *et al.*, and Kennedy *et al.*, reported that obesity leads to elevated SVR and reduced vascular compliance [19, 31]. These findings suggest that maternal anthropometry and metabolic profile should be factored into antenatal risk assessment. Although measurement modalities varied, ranging from NICOM and Doppler to MRI, the consistency of physiological trends supports their reliability. Langham *et al.*, [20] MRI-based vascular data reinforced earlier work by Duvekot and Peeters [32], who emphasized the interplay between vascular tone and cardiac function as central to pregnancy adaptation. Many studies lacked early first-trimester data, missing a crucial window where maladaptation may begin. Reijnders *et al.*, Mecacci *et al.*, and Warren *et al.*, emphasized that elevated uterine artery resistance early in pregnancy can predict later complications [33-35].

This review is limited by the small number of eligible studies, heterogeneity in study designs, populations, and hemodynamic assessment methods, which restricted direct comparison across studies. Additionally, several studies lacked first-trimester data and included relatively small sample sizes, reducing the generalizability of findings. Future research should adopt standardized measurement protocols, include larger multicenter longitudinal cohorts beginning in early pregnancy, and evaluate the relationship between maternal hemodynamic profiles and maternal-fetal outcomes. Such studies may facilitate the development of personalized monitoring strategies and earlier identification of pregnancy-related complications.

CONCLUSIONS

This review confirms that pregnancy requires dynamic, trimester-specific cardiovascular adaptation characterized by increased cardiac output and reduced vascular resistance, which is crucial for fetal development. In high-risk pregnancies (fetal growth restriction (FGR), preeclampsia (PE), and obesity), these adaptations are often impaired and may signal early complications. Routine use of non-invasive hemodynamic monitoring could aid in early risk detection. Future studies should standardize measurements, begin assessments in the first trimester, and link maternal profiles with perinatal outcomes to support personalized care.

Authors' Contribution

Conceptualization: NF, MU

Methodology: SA, OK, MA, MU

Formal analysis: OK, NF

Writing and Drafting: AJ, SA, OK, MA, MU

Review and Editing: AJ, SA, OK, MA, MU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Systematic Review



Evaluating Preventive Strategies for Bronchopulmonary Dysplasia in Preterm Neonates: A Systematic Review

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ABSTRACT

Bronchopulmonary dysplasia (BPD) remains a major complication in preterm neonates, affecting long-term respiratory health and quality of life. Despite advances in neonatal care, identifying consistently effective preventive strategies remains a clinical challenge.

Objectives: To evaluate recent evidence on interventions used to prevent BPD in preterm neonates, focusing on identifying effective strategies and addressing current research gaps.

Methods: A structured literature search was conducted using PubMed, Embase, Cochrane Library, and Web of Science for studies published between January 2016 and March 2025. Eligible studies included randomized controlled trials, prospective cohorts, and observational studies evaluating interventions in neonates born before 32 weeks of gestation or weighing under 1500 grams. Screening and data extraction were performed independently. Methodological quality was assessed using standard tools. **Results:** Eighteen studies met the inclusion criteria. Interventions evaluated included non-invasive ventilation, minimally invasive surfactant therapy (MIST), pharmacologic agents (melatonin, corticosteroids, intra-tracheal budesonide), and nutritional supplementation (vitamins A and D, fatty acids). MIST, melatonin, budesonide with surfactant, and early vitamin D supplementation consistently reduced BPD incidence. In contrast, vitamin A, maternal DHA supplementation, and systemic hydrocortisone showed limited or inconsistent benefit. **Conclusions:** Several interventions, particularly MIST, budesonide with surfactant, melatonin, and vitamin D, appear effective in preventing BPD in preterm infants. However, inconsistencies in outcomes from other therapies underscore the need for further high-quality trials to guide clinical practice.

INTRODUCTION

Bronchopulmonary dysplasia (BPD) remains a serious and common complication among preterm neonates, especially those born at ≤ 32 weeks of gestation or with birth weights less than 1500 grams [1]. Despite advances in neonatal care, BPD continues to impact neonatal survival and long-term respiratory and neurodevelopmental outcomes significantly [2]. Preterm infants with BPD often experience extended hospital stays, increased healthcare costs, and higher risks of chronic lung disease, making its prevention a priority in neonatal intensive care settings [3, 4]. Over recent years, various strategies have been investigated to prevent or reduce the severity of BPD.

These include non-invasive respiratory support modalities, pharmacological agents, nutritional supplementation, and early developmental interventions [5]. While multiple individual studies and previous systematic reviews have explored these options, most have focused on isolated interventions or a narrow subset of strategies [6]. Furthermore, many existing reviews are outdated and do not incorporate findings from the most recent randomized controlled trials or observational studies. Importantly, the available evidence often lacks consistency in recommendations, partly due to heterogeneity in study design, outcomes assessed, and



population characteristics. For example, while some reviews report the benefits of non-invasive ventilation, others fail to demonstrate a clear advantage over conventional methods. Similarly, studies investigating pharmacological therapies like corticosteroids or antioxidants like melatonin vary widely in methodology and outcomes. Thus, there remains a lack of consolidated and up-to-date evidence to guide clinicians in selecting the most effective preventive measures. By analysing recent evidence from randomized controlled trials, cohort studies, and prospective observational studies, this review seeks to identify evidence-based interventions that show promise in reducing the incidence and severity of BPD. Interventions covered include non-invasive ventilation, minimally invasive surfactant therapy (MIST), pharmacologic therapies (such as corticosteroids and melatonin), nutritional approaches (including vitamin and fatty acid supplementation), and early developmental care strategies. This review synthesizes current evidence and highlights knowledge gaps and areas for future investigation, supporting evidence-based clinical decision-making in neonatal care.

Abdominal ectopic pregnancy is a rare and life-threatening condition with limited documented evidence, especially in low-resource settings like Pakistan. Moreover, due to its nonspecific presentation, delayed diagnosis remains a major challenge, and local data on its clinical outcomes are scarce. This study aims to evaluate original research studies published between 2016 and 2025 that assess various preventive strategies for BPD in preterm neonates.

METHODS

A comprehensive search was performed in four major databases: PubMed, Embase, Web of Science, and Cochrane CENTRAL, covering studies published between January 2016 and March 2025. This systematic review evaluated recent evidence on interventions to prevent bronchopulmonary dysplasia (BPD) in preterm neonates. Keywords and MeSH terms included: bronchopulmonary dysplasia, BPD, preterm neonates, prevention, non-invasive ventilation, surfactant therapy, vitamin supplementation, corticosteroids, and melatonin. Boolean operators such as "AND" were used to improve search specificity. Reference lists of selected studies were also checked to identify additional eligible articles. Studies were included if they involved preterm infants (≤ 32 weeks' gestation or ≤ 1500 g birth weight) and evaluated interventions aimed at preventing BPD. These included non-invasive ventilation strategies (NIPPV, NCPAP, NHFOV, MIST), pharmacological agents (e.g., budesonide, melatonin, corticosteroids), nutritional supplements (e.g., vitamin A, vitamin D, DHA), and early developmental care. Only randomised controlled trials, prospective/retrospective cohort studies, and observational studies reporting BPD-related outcomes were included. Exclusion

criteria included studies on term infants, animal models, reviews or editorials, and non-English publications. Two independent reviewers screened the identified studies' titles, abstracts, and full texts. A third reviewer resolved disagreements. Data were extracted using a standardised form, including the author's name, year, study design, sample size, intervention type, outcomes, and key findings. Eighteen studies met the inclusion criteria. Risk of bias was assessed using the Cochrane Risk of Bias Tool for RCTs and the Newcastle-Ottawa Scale for cohort and observational studies. Due to heterogeneity in interventions and outcome measures, data were synthesized narratively rather than through meta-analysis. The PRISMA 2020 flow diagram summarises the selection process (Figure 1).

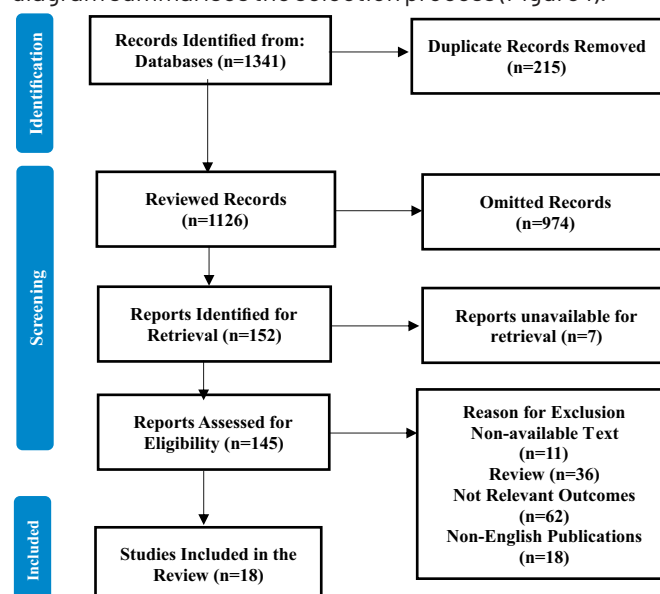


Figure 1: Process of Study Selection for This Systematic Review, Including Identification, Screening, Eligibility Assessment, and Final Inclusion of Studies

RESULTS

This systematic review included 18 studies assessing interventions to prevent bronchopulmonary dysplasia (BPD) in preterm neonates. The interventions comprised non-invasive ventilation, nutritional and pharmacological therapies, and early developmental support. Non-invasive ventilation strategies showed varied effectiveness. Foglia *et al.*, compared nasal intermittent positive-pressure ventilation (NIPPV) to nasal continuous positive airway pressure (NCPAP) in infants ≤ 28 weeks of gestation and found no significant reduction in BPD or mortality [7]. In contrast, Rachana *et al.*, demonstrated that non-invasive high-frequency oscillatory ventilation (NHFOV) significantly reduced BPD incidence and need for mechanical ventilation compared to non-invasive intermittent mandatory ventilation (NIMV). Nutritional interventions had mixed results [8]. Wendel *et al.*, and Abiramalatha *et al.*, investigated arachidonic acid (ARA)

and docosahexaenoic acid (DHA) supplementation, but neither study showed significant benefits [9, 10]. Similarly, Ndiaye *et al.*, found that SMOF lipid emulsion failed to improve BPD-free survival [11]. Marc *et al.*, also reported no benefit from maternal DHA supplementation. Vitamin supplementation yielded inconsistent outcomes [12]. Ge *et al.*, found that early vitamin D supplementation (800 IU/day) significantly reduced BPD and inflammatory markers [13]. However, Rakshasbhuvarkar *et al.*, reported no benefit of enteral vitamin A on BPD incidence or inflammation. Pharmacological therapies produced variable effects [14]. Manley *et al.*, and Liu *et al.*, noted that intra-tracheal budesonide combined with surfactant significantly reduced BPD and mortality [15, 16]. Conversely, systemic hydrocortisone administered after the first week of life showed no effect on BPD or death in a trial by Onland *et al* [17]. As reported by Remy *et al.*, oral betamethasone was beneficial for patent ductus arteriosus (PDA) closure and

ventilator weaning [18]. Melatonin demonstrated significant reduction in BPD, mortality, and hospital stay when used with surfactant [19]. Surfactant delivery techniques were also explored. Dai *et al.*, suggested that optimising surfactant administration angle may reduce BPD and intracranial haemorrhage [20]. Dargaville *et al.*, showed that minimally invasive surfactant therapy (MIST) significantly decreased BPD and mortality compared to CPAP alone [21]. Developmental interventions also proved valuable. Van *et al.*, found that early behavioural programs enhanced long-term motor and cognitive outcomes in preterm infants with BPD [22]. In summary, the most promising interventions were MIST, intra-tracheal budesonide with surfactant, melatonin, and early vitamin D supplementation. Other therapies, particularly nutritional supplements and systemic steroids, showed limited or inconsistent benefits (Table 1).

Table 1: Study Involved for This Research

Sr. No.	References	Study Design	Sample Size	Intervention	Primary Outcome (s)	Key Findings
1	[7]	RCT	1009	NIPPV vs. NCPAP (non-invasive ventilation)	(BPD incidence, mortality)	NIPPV was not superior to NCPAP in reducing BPD or mortality.
2	[8]	RCT	140	NHFOV vs. NIMV (non-invasive modes)	BPD incidence, need for ventilation	NHFOV is more effective in reducing BPD and ventilation need.
3	[9]	RCT	200	ARA + DHA supplementation	BPD incidence, respiratory morbidities	No significant impact on BPD or other neonatal morbidities.
4	[10]	RCT	251	Enteral ARA + DHA	Severe ROP, BPD	Reduced ROP risk, but no effect on BPD, sepsis, or IVH.
5	[11]	Cohort	222	SMOF lipid emulsion vs. standard	BPD-free survival	No improvement in BPD-free survival among very preterm infants.
6	[12]	RCT	528	Maternal DHA supplementation	BPD-free survival	No significant improvement in BPD-free survival.
7	[13]	RCT	112	Vitamin D (800 IU/day)	BPD incidence, inflammation	Early vitamin D reduced BPD and inflammatory markers.
8	[14]	Nested Observational	66	Enteral Vitamin A	BPD incidence, faecal calprotectin	No significant change in BPD or inflammation biomarkers.
9	[15]	RCT	1160	Budesonide + surfactant (intra-tracheal)	BPD incidence, mortality	Significantly reduced BPD and mortality in preterm neonates.
10	[16]	RCT	122	Budesonide + surfactant	BPD severity, Oxygen therapy duration	Improved ventilation outcomes without steroid-related complications.
11	[17]	RCT	372	Postnatal hydrocortisone	Death or BPD at 36 weeks PMA	No significant reduction in BPD or mortality.
12	[18]	Retrospective Cohort	101	Oral betamethasone	BPD incidence, PDA closure	Improved PDA closure and ventilator weaning; aided BPD recovery.
13	[19]	RCT	80	Melatonin + surfactant vs. surfactant alone	BPD incidence, mortality	Melatonin reduced BPD, mortality, and length of hospital stay.
14	[20]	RCT	96	Surfactant administration angles	BPD, intracranial haemorrhage	Certain angles reduced BPD and intracranial haemorrhage rates.

15	[21]	RCT	485	MIST vs. CPAP	Death or BPD at 36 weeks PMA	MIST significantly lowered rates of death or BPD.
16	[22]	RCT	176	Early behavioural program	Motor and cognitive outcomes	Improved long-term development in infants with BPD.
17	[23]	Prospective Cohort	2693	Combined perinatal interventions	Severe BPD or death	Synergistic interventions reduced the risk of severe BPD or death.
18	[24]	RCT	800	Inhaled nitric oxide (iNO)	Neurodevelopmental outcomes	No significant benefit on long-term outcomes at 7 years.

DISCUSSION

A systematic review highlights multiple strategies for preventing bronchopulmonary dysplasia (BPD) in preterm neonates. Several interventions demonstrated promising clinical benefits, while others showed inconsistent or limited effects. Existing literature largely supports these findings, though some discrepancies persist [25, 26]. Non-invasive ventilation techniques effectively reduced BPD incidence, particularly non-invasive high-frequency oscillatory ventilation (NHFOV). Rachana *et al.*, reported significantly lower rates of BPD and reduced mechanical ventilation needs with NHFOV [8]. This aligns with a meta-analysis by Minamitani *et al.*, which confirmed superior outcomes for high-frequency non-invasive ventilation over conventional methods such as NCPAP and NIPPV [27]. However, Jensen *et al.*, observed no significant advantage of nasal intermittent positive-pressure ventilation (NIPPV) over nasal continuous positive airway pressure (NCPAP) [25]. This finding is also supported by earlier systematic reviews conducted by Mitra *et al.*, [28]. These mixed outcomes suggest that timing, technique, and patient characteristics may influence the effectiveness of non-invasive respiratory strategies. Pharmacological agents showed variable effectiveness. Melatonin, for example, demonstrated consistent benefit in reducing BPD, mortality, and hospital stay duration¹⁰. This is supported by Häusler *et al.*, who emphasised melatonin's antioxidant and anti-inflammatory properties as protective against neonatal lung injury [29]. Similarly, intra-tracheal administration of budesonide mixed with surfactant significantly reduced the incidence and severity of BPD [14]. These findings are consistent with prior meta-analyses such as Venkataraman *et al.*, which endorsed the safety and efficacy of this combined therapy [30]. Vitamin-based interventions yielded mixed results. Ge *et al.*, found that early vitamin D supplementation reduced BPD incidence and inflammatory markers [13]. This aligns with other systematic reviews that support vitamin D's anti-inflammatory role in improving respiratory outcomes [31]. On the other hand, vitamin A supplementation showed no clear benefit. Rakshasbhuvarkar *et al.*, observed no improvement in BPD outcomes or faecal inflammation [14]. This mirrors the findings by Ding *et al.*, who questioned the

practical value of routine vitamin A use in this population [32]. Maternal supplementation with docosahexaenoic acid (DHA) also produced a limited benefit. Marc *et al.*, reported no significant improvement in BPD-free survival [33]. This result corresponds with findings from Tanaka *et al.*, who also noted negligible respiratory advantages in preterm infants whose mothers received DHA [34]. These outcomes highlight the need for more targeted nutritional interventions and larger studies to confirm clinical efficacy. Minimally invasive surfactant therapy (MIST) consistently showed positive results. Dargaville *et al.*, reported a significant reduction in BPD [21] and mortality when MIST was used compared to standard CPAP [23]. These outcomes align with earlier systematic reviews, such as Rigo *et al.*, which emphasised the effectiveness of MIST in spontaneously breathing preterm infants [35]. Postnatal corticosteroid therapy produced contrasting outcomes. Oral betamethasone aided ductus arteriosus closure and supported ventilator weaning [13]. Systemic hydrocortisone therapy did not significantly affect BPD or survival outcomes²³. This is consistent with a meta-analysis by De *et al.*, who advised caution in using systemic corticosteroids due to their limited benefits and potential risks [36]. Lastly, developmental care strategies also warrant consideration. Van *et al.*, demonstrated that early behavioural intervention programs significantly improved motor and cognitive outcomes in infants with BPD²⁴. These findings support previous systematic reviews that promote early neurodevelopmental support for high-risk preterm infants [22].

This review is limited by heterogeneity among included studies in terms of patient populations, interventions, and outcome definitions, which may affect comparability. Additionally, variability in study quality and the presence of inconsistent reporting across trials may influence the strength of the conclusions. Continued research is needed to standardize treatment protocols, evaluate long-term safety, and identify patient-specific factors influencing intervention effectiveness.

CONCLUSIONS

This systematic review identifies several preventive strategies that show meaningful potential in reducing the incidence and severity of bronchopulmonary dysplasia (BPD) in preterm neonates. Among the most consistently effective interventions were minimally invasive surfactant therapy (MIST), intra-tracheal budesonide with surfactant, melatonin, and early vitamin D supplementation. These strategies demonstrated favourable outcomes across multiple high-quality studies and may serve as reliable options in neonatal clinical practice. On the other hand, interventions such as systemic hydrocortisone, vitamin A, and maternal DHA supplementation showed limited or inconsistent benefits. While they hold theoretical and biological plausibility, current evidence does not support their routine use without further validation through large-scale, well-designed trials. In conclusion, a combination of non-invasive respiratory techniques, targeted pharmacological therapies, and early nutritional support appears to be the most effective approach for BPD prevention.

Authors' Contribution

Conceptualization: MG

Methodology: MG, SA, AD, MR, HMNJ

Formal analysis: MG, HU

Writing and Drafting: SA, AD, MR, HMNJ, HU

Review and Editing: SA, AD, MR, HMNJ, HU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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