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Aims and Scope

PJHSL aims to advance scientific knowledge, promote evidence-based research, and facilitate the practical application of findings to improve health outcomes.

The Pakistan Journal of Health Sciences (Lahore) covers all areas of health sciences, clinical medicine, biomedical sciences, health systems and policy, nursing and allied health sciences, public health, including preventive measures and community-level health initiatives.

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Type of Article

Research Article/ Case Report/ Review Article/ Opinion/ Short Communication/ Mini Review.

Running Title: A short version of the paper title.

Keywords: The major keywords used in the article have to be mentioned.

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Study Design, Inclusion / Exclusion Criteria, Data collection Procedure and Statistical analysis.

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Do not repeat the data in text and in the tables or illustrations; emphasize or summarize only important observations. When data are summarized in the results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them. Table font should be 10 and caption should be above table and below the figure.

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Discuss your findings by comparing your results with other literature.

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A Climate Wake-Up Call: Pakistan's Floods Reveal a Healthcare Crisis



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Flooding has become a recurring nightmare in Pakistan, exacerbated by both natural and human-induced factors. The devastating monsoon floods of 2022 exposed the country's deep vulnerability, damaging nearly 2,000 health facilities showing 13% of all in the country, and displacing more than 600,000 people. Vast areas of farmland, including three million acres of cereal crops and over 1.2 million livestock, were lost, severely disrupting food security and livelihoods.

Since July 2022, floods have inundated 116 districts, affecting 33 million people and placing immense strain on the already fragile healthcare system. More than 1,000 people lost their lives, 1,500 were injured, and over 161,000 were forced into overcrowded and unhygienic relief camps. As of now, 66 districts remain critically impacted. This crisis is not just a one-off disaster it is a symptom of worsening climate extremes, poor planning, and under-resourced public infrastructure. In 2025 alone, Pakistan has already witnessed deadly spring weather, including severe hailstorms, which claimed at least 32 lives.

The 2025 Climate Risk Index ranks Pakistan as the world's most climate-impacted country, based on data from 2022. A third of the country was submerged, over 1,700 lives were lost, and economic damages surpassed \$30 billion. At least 6.4 million people still require humanitarian assistance, and healthcare access remains dangerously limited. Although roughly half of the displaced population has returned home, the absence of clean water and sanitation continues to drive the spread of disease.

As the nation reels under relentless monsoon rains and deteriorating conditions, a public health emergency is unfolding silently alongside the visible destruction. The World Health Organization (WHO) has warned that flooding is fueling outbreaks of diseases such as dengue, malaria, acute watery diarrhea, COVID-19, and polio. With immunization campaigns disrupted and stagnant water everywhere, disease is spreading unchecked. Even before the floods, Pakistan had recorded over 4,500 measles cases and 15 instances of wild poliovirus. These fragile public health gains are now at grave risk.

In response, the World Health Organization (WHO) and Pakistan's Ministry of National Health Services are maintaining emergency operations in the affected regions. They are concentrating on long-term preparedness, healthcare restoration, medicine supply, and disease surveillance. However, it is imperative that these endeavors be dramatically increased. Millions of individuals continue to be vulnerable to preventable illnesses due to their lack of access to basic care and proper sanitation. This crisis is no longer solely about water; it is also about the future of healthcare, resilience, and survival in a world that is warming. Pakistan's silent emergency may soon become too loud to ignore if sustained action is not taken.

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Review Article

Effect of Exercise and Nutrition on Oxidative Stress in Females with Polycystic Ovary Syndrome, a Current Status and Future Perspective in Narrative Review

Maria Mustafa^{1,2*}, Naveed Babur¹, Saleh Shah¹, Almina Shafiq² and Rabia Aslam²¹Department of Physical Therapy and Rehabilitation, Superior University, Lahore, Pakistan²Department of Biomedical Laboratory Sciences, School of Health Sciences, University of Management and Technology, Lahore, Pakistan

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ABSTRACT

Women in their reproductive years are prone to the widespread endocrinological disorder known as Polycystic Ovarian Syndrome (PCOS). To provide in-depth insights into the factors contributing to hormonal imbalances, inflammation, and oxidative stress in women with PCOS. Additionally, it evaluates the impact of exercise and nutritional interventions on oxidative stress and overall metabolic health in PCOS women to improve their quality of life. This review analyzed existing literature and clinical evidence related to endocrine disturbances in PCOS, including hormonal changes such as elevated androgens, insulin resistance, inflammation, and oxidative stress. The effects of lifestyle interventions specifically physical exercise, dietary modifications, and supplementation on these metabolic and hormonal abnormalities were studied. Hormonal Imbalance: Women with PCOS show dysregulated production of Growth Hormone (GH), ghrelin, LEAP-2, Gonadotropin-Releasing Hormone (GnRH), insulin, LH/FSH ratio, androgens, and estrogens. Inflammation and Oxidative Stress: Hyperandrogenism and insulin resistance promote chronic inflammation and increased Reactive Oxygen Species (ROS), leading to oxidative stress, gut microbiome alterations, and metabolic dysfunction. PCOS is a multifactorial disorder influenced by hormonal imbalance, chronic inflammation, and oxidative stress. Lifestyle modifications, particularly tailored exercise regimens and nutritional strategies, play a critical role in mitigating these factors.

INTRODUCTION

A prevalent endocrinological condition that affects women in their reproductive years is polycystic ovarian syndrome, or PCOS. The World Health Organization (WHO) estimates that 8-13% of women in their reproductive years have PCOS. While about 70% of females are still undiagnosed in general. Specifically, in Pakistan, this has a very alarmingly high prevalence of 52% [1]. The key features of PCOS are hyperandrogenism, metabolic disorder, and polycystic ovaries causing chronic anovulation. The most common hormones altered in females with PCOS are androgen, estrogen, insulin, cortisol, gonadotropin-releasing hormone (GnRH), luteinizing hormone/follicle-stimulating

hormone (LH/FSH) ratio, and Growth Hormone (GH). Consequently, this imbalance may enhance the likelihood of resistance to insulin and being overweight while directly affecting psychological health. Furthermore, increased prevalence of obesity, long-term cardiovascular diseases, infertility, and pregnancy complications have been observed. Some evidence suggests that females taking medicine for the condition have increased chances of osteoporosis and the likelihood of bone fracture [2]. There are many different criteria for diagnosing PCOS, but the most commonly used clinical diagnosis criteria are NIH and Rotterdam. According to the former, a patient can only be



diagnosed if symptoms like hyperandrogenism, or when the ovarian size and morphology on ultrasonography reveal the presence of 12 or more follicles measuring 2–9 mm in diameter or an increased ovarian volume > 10 ml, or there must be a disordered menstrual history (oligo or anovulation) [3]. Whereas the former defines PCOS as a syndrome characterized by ovarian dysfunction. The hallmarks include polycystic ovarian morphology and hyperandrogenism, as well as clinical symptoms that may include obesity, irregular menstruation, and indicators of androgen excess. The main symptoms of hyperandrogenism are irregular menstruation, acne, and hirsutism, which is excessive growth of terminal hair in masculine pattern distribution in women [4]. It is worth noticing that around 75% of females suffer from ovulatory infertility. These females choose in Vitro Fertilization (IVF) for conception, which in turn increases the chances of developing ovarian hyperstimulation syndrome. Furthermore, it also increases the risk of miscarriages and gestational diabetes during pregnancy [5].

Although the increasing awareness of oxidative stress as a major contributor to the pathophysiology of PCOS, there is a large gap in the literature on standardized, evidence-based protocols of exercise and nutritional interventions, specifically aimed at reducing oxidative stress in the patients of PCOS. The main issue is that there is the lack of high-quality, randomized controlled trials with sufficient sample sizes that directly measure the oxidative stress biomarkers as the main outcomes of response to lifestyle interventions in PCOS women. This study aims to analyze existing literature and clinical evidence related to endocrine disturbances in PCOS, including hormonal changes such as elevated androgens, insulin resistance, inflammation, and oxidative stress.

Contributing Factor

Many earlier studies showed several contributing factors that can be characterized as internal and external for the PCOS occurrence. Internal factors include but are not limited to oxidative stress, inflammation, hyperandrogenism, obesity, and insulin resistance. Some of the external factors include food, stress, and environmental toxins [6]. The pathological imbalance of the hormones (mentioned earlier) increases the prevalence of osteoporosis. Therefore, there is little evidence that the medications used to treat PCOS raise the likelihood of bone fracture via disrupting hormones [6]. Additionally, research has shown that the gut microbiota is the main factor contributing to obesity, diabetes, and inflammation in PCOS. It has been reported in studies that poor diet and lifestyle cause gut dysbiosis, which ultimately leads to the activation of lipopolysaccharides. Consequently, it results in the inactivation of the immune system, hyperandrogenism, and insulin resistance [7].

Chronic Low-Grade Inflammation

It has been seen in earlier studies that females suffering from PCOS experience chronic low-grade inflammation. This inflammation usually shows itself as an increased level of inflammatory markers and AGEs among them. Neutrophils, macrophages, and lymphocytes are the main cells that secrete cytokines, which are small proteins that function as signaling molecules to regulate the immune system, including initiating and controlling inflammatory response. Dysregulation of cytokines is strong enough to cause low-grade inflammation and, ultimately, cell death. Likewise, an additional element is Reactive Oxygen Species (ROS), engaged in producing chronic low-grade inflammation and a subsequent rise in oxidative stress load. An imbalance between the generation of free radicals and anti-oxidant defense mechanisms is known as oxidative stress. Elevated levels of Reactive Oxygen Species (ROS) cause cellular damage including DNA, protein, and lipid, which subsequently causes increased oxidative stress and inflammation [8]. All of this puts PCOS-afflicted women at higher risk for cardiovascular illness and other pregnancy issues, such as infertility or miscarriages [9].

Oxidative Stress

Oxidative stress is a normal physiological process in a body because of an imbalance between oxidant free radicals and antioxidants. Oxidants are free radicals with an unstable single electron in the outer shell of an atom which are highly reactive. These oxidants achieve stability by stealing electrons from antioxidants. A condition known as oxidative stress occurs when the quantity of free radicals exceeds that of antioxidants. This oxidative stress causes cell damage or even cell death leading to various pathologies, chronic inflammation, and the aging process [10]. These free radicals can be divided into two main classes namely, both reactive oxygen and reactive nitrogen species. These free radicals play a significant role in metabolic derangements like diabetes mellitus, cardiovascular disease, and obesity. Biomarkers for assessing the antioxidants can be used for early diagnosis and treatment and as a preventive measure for metabolic disorders [11]. A strong immune response is essential for the recovery of inflammation in the body caused by the oxidants. Inflammation and oxidative stress often create a vicious cycle where one process fuels the other, leading to a cascade of cellular damage and ultimately, decreased health outcomes. In contemporary research, lifestyle modifications have been considered fundamental in addressing PCOS. They serve as the primary treatment for individuals with obesity. Key interventions include dietary changes and enhanced physical activity. These modifications are associated with the normalization of ovulation and menstrual cycles, thereby improving

pregnancy outcomes in PCOS females. Researchers have shown that nearly 50% of PCOS patients experience enhancements in menstrual regularity and ovulation due to lifestyle changes. Furthermore, such modifications can lead to reductions in anxiety and enhancements in life quality, especially for obese women with PCOS [12]. According to another study, women with PCOS are more likely to suffer from eating disorders, including binge eating disorder and bulimia nervosa. Major characteristic symptoms of the eating disorder are associated with behavioral, cognitive, and emotional features. A person with PCOS who suffers from eating disorders is more likely to experience body dysmorphia, stress, anxiety, and depression, all of which have a negative impact on their quality of life [13]. The variety of eating disorders associated with PCOS, including atypical anorexia nervosa, require more research. Significant detrimental effects on the health and quality of life of people with PCOS may be avoided with early detection and appropriate treatment of an eating disorder.

Current Status and Future Perspective Regarding Treatment of PCOS

This paper examines a detailed review of the health status of women with PCOS. It is an endocrine and metabolic disorder that causes hormonal imbalance as mentioned earlier. It describes the affirmative actions needed to avert and/or reduce the risk associated.

Exercise

For women with PCOS, lifestyle change has been proposed as the first-line therapy in along with medical intervention [14]. An essential component of PCOS management is physical activity, which helps alleviate symptoms and lower the chance of long-term illnesses like type 2 diabetes and cardiovascular disease. Both continuous and intermittent aerobic training exercise regimens are recommended by the American College of Sports Medicine (ACSM). Numerous previous research used submaximal heart rate aerobic activities, adhering to the American College of Sports Medicine's (ACSM) approved guidelines [15]. Women of normal weight should exercise an average of 150 minutes per week at a moderate effort, 75 minutes per week at an intense frequency, or an equal quantity of both, according to worldwide PCOS guidelines. Obese or overweight women with PCOS are advised to engage in moderate-intensity activity for 250 minutes per week, intense exercise for 150 minutes per week, or a combination of both [14]. Additionally, research on the effects of exercise therapy on fertility has shown improvements in the regularity of cycles of menstruation and/or ovulation [16]. The significance of exercise further increases due to the significant risk for Cardiovascular Diseases (CVD) in these women [16]. Exercise also improves insulin sensitivity and lowers hyperinsulinemia, which is the fundamental

mechanism by which it decreases CVD risk variables. Meanwhile, PCOS has been linked to a higher prevalence of mental health conditions in addition to cardio metabolic and reproductive issues. The psychological health of the sick population is enhanced by exercise. Given the extremely individualized nature of PCOS, it may not be possible to establish an ideal dose-response connection with exercise [15]. According to current recommendations, one should engage in physical activity for at least 150 minutes per week; however, the optimal exercise regimen may vary among individuals. Exercise regimens that are customized for each PCOS-afflicted female based on her particular traits and reactions, are essential for maximizing health benefits in coordination with clinician or healthcare professional prescription [17]. To lessen the consequences of PCOS, some non-pharmacological strategies should be used. This suggests that engaging in regular exercise is a valuable strategy for reducing some of the symptoms associated with PCOS [18, 19]. As stated by Covington *et al* [18]. Because skeletal muscles produce cytokines and other peptides called myokines, they are regarded as organs with an endocrine role. As stated by Moro *et al.*, and Aghaie *et al.*, through the regulation of guanylyl triphosphatase GTPases, perilipin 3 PLIN3, catecholamine, and the atrial natriuretic peptide, both found that prolonged aerobic exercise was sufficient to improve lipolysis activity, which is reduced in individuals suffering from PCOS [19, 20]. These physical exercise regimes could be acute or chronic with varying intensities (low, moderate, or high intensity) based on the patient's needs. Anaerobic or aerobic metabolic processes may also be involved [21, 22].

Oxidative Stress and Exercise Relationship in PCOS Patients

The generic phrase "oxidative stress" refers to a disproportion between the body's capacity to use antioxidants to protect itself from the damaging effects of free radicals and the generation of these radicals. Cell death and/or mutations in DNA result from the imbalance [23]. Disruptions to the cells' normal oxidation response and the production of peroxides and free radicals can have toxic effects that damage the cell. To evaluate this imbalance, oxidative and anti-oxidative stress markers can be tested in the patients for timely intervention through pharmacological as well as physical therapy/exercise regimes. Some of these markers are mentioned in the following table 1 [24].

Table 1: PCOS Patients' Oxidative Stress Indicators [25]

Indicators of the Degree of Oxidative Stress	Source	OS Concentrations in PCOS Patients Compared to Normal
Malondialdehyde (MDA)	Serum; RBCs	High
Nitric Oxide (NO)	Serum	High

Advanced Glycosylated End Products (AGEs)	Serum	High
Xanthine Oxidase (XO)	Serum	High

Table 2 summarized the variations in oxidative stress indicators among PCOS patients compared to healthy individuals.

Table 2: PCOS Patients' Oxidative Stress Indicators [26]

Indicators of the Degree of Oxidative Stress	Source	OS Concentrations in PCOS Patients Compared to Normal
Superoxide Dismutase (SOD)	Serum, Erythrocyte, and Follicular Fluid	High/Low
Glutathione Peroxidase (GPx)	Serum	Low
Total Antioxidant Capacity (TAC)	Follicular Fluid; Serum	High/Low
Vitamin E	Serum	Low
Vitamin C	Serum	Low

Both patients and medical professionals benefit from exercise training, which is important in the treatment of PCOS. Enhancing glucose transport and metabolism through physical activity results in improved insulin sensitivity. Increased glucose transport and metabolism brought about by physical activity improve insulin sensitivity. Exercise intensity affects how much a variety of physical characteristics improve. PCOS-affected women's levels of androgen and insulin sensitivity can be improved by engaging in strenuous activity, such as weight training and vigorous aerobic exercise for at least 120 minutes each week. Chronic inflammation in PCOS women can lead to increase ROS level which can be reduced mindful exercise and Yoga [27]. Nonetheless, yoga-based relaxation methods have been associated with lower oxygen consumption and are useful in lowering PCOS metrics [28]. Yoga can help lower the likelihood of PCOS by promoting conception and regulating endocrine factors [28]. Notably, exercise alone may not be sufficient to address a gynecological problem associated with hormones. Via the Hypothalamic-Pituitary-Gonadal (HPG) pathway, the hypothalamus is in charge of producing androgen and ovarian hormones. Follicle-stimulating hormone and luteinizing hormone, two gonadotropins that are of particular importance in PCOS, are produced and released by GnRH. The HPG axis releases LH in response to irregular GnRH discharge from the hypothalamus to the pituitary. Both inflammation and oxidative stress are disruptive factors that elevate the LH-FSH ratio and cause hyperandrogenism. Hypothalamic pathologies in PCOS result in hormonal imbalance and consequent metabolic disturbances like insulin resistance. Studies suggest that physical exercise plays a significant role in improving insulin sensitivity. Furthermore, a usual androgenic rhythm with a lower concentration of LH is the outcome of this insulin sensitivity. According to research by Bonab and Parvaneh, aerobic exercise has an impact on adolescent

females suffering from PCOS [21]. Aerobic conditioning for 12 weeks was found to have a beneficial effect on lipid profile and to raise testosterone and estrogen levels. Jedel and colleagues demonstrated that 16 weeks of aerobic exercise was beneficial in treating hyperandrogenism and oligo/amenorrhea [29]. Physical activity training is progressively employed in the treatment of PCOS. Examination shows that intense exercise significantly boosts cardiorespiratory fitness, body composition, and insulin sensitivity. Evidence suggests that engaging in at least 120 minutes of intense exercise weekly is vital for achieving favorable health results in female PCOS patients [30]. Exercise has been shown to have enormous positive impacts on insulin resistance, particularly in women with PCOS, according to certain research. Health outcomes can get better from vigorous exercise, especially insulin resistance, cardiovascular fitness, and body fat or adiposity. High-intensity exercises, especially resistance exercises, increase insulin sensitivity and improve hyperandrogenic measurements [31].

Diet

One of the main risks associated with the environment that can be changed for preventative measures and early treatment of non-communicable illnesses is diet. One thing observe in PCOS female is lack of knowledge and poor quality of diet. The major portion of diet is on carbohydrate that contribute to weight gain and further lead to complication like insulin resistance, metabolic abnormalities [32]. A diet with fewer calories with lower levels of Glycemic Index (GI) is associated with a significant improvement in insulin resistance, oxidative stress, and chronic inflammation. Herbs with antioxidant properties are of importance in reducing chronic inflammation, along with liver steatosis. These are the supplements (inositol, thiamine, coenzyme Q10, vitamin D, zinc, and selenium) suggested for reducing chronic inflammation and having antioxidant properties [31]. Good intake of vitamins, and minerals like calcium, vitamin D, and herbs with antioxidant property could improve healthy hormonal balance, regular ovulation, increased estrogen level and healthy uterine lining in PCOS women [33]. Increased weight gain is more common in PCOS women and is causative factor of insulin resistance resulting in metabolic abnormalities and reproductive issues. These issues are more common in obese PCOS women as compared to lean PCOS women. so that's means IR is major complication of PCOS women so first line of treatment is life style modification, dietary changes and physical exercises are recommended along with medical treatment. Evidence proved that weight loss, by 5–10%, can increased insulin and testosterone levels and improve menstrual hormones. Among all different nutritional plans, the MD and KD is recognized as a best dietary plan due to its characteristics, like consumption of

omega-3 unsaturated fatty acid, fatty acids, and diminished consumption of animal-derived proteins that may lower many risk factors for metabolic disorders such as endothelial dysfunction, fatty acids alterations and IR [33]. Single diet could not benefit a woman with PCOS. It is observed that mediterranean diet and KD diet have beneficial effect on PCOS women. Pharmacological intervention plays important role in regulating menstrual cycle and reducing hyperandrogenism symptoms [34]. Increased carbohydrate consumptions always major source of obesity and this leads to insulin resistance [32].

Treatment/Management

Treatment for PCOS is symptomatic. Evidence showed that the use of oral contraceptives along with metformin improves hyperandrogenism response in PCOS. Particularly females who are obese showed a remarkable change in BMI [4]. To manage irregular menstruation, oral contraceptives are the primary line of treatment for female PCOS patients. Hirsutism, acne, and Oral contraceptives indirectly reduce the androgen hormone because of its impact on both the pituitary and hypothalamus, which promotes negative feedback for LH. Estrogen (ethinylestradiol) and anti-androgens (Cyproterone Acetate (CPA), drospirenone, norgestimate, levonorgestrel, and desogestrel) are found in most oral contraceptive preparations. Although the exact processes are not yet understood, prebiotic, probiotic, and symbiotic treatment appears to have positive benefits and enhance many biochemical findings in women with PCOS [35].

Vitamin D

All vitamins have some importance in metabolic activities. Above all, vitamin D is necessary to preserve bone homeostasis and calcium metabolism. It is available from dietary sources and mainly from sunlight. Some studies have proved that vitamin D has a positive effect on glycemic control by increasing insulin resistance. It was more effective with a daily low dose of vitamin D. Folic acid, commonly referred to as vitamin B-9, and possesses neuroprotective, cardiac, anticancer, and antioxidant qualities. Additionally, in women with PCOS, folic acid supplementation affects glycemic, inflammatory, and oxidative stress markers [9]. Guidelines for women with PCOS include a physical activity component. Increased levels of insulin sensitivity markers are improved with regular prolonged bouts of aerobic exercise conducted with heart rate and/or VO₂max monitoring. While some data suggest that strength or resistance exercise improves many androgens, further studies are necessary to validate this. The influence of yoga on androgens and insulin sensitivity suggests more research. To find out how various types of exercise impact adipokines and anti-Mullerian hormone levels in females with PCOS, more research is also required [36]. Using supplements like vitamins, minerals,

probiotics, and other dietary supplements may help with PCOS symptoms [37]. A diet high in protein, moderate in carbohydrates, and low in fat, together with an active lifestyle, may greatly reduce PCOS symptoms. Accordingly, a suggestion has been made that future research studies and clinical trials should incorporate various issues such as diet and eating patterns, changes in behavior, herbal and supplemental treatment, and other practices related to lifestyle to draw reliable conclusions [38].

Limitations and Future Recommendations

The inherent weaknesses of the narrative review design are that the design does not have a systematic method of search, quality evaluation of the included studies, and quantitative synthesis, which may introduce selection bias and compromise the reproducibility of drawn conclusions. The majority of primary studies, listed in this review, have small sample sizes (most of them contain less than 50 participants, divided into two or more groups), short intervention periods (most of them include less than 8-16 weeks), and insufficient follow-up periods to determine the long-term sustainability of oxidative stress reduction. Multicenter randomized controlled trials with adequate sample sizes with a long period of follow-up (more than 12 months) of large scale and multicentric nature are urgently required to provide definitive evidence on exercise and dietary interventions aimed at oxidative stress reduction in PCOS women with stratification by PCOS phenotype and a diverse ethnic population including South Asians.

CONCLUSIONS

Based on all the description mentioned in this article, the management of the PCOS depends on sign and symptoms of the disease. The exercise and nutrition has proved to be beneficial effects in the management of PCOS women. The insulin sensitivity improved with regular aerobic exercises with some relaxation techniques to neutralize the effect of ROS. While some data suggest that strength or resistance exercise improves androgens which also help to reduce oxidative stress. Using ketogenic and mediterranean diet along with supplements like vitamins, probiotics are helpful in the reduction of oxidative stress in PCOS women. Meanwhile, PCOS woman are advised to take diet high in protein, moderate in carbohydrates, and low in trans-fat, together with an active lifestyle to get rid of these symptoms.

Authors' Contribution

Conceptualization: MM

Methodology: MM

Formal analysis: MM, NB, SS

Writing and Drafting: MM, NB, SS, AS, RA

Review and Editing: MM, NB, SS, AS, RA

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



Obstetric Outcomes after Cervical Cerclage in Women with Cervical Insufficiency

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ABSTRACT

Most of the local studies in Pakistan have focused only on the prevention of preterm labour after cervical cerclage in women with cervical insufficiency. Still, these studies lack data regarding other outcomes like abortion and premature rupture of membranes after cervical cerclage in women with cervical insufficiency. **Objective:** To determine the obstetric outcomes after cervical cerclage in women with cervical insufficiency. **Methods:** This descriptive study was carried out at the Gynaecology Department, Khyber Teaching Hospital, during the period 22nd May 2024 till 31st March 2025. Women aged 18-35 years with gestational age 13 to 20 weeks and transvaginal ultrasound showing cervical length <2.5cm were enrolled. Cervical cerclage was performed, and pregnancy outcomes were noted in terms of miscarriage, preterm, PROM, prolonged pregnancy and term pregnancy. **Results:** Mean age of the participants was 30.42 ± 5.616 years, mean BMI was 24.070 ± 2.704 kg/m² and mean gestational age was 24.37 ± 4.844 weeks. 85 patients (50.3%) were aged more than 30 years. Participants with parity up to 3 were 94 (55.6%), and 126 patients (74.6%) were housewives. Preterm was the most common pregnancy outcome, recorded in 58 patients (34.3%), 34 patients (20.1%) had a term pregnancy, and prolonged labor was the least common (n=8, 4.7%). **Conclusions:** Preterm delivery was the most common pregnancy outcome after cervical cerclage in this cohort of patients. However, a reasonable number of patients were found with a term pregnancy, showing the adequate prolongation of pregnancy with cerclage in cervical insufficiency.

INTRODUCTION

The demise of conception in the middle month and preterm delivery are significantly influenced by cervical insufficiency. It is characterized as the cervix's anatomical or functional impairment that prevents it from supporting a pregnancy until full term [1]. Characteristics of cervical incapacity frequently encompass uncomfortable dilatation of the cervical canal without spasms or intrauterine infections, as well as a previous preterm delivery or repeated mid-trimester miscarriage [2]. Frequently, labor is brief, and the early fetus is born alive. About 15% of pregnancy-related failures around 16 and 28 weeks are thought to be caused by cervical incompetence, which is believed to occur at a rate of 0.1% to 2% [3]. Mechanically supporting a weak cervix is considered the primary aspect

needed to sustain pregnancy in situations of cervical incompetence [4]. Shirodkar was the first to describe cervical cerclage, and McDonald subsequently made modifications [5]. To extend the gestation until a successful development, women experiencing dilatation of the cervical canal and protruding uterine membranes in the middle of the third trimester may have urgent cervical cerclage surgery as a rescue treatment [6]. Nevertheless, the safety and efficacy of emergency cervical cerclage are still up for debate, and it has the potential to raise the probability of transmission since it exposes the fetal membranes to more genital infectious agents [7]. The cervix is made up of blood vessels and fibromuscular tissue. Although it makes up 15% of the cervical stroma,

muscular connective tissue has an uneven distribution across various levels of the cervix. Early cervical dilatation and miscarriage are believed to result from anomalies in fibromuscular tissue. Cervical insufficiency danger can be accurately predicted among individuals by transvaginal ultrasound assessment of the cervix. Sonographic indicators for this obstetrical syndrome include dilatation of the cervical opening (internal OS), shortening of the endocervical canal length [8]. A study by Prasad *et al.*, has shown that the frequency of abortion was 12.5%, Premature Rupture of Membranes 25%, and preterm labour was 42% after cervical cerclage in women with cervical insufficiency [9]. He *et al.*, in another study, have shown that the frequency of live birth was 82.28% after cervical cerclage in women with cervical insufficiency [1]. Chan *et al.*, in another study, have shown that the frequency of prolonged pregnancy was 61.7% after cervical cerclage in women with cervical insufficiency [8].

Most of the local studies in Pakistan have focused only on the prevention of preterm labor after cervical cerclage in women with cervical insufficiency, but these studies lack data regarding other outcomes, like abortion, premature rupture of membranes after cervical cerclage in women with cervical insufficiency. Moreover, no such study has been done before in our part of the world (the northwestern region of the country), so the results of my study would not only provide further local evidence on this subject but also help to fill the gap outside Pakistan in neighboring countries. The study aims to determine the obstetric outcomes after cervical cerclage in women with cervical insufficiency, as there is a paucity of data on this subject in our local population.

METHODS

This descriptive study was conducted at the Gynecology Department of Khyber Teaching Hospital, Peshawar. Participants were enrolled during the period from 22nd May 2024 till 31st March 2025. Approval for the conduct of the study was taken vide no 316/DME/KMC and CPSP/REU /OBG-2022-020-11423. Women aged 18 to 45 years, gestational age 13 to 20 weeks, prior history of cervical insufficiency in the previous pregnancy and cervical length less than 2.5cm on ultrasound were enrolled. Patients with a history of antiphospholipid syndrome, >4cm cervical dilatation on PV examination, uterine contraction with pain (VAS>3) and diabetic and hypertensive patients were excluded. Cervical insufficiency was confirmed on transvaginal ultrasound with cervical length <2.5cm. Pregnancy outcomes were noted in terms of miscarriage (expulsion of product of gestation before 24 weeks of gestation, PROM (pooling of amniotic fluid in the vaginal fornices before 37 weeks POG, prolonged labor (labor duration >20 hours) and term pregnancy. The sample size was 169, calculated using the WHO sample size formula, Open-epi software, taking a 5% margin of error, 95 %

confidence level, taking the least expected percentage of abortion after cerclage in women with cervical insufficiency, i.e. 12.5% [9]. The sampling technique was non-probability, convenient sampling. After approval from the hospital ethical board, patients fulfilling the inclusion criteria were enrolled. Basic demographics like age, gestational age, parity, cervix length, residence, education, profession and socioeconomic status were noted. The effects, procedure and possible side effects of cervical cerclage were explained to patients. Informed consent was taken from all enrolled participants. By hospital practice, patients had the routine preoperative assessment and care was given. General anesthesia was used throughout the whole surgery. Lithotomy posture was applied. The surgical region was scrubbed and draped, and then a round-bodied needle was used to apply silk at the level of the internal cervical os. All the procedures were done by a consultant gynecologist. Post operatively patients were observed for any contractions, vaginal leak or bleed. Fetal cardiac activity was checked before discharge. The patient was discharged on the first post-operative day. Following discharge, avoidance of coitus was advised. Patients were followed up till delivery (patients who were lost to follow-up were contacted by phone and reminded of their appointment), cervical cerclage was removed at the end of 37 weeks' gestation, electively or in emergency, when patients came in with preterm labor. Obstetric outcomes were noted. Data were analyzed with a statistical analysis program (IBM-SPSS version 22.0). Frequency and percentage were computed for categorical variables like residence, education, profession, and socioeconomic status, history of preterm delivery, abortion, PROM, preterm labor, live birth and prolonged pregnancy. Mean $\pm$ SD was presented for quantitative variables like age, gestational age, parity, cervical length, weight and BMI. Stratification was done about age, gestational age, parity, history of preterm delivery, cervical length and BMI to control the effect of modifiers. Post-stratification, the chi-square test was used, keeping $p \leq 0.05$ as statistically significant.

RESULTS

In this study mean age of the participants was 30.42 ± 5.616 years, mean BMI was $24.070 \pm 2.704 \text{ kg/m}^2$ and mean gestational age was 24.37 ± 4.844 weeks. 85 patients (50.3%) were aging more than 30 years. Participants with parity up to 3 were 94 (55.6%), and 126 patients (74.6%) were housewives (Table 1).

Table 1: Baseline Characteristics of Study Cohort (n=169)

Baseline Parameters		Frequency (%)
Age (Years)	30 or Below	84 (49.7%)
	More Than 30	85 (50.3%)
Parity	3 or Below	94 (55.6%)
	More Than 3	75 (44.4%)

Education	Matric or Below	69 (40.8%)
	Above Matric	100 (59.2%)
Profession	Employed	43 (25.4%)
	House Wife	126 (74.6%)

Preterm was the most common obstetric outcome, recorded in 58 patients (34.3%), followed by miscarriage in 39 participants (23.1%). 34 patients (20.1%) had a term pregnancy. PROM was recorded in 30 participants (17.8%), and prolonged labor was least common (n=8, 4.7%)(Figure 1).

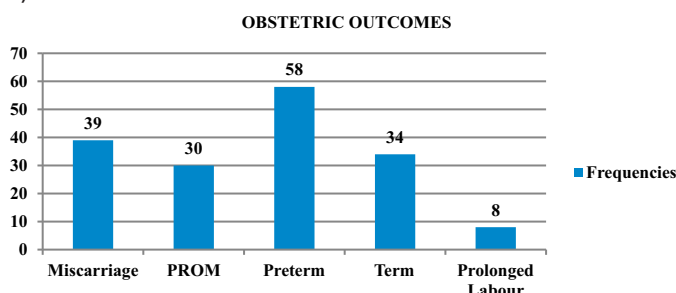


Figure 1: Obstetric Outcomes in Study Cohort (n=169)

Subgroup analysis of obstetric outcomes with patient age showed that the association did not reach statistical significance ($p > 0.05$)(Table 2).

Table 2: Stratification of Obstetric Outcomes with Age (n=169)

Variables		Age (years)		Total	p-value
		30 or Below	More Than 30		
Miscarriage	Yes	17 (43.6%)	22 (56.4%)	39 (100.0%)	0.384
	No	67 (51.5%)	63 (48.5%)	130 (100.0%)	
PROM	Yes	16 (53.3%)	14 (46.7%)	30 (100.0%)	0.661
	No	68 (48.9%)	71 (51.1%)	139 (100.0%)	
Preterm	Yes	33 (56.9%)	25 (43.1%)	58 (100.0%)	0.176
	No	51 (45.9%)	60 (54.1%)	111 (100.0%)	
Term	Yes	17 (50.0%)	17 (50.0%)	34 (100.0%)	0.969
	No	67 (49.6%)	68 (50.4%)	135 (100.0%)	
Prolonged	Yes	5 (62.5%)	3 (37.5%)	8 (100.0%)	0.458
	No	79 (49.1%)	82 (50.9%)	161 (100.0%)	

Miscarriage was more frequent among patients with parity 3 or below (n=23, 59.0%); however, the chi-square p-value was 0.631. Though term pregnancy was more often in patients with parity above 3, the difference was statistically insignificant with a p-value of 0.131 (Table 3).

Table 3: Stratification of Obstetric Outcomes with Parity (n=169)

Variables		Parity		Total	p-value
		30 or Below	More Than 3		
Miscarriage	Yes	23 (59.0%)	16 (41.0%)	39 (100.0%)	0.631
	No	71 (54.6%)	59 (45.4%)	130 (100.0%)	
PROM	Yes	16 (53.3%)	14 (46.7%)	30 (100.0%)	0.781
	No	78 (56.1%)	61 (43.9%)	139 (100.0%)	
Preterm	Yes	30 (51.7%)	28 (48.3%)	58 (100.0%)	0.461
	No	64 (57.7%)	47 (42.3%)	111 (100.0%)	

Term	Yes	15 (44.1%)	19 (55.9%)	34 (100.0%)	0.131
	No	79 (58.5%)	56 (41.5%)	135 (100.0%)	
Prolonged	Yes	5 (62.5%)	3 (37.5%)	8 (100.0%)	0.688
	No	89 (55.3%)	72 (44.7%)	161 (100.0%)	

Subgroup analysis of obstetric outcomes with patient education status showed that 27 (79.4%) participants with an education level above matric achieved term pregnancy compared to 07 (20.6%) patients with an education level of matric or below. The chi-square p-value was 0.007 (Table 4).

Table 4: Stratification of Obstetric Outcomes with Education (n=169)

Variables		Education		Total	p-value
		Matric or Below	Above Matric		
Miscarriage	Yes	20 (51.3%)	19 (48.7%)	39 (100.0%)	0.130
	No	49 (37.7%)	81 (62.3%)	130 (100.0%)	
PROM	Yes	16 (53.3%)	14 (46.7%)	30 (100.0%)	0.124
	No	53 (38.1%)	86 (61.9%)	139 (100.0%)	
Preterm	Yes	27 (46.6%)	31 (53.4%)	58 (100.0%)	0.274
	No	42 (37.8%)	69 (62.2%)	111 (100.0%)	
Term	Yes	7 (20.6%)	27 (79.4%)	34 (100.0%)	0.007
	No	62 (45.9%)	73 (54.1%)	135 (100.0%)	
Prolonged	Yes	4 (50.0%)	4 (50.0%)	8 (100.0%)	0.589
	No	65 (40.4%)	96 (59.6%)	161 (100.0%)	

DISCUSSION

The mean age of the participants was 30.42 ± 5.616 years, mean BMI was $24.070 \pm 2.704 \text{ kg/m}^2$ and mean gestational age was 24.37 ± 4.844 weeks. 85 patients (50.3%) were aged more than 30 years. Participants with parity up to 3 were 94 (55.6%), and 126 patients (74.6%) were housewives. Preterm was the most common pregnancy outcome, recorded in 58 patients (34.3%), 34 patients (20.1%) had a term pregnancy and prolonged labour was least common (n=8, 4.7%). The cornerstone and crucial element in extending pregnancy is surgical treatment [10, 11]. The most popular technique for treating cervical insufficiency is cervical cerclage [12]. Prior research on ECC has primarily used previous research [12]. Those receiving treatment for ECC had a substantially greater length of gestation and a lower risk of preterm birth than those managed with bed rest [13, 14]. Comparable to the current investigation, a prior retrospective study assessed the efficacy of ECC and reported a comparable suture-to-delivery latency [15]. By lengthening the interval between identification and delivery, physical examinations that reveal ECC might raise the risk of spontaneous preterm birth, according to some earlier research [10, 16]. To assess the actual therapeutic impact of ECC in real life, a deeper examination of variables that anticipate favourable pregnancy outcomes is required. Educating women who get ECC requires knowledge of the risk markers associated with the condition, along with all individuals who ought to be properly informed of the potential risks associated with

surgery. Warning signs for birth after 28 gestational weeks were identified in an earlier study of individuals with singleton pregnancies after ECC [16]. While ECC is linked to improved obstetric outcomes if the protruding coverings remain within the cervix, it has been linked to a lower chance of a birth lasting more than 28 gestational weeks if the protruding membranes stretch beyond the cervix. Optimal conception outcomes were linked to gestational ages of more than 22 weeks at ECC, while more serious pregnancy outcomes were linked to gestational ages of less than 22 weeks at ECC [17]. This falls in line with what we discovered. New research has indicated that emergency cervical cerclage is a good way to dilate the cervical cavity in the latter stages of the third trimester, which may result in an increasingly healthy baby [18-20]. The average duration of pregnancy extension increased significantly when Miller *et al.*, contrasted the impact of confinement with emergency cervical cerclage. Additionally, the cerclage group experienced considerably more births than the bed rest group ($p < 0.05$). Research indicates that the emergency cervical cerclage group had a much higher live birth rate (72% vs. 25%) [21]. Additionally, Yang *et al.*, found that women who had emergency cervical cerclage performed after 20 weeks had significantly higher infant birth weights and longer gestation durations at birth [22]. According to Siqueira *et al.*, over eighty percent of women gave birth within 28 weeks, the median pregnancy age at birth was just under 26 weeks, and the mean cerclage-delivery gap was 20 days. Additionally, they proposed that an additional advantage of emergency cervical cerclage is the notable decrease in newborn complications [23]. According to Nutter *et al.*, women who undergo cerclage have a higher chance of giving birth prematurely in their pregnancy if their cervical dilatation is ≥ 2 cm at the time of the surgery [24]. This might be due to women with protruding membranes tend to be more prone to illness, and since fetal membranes are exposed to vaginal germs more frequently. Furthermore, when the degree of cervical dilatation increases, the process becomes more difficult. According to reports, women who had cervical dilatation of at least 2 cm at the time of cerclage implantation were more inclined to obtain an intracervical Foley balloon catheter used for membrane clearance.

This study was limited by its single-center design and lack of a control group managed without cerclage, which may affect the strength of comparative conclusions. Additionally, limited adjustment for confounding factors such as infection status and cervical dilation at presentation may have influenced outcomes. Future studies should include multicenter randomized designs with better stratification of cervical findings and standardized management protocols to more accurately evaluate the effectiveness of emergency cervical cerclage.

CONCLUSIONS

Preterm delivery was the most common pregnancy outcome after cervical cerclage in this cohort of patients. However, a reasonable number of patients were found with a term pregnancy, showing the adequate prolongation of pregnancy with cerclage in cervical insufficiency. Patients with a higher education level were more likely to achieve a term pregnancy compared to patients with lower education. Moreover, miscarriage was frequent in housewives compared to employed women.

Authors' Contribution

Conceptualization: MB

Methodology: MB, UR, AS, S, SY

Formal analysis: UR, AS, SY

Writing and Drafting: MB, AS, MH

Review and Editing: MB, UR, AS, MH, S, SY

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



Diagnostic Accuracy of Chest Ultrasound in Diagnosing Rib Fractures, Keeping CT Chest as Gold Standard

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ABSTRACT

Blunt chest trauma is a frequent cause of emergency visits with a high risk of rib fractures, timely identification of which is crucial for effective patient management. **Objectives:** To assess the accuracy of chest ultrasound in diagnosing rib fractures, keeping CT chest as a gold standard. **Methods:** A cross-sectional validation study was conducted at the Radiology Department, Holy Family Hospital, Rawalpindi, for six months (Jun–Nov 2023). Adult patients presenting with blunt chest trauma in the Emergency Department who fulfilled eligibility criteria were included. The presence of rib fractures was assessed in each patient by chest ultrasound and verified by CT chest. The diagnostic power of the ultrasound method was assessed and reported as sensitivity, specificity and predictive values by comparison with the gold standard. **Results:** The mean age reported was 35.3 ± 5.93 years; there were 61 (57.5%) male and 45 (42.4%) female. The accuracy of chest ultrasound in detecting rib fracture, with CT-chest as the reference standard, demonstrated 92.1% sensitivity, 95.2% specificity, 96.7% and 88.8% positive and negative predictive values, and an accuracy of 93.3%. **Conclusions:** It was concluded that chest ultrasound has good diagnostic power (93.3%) to establish the diagnosis of broken ribs in patients with trauma in emergency settings compared with CT-chest scan.

INTRODUCTION

The third most frequent injury in trauma patients is blunt chest trauma (BCT), which affects 15% of emergency visits [1]. The most frequent causes include falls, car accidents, and direct strikes. The prevalence of fractured ribs in blunt trauma is quite high and is reported to be 39.0% [2]. When rib fractures are swiftly and accurately diagnosed, early management can be initiated in the emergency department, relieving patient symptoms [3]. The lungs can suffer catastrophic consequences, including tearing of the lung or chest wall, causing pneumothorax due to rib fractures. To avoid these life-threatening complications, early diagnosis is crucial [4]. Radiological evaluation is

almost always considered in such individuals; as physical examination rarely reveals any distinguishing indicators for fractured rib diagnosis [5]. The early diagnosis of fractured ribs has historically been a chest x-ray scan, ideally in the standard postero-anterior position. The detection of major diseases like pneumothorax, hemothorax, or contusion has made the chest x-ray study beneficial in some instances, although studies have regularly and continuously indicated low sensitivities for the diagnosis of rib fracture [6, 7]. The most reliable imaging method for identifying rib fractures and ruling out other concurrent diseases is computed tomography (CT). The CT was ranked



first for blunt trauma chest by the American College of Radiology. However, the traditional drawbacks, such as exposure to radiation, higher expenses, and the requirement of leaving the emergency department, continue to exist [8, 9]. Another effective screening method for quickly evaluating trauma patients in the emergency department is ultrasonography [10]. To diagnose rib fractures, chest ultrasound can potentially be as good as a CT scan and can also offer some distinct advantages over chest CT as well for example, being quicker, more convenient, and less exposure to harmful radiation [11]. Contrarily, some studies highlighted drawbacks of chest ultrasound as well, including prolonged examination times, discomfort due to the pressure of the ultrasound probe and missed diagnosis [8, 12]. However, literature supports the utility and diagnostic value of chest ultrasound compared with CT chest [13, 14], but data from lower and middle-income countries like Pakistan are deficient. In the context of low-income countries, health system constraints exist, and in low-resource settings availability of chest CT might be questionable. In such circumstances, ultrasonography can serve the purpose of quickly diagnosing the patients for rib fracture, timely management of which is crucial for better patient outcomes. In a poor country like Pakistan with limited resources, chest ultrasonography can be demonstrated to be cost-effective in the identification of rib fractures in patients visiting the emergency room owing to traumatic chest trauma. The goal is to inspect the practicality and benefit of utilizing chest ultrasonography to detect rib fractures in acute chest trauma using CT chest as the gold standard.

Although computed tomography (CT) is considered the gold standard for detecting rib fractures in blunt chest trauma, its limited availability, high cost, and radiation exposure restrict its routine use in resource-limited settings like Pakistan, where local evidence comparing alternative modalities is scarce. This creates a need for accessible and reliable diagnostic tools for early detection and management. This study aims to compare the accuracy of ultrasound and computed tomography in detecting fractured ribs in the Emergency Department.

METHODS

This study employed an analytical cross-sectional validity study, conducted in the Radiology Department of Holy Family Hospital, Rawalpindi, over six months (Jun-Nov 2023) following synopsis approval by the CPSP (RAD-2027-726-3677). The sample size was determined by an online sample size calculator [15] using a mathematical formula for validity studies as mentioned below [16], based on sensitivity and specificity values reported by Gilbertson et al., [14]. $TP + FN = (Za/2)^2 \text{ Sensitivity} (1 - \text{Sensitivity}) / e^2$.

Sample size (n_1) = $TP + FN / \text{Prevalence of Disease}$. Key parameters considered in the calculation include a sensitivity of 89.3% and specificity of 98.4% for chest ultrasonography in detecting rib fractures, a prevalence of rib fractures in blunt chest trauma of 39.0%, a confidence level of 95%, and an absolute precision of 5.0% for both sensitivity and specificity [14]. The final sample size was estimated to be 106 patients, recruited through non-probability consecutive sampling. Eligible participants included adult patients of either gender presenting to the Emergency Department with chest trauma, suspected fractured ribs with signs/symptoms including chest pain, swelling or tenderness, bruising of skin at the site of trauma and pain during breathing. Patients with critical illness, severe or penetrating trauma, unstable hemodynamic conditions, or those who did not provide consent were excluded. Before data collection, the study obtained ethics approval, and informed consent was taken from all eligible participants or their attendants. Demographic and clinical data were recorded for each patient. Chest ultrasonography was performed using a Honda HS-2600 ultrasound machine along with a high-frequency (5–10 MHz) linear probe. The transducer was placed along the long axis of the rib at the site of maximal pain as indicated by the patient. Rib fractures, costochondral junction involvement, and costal cartilage interruptions were identified based on specific sonographic findings, including interruption of the anterior margin, linear acoustic edge shadowing, or focal hematoma. The duration of each ultrasound examination was also recorded. Following ultrasonography, all patients underwent a CT scan of the chest, which served as the reference standard. A radiologist, blinded to the ultrasound results, interpreted all CT scans to confirm the diagnosis. Data were extracted from the collection tool and analyzed using IBM SPSS software (version 29.0). Descriptive statistics of quantitative variables were expressed as mean $\pm$ SD. A 2 $\times$ 2 contingency table was used to classify true and false, positive and negative cases. Standard formulas were used to calculate and report accuracy. Significance was calculated using the Fisher-Exact test, where a p-value of ≤ 0.05 was considered statistically significant. Rib fractures, costochondral junction involvement, and costal cartilage interruptions were identified based on specific sonographic findings, including interruption of the anterior margin, linear acoustic edge shadowing, or focal hematoma (Table 1).

Table 1: Ultrasound Findings Suggestive of Rib Fractures

Ultrasound Parameters	Availability
Breaks in Cortical Alignment	Present
	Absent

Linear Edge Shadow	Present
	Absent
Interruption in Anterior Margin	Present
	Absent
Focal Hematoma	Present
	Absent

The image of normal echogenic border of the rib shows these specific ultrasound signs (Figure 1).

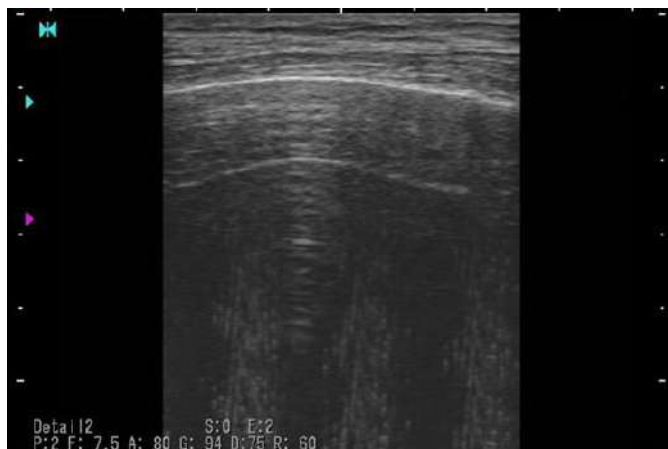


Figure 1: Normal Echogenic Border of Rib

The image of breaks in the cortical alignment of the rib shows these specific ultrasound signs (Figure 2).



Figure 2: Breaks in Cortical Alignment

The image of a linear edge shadow (arrow) and focal hematoma (solid arrow) of the rib shows these specific ultrasound signs (Figure 3).



Figure 3: A Linear Edge Shadow (Arrow) and Focal Hematoma (Solid Arrow)

The image of interruption in anterior margin of the rib shows these specific ultrasound signs (Figure 4).



Figure 4: Interruption in Anterior Margin

RESULTS

There were a total of 106 participants; the mean age reported was 35.3 ± 5.93 years. A majority of the participants, comprising 78 individuals (73.5%), were above 40 years of age. Of the 106 patients, 61 (57.5%) were male, and 45 (42.4%) female. The demographic data are summarized (Table 2).

Table 2: Sociodemographic of Participants (n=106)

Characteristics	Frequency (%)
Age (Year)	35.3 ± 5.93
Age Categories (Year)	
≤40 Years	78 (73.58%)
>40 Years	28 (26.41%)
Sex Distribution	
Female	45 (42.45%)
Male	61 (57.54%)

All patients underwent chest ultrasonography followed by computed tomography (CT) for confirmation of fractures. The pattern of ultrasound findings among the study

participants is given (Figure 5).

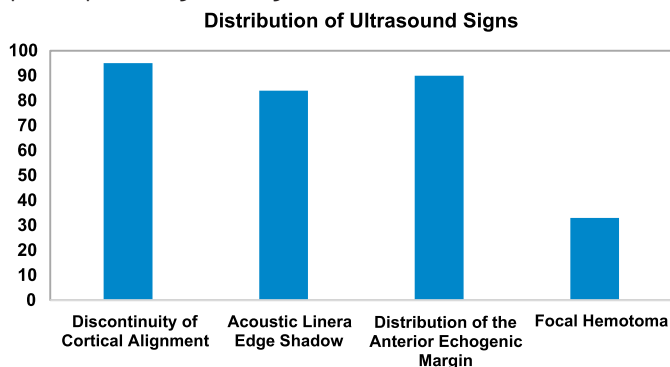


Figure 5: Distribution of Ultrasound Signs Suggestive of Rib Fracture (n=61)

Discontinuity of cortical alignment was present in 58 (95.0%) participants, acoustic linear edge shadow was present in 51 (83.6%), disruption of the anterior echogenic margin was found in 55 (90.1%), while the focal hematoma was evident in 21 (34.4%) participants. Among patients who tested positive on ultrasonography, 59 were confirmed as true positives, whereas 2 were identified as false positives. In contrast, among those who tested negative on ultrasonography, 40 were confirmed as true negatives, while 5 were classified as false negatives. Some of the true positive cases missed rib fracture diagnosis on the ultrasound and vice versa; the difference was significant ($p=0.001^*$) (Table 3).

Table 3: Distribution of Patients as Per Test and Confirmed Diagnosis

Variables	Rib Fracture Present on CT	Rib Fracture Absent on CT	p-Value
Rib Fracture Present on USG Scan	59 (TP)**	02 (FP)****	0.001*
Rib Fracture Absent on USG Scan	05 (FN)***	40 (TN)*****	

The p-value was calculated using Fisher-exact test, *significant p-value, **-TP=True positive ***-FP=False positive ****-FN=False negative *****-TN=True negative

The ability of ultrasound to detect fractured ribs, considering CT-chest as reference standard, demonstrated 92.1% sensitivity, 95.2% specificity, 96.7% and 88.8% positive and negative predictive values, and overall accuracy of 93.3% (Table 4).

Table 4: Diagnostic Parameters for Ultrasound Technique to Diagnose Rib Fractures

Parameters	Value %
Sensitivity	92.18%
Specificity	95.23%
Positive Predictive Value	96.72%
Negative Predictive Value	88.88%
Diagnostic Accuracy	93.3%

DISCUSSION

Chest ultrasound is a promising diagnostic technique to diagnose fractured ribs in chest trauma presenting in the emergency center. Ultrasound technique has several pros over conventional chest CT scan as it avoids ionizing radiation exposure, is mobile, is capable of quick imaging and is more acceptable to patients at the same time. Nonetheless, it is easily accessible and cost-effective as well. The literature reports the efficiency and utility of chest ultrasound in diagnosing rib fractures in emergency settings, but studies from Pakistan are relatively few. The goal was to establish the efficacy of chest ultrasonography in Pakistan's local context to diagnose fractured ribs in emergency settings. We included one hundred and six patients from the Emergency Department, presenting with blunt chest trauma suspected to have fractured ribs. Ultrasound chest was found to be sensitive (92.1%) and specific (95.2%) in correctly diagnosing rib fractures. The predictive values were also reported, 96.7% and 88.8% positive and negative, respectively, along with an accuracy of 93.3%. The negative predictive value was found to be slightly lower in this study; the reasons can be due to the limited sample size. Several studies done worldwide demonstrated the ultrasound method to be as effective as chest CT in terms of sensitivity and specificity to diagnose rib fractures [17-19]. Results of the current study also demonstrated similar results with fairly high diagnostic test parameters for the ultrasound technique compared with CT chest as a standard. A systematic review by Gilbertson et al., based on seven studies from the literature, reported a pooled sensitivity of 89.3% for the chest ultrasound to diagnose rib fracture, and a pooled specificity of 98.4% [14]. The most significant of the ultrasound parameters used in included studies was the cortical irregularity. The results reported in this systematic review are almost identical to the results of the current study, where relatively high diagnostic power is reported for the chest ultrasound method. In the current study, the discontinuity of cortical alignment was found in 95% of the participants, while 83.6% showed acoustic linear edge shadow, 90.1% had disruption of the anterior echogenic margin, and 34.4% had focal hematoma. Authors, including Çelik et al., conducted a study on one hundred and forty-five patients presenting in the ER with blunt chest trauma injury and assessed the utility of ultrasound to diagnose the rib fractures [17]. The authors reported an overall accuracy of 80%, which is slightly less than what was reported in the current study, along with 72.7% specificity, which is also somewhat lower than what was reported in the current study and 91.2% sensitivity, which is similar to the value reported in the current study. The differences in these

values can be due to variations in sample size, study population and other contextual factors. The authors concluded that if a patient with blunt chest trauma comes to the emergency with pain on one side, ultrasound can be used to check for rib fractures, and if the ultrasound does not show any fractures at the most painful spot and nearby ribs, it strongly suggests that a rib fracture is unlikely [17]. Jelyani *et al.*, conducted a study on one hundred and thirteen patients to compare the diagnostic power of chest ultrasound to diagnose rib fractures, and the authors reported that out of the total, 66.3% of patients were found to have at least one broken rib by CT and 54.9% by ultrasound [18]. Overall, the authors reported 81.5% sensitivity of ultrasound, but with one fractured rib, the sensitivity was reported to be 73.1%, while for five fractured ribs, the sensitivity was reported as 100%. In the current study, researchers did not consider the number of fractured ribs while determining the diagnostic power of ultrasound, but overall, the findings of both studies tend to be in a similar direction. Kumar *et al.*, conducted a study in India with a similar aim. The authors considered data from sixty consecutive patients presenting with chest trauma in the ER and reported that in sixty patients, there were 72 fractured ribs, out of which 62 were correctly picked up on the ultrasound test [19]. The authors did not report diagnostic accuracy in terms of sensitivities or specificities, but the conclusion supports that chest ultrasound is as effective in picking up broken ribs as chest X-ray and Chest CT scan, so these can be used alternatively in clinical settings. Devadoss *et al.*, reported the diagnostic accuracy of e-Fast ultrasound in stable blunt trauma injury to diagnose fractured ribs, and the authors reported that this technique is a good alternative to conventional techniques to diagnose fractured ribs in patients with chest trauma [20]. This study emphasizes the importance of using chest ultrasound to diagnose broken ribs compared to chest CT scan. As a non-invasive and cost-effective imaging method, ultrasound avoids ionizing radiation exposure, making it a safer alternative to traditional techniques like chest X-rays and CT scans. Additionally, its affordability, widespread availability, and ability to be performed at the bedside make ultrasound highly valuable in emergency settings and resource-limited areas. If a high diagnostic yield is established, ultrasonography (USG) may serve as a valuable alternative for patients with multiple trauma who are hemodynamically unstable or in intensive care settings, where mobilizing the patient for CT can be challenging. By enabling timely and accurate diagnoses, ultrasound can help clinicians improve patient outcomes. This study was limited by a single-center design and

relatively small sample size, which may affect the generalizability of the findings. Additionally, operator dependency of ultrasound and lack of long-term follow-up may have influenced diagnostic consistency. Future studies should include larger, multicenter cohorts and standardized operator training protocols to further validate the diagnostic accuracy of chest ultrasound for rib fractures.

CONCLUSIONS

It was concluded that chest ultrasound was found to have good diagnostic power (93.3% accuracy) to establish the diagnosis of broken ribs in blunt chest trauma patients in emergency settings compared with chest CT scan.

Authors' Contribution

Conceptualization: RR

Methodology: SR, RR

Formal analysis: AZ

Writing and Drafting: SR, SBK, NK, BN

Review and Editing: SR, RR, SBK, NK, AZ, BN

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 C-Reactive Protein and D-dimer Status with Maternal Outcomes in Pregnant Women with COVID-19

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ABSTRACT

C-reactive protein (CRP) and D-dimer are crucial biomarkers that play a key role in maternal health, helping to assess risks and minimize complications. **Objectives:** To find the association of CRP and D-dimer status with maternal outcomes in pregnant women with COVID-19.

Methods: The prospective cohort study was carried out at the Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore, from July to September 2020. Demographic data, laboratory parameters including COVID-19, D-dimer and CRP levels and maternal outcomes were recorded. Crosstabs and binary logistic regression analyses were performed to measure the risk of adverse maternal outcomes. **Results:** Among 112 COVID-19 suspects, 58 (51.8%) were diagnosed as COVID-19 positive, 82 (73.2%) tested positive for CRP, and 19 (17.0%) were D-dimer positive. COVID-19 positive women exhibited twice the mean D-dimer levels (0.92 ± 1.36 vs. 0.43 ± 0.70 $\mu\text{g/mL}$) and a slightly lower mean CRP level (26.47 ± 31.55 vs. 29.30 ± 32.79 mg/L). Ventilator requirement (32.8% vs. 11.1%) and maternal death rate (29.3% vs. 11.1%) were three times higher in COVID-19 positive cases as compared to the COVID-19 negative cases. CRP positive status and COVID-19 positive showed a statistically significant association and higher risk for ventilator requirement as well as maternal death. However, D-dimer positive status did not show any association with ventilator requirement and maternal death. **Conclusions:** COVID-19 positivity and CRP positivity in pregnant women are associated with adverse maternal outcomes, including increased ventilator requirement and mortality. However, D-dimer positivity was not related to these adverse maternal outcomes.

INTRODUCTION

C-reactive protein (CRP) and D-dimer are crucial biomarkers that play a key role in maternal health, helping to assess risks and minimize complications [1]. CRP, a protein produced by the liver in response to inflammation, serves as an important marker of systemic health issues. Likewise, D-dimer, which results from fibrin breakdown, provides insight into coagulation activity. Elevated levels of these biomarkers have been strongly linked to increased

mortality in patients suffering from COVID-19 [2]. Among pregnant women, these biomarkers act as significant predictors of future health risks, allowing early identification of those who may experience severe complications. Research suggests that CRP and ferritin levels can signal a heightened risk of mortality and the need for intensive medical interventions such as mechanical ventilation [3]. Additionally, CRP levels have been

correlated with conditions like preeclampsia and infections, which negatively impact placental health. These disruptions can lead to complications such as preterm birth and low birth weight, necessitating early monitoring and intervention to protect maternal and fetal well-being [4]. Elevated D-dimer levels in pregnant women indicate potential coagulation disturbances, increasing their vulnerability to serious health conditions. High levels have been associated with a greater likelihood of thromboembolic events, such as deep vein thrombosis and pulmonary embolism, which pose severe risks to maternal health [5]. Coagulation imbalances can also interfere with placental blood flow, potentially leading to fetal growth restriction and placental abruption. Beyond maternal complications, neonates may also be affected, with elevated D-dimer levels linked to conditions such as neonatal sepsis, requiring immediate medical intervention. Recognizing the potential impact of these biomarkers, healthcare providers emphasize the importance of regular monitoring to facilitate timely intervention. Effective management strategies, including anticoagulation therapy and measures to regulate inflammation, help mitigate associated risks. Addressing these biomarkers through proactive medical approaches enhances obstetric care, reducing the likelihood of severe complications and ensuring better health outcomes for both the mother and baby. The COVID-19 pandemic has further emphasized the relevance of CRP and D-dimer in maternal healthcare. Studies indicate that elevated levels of these biomarkers are associated with severe pregnancy complications, including increased hospitalizations, ICU admissions, and higher maternal mortality rates [1, 6]. Despite the growing attention to CRP and D-dimer in predicting disease severity and outcomes in various populations [7], their specific relationship with maternal outcomes in pregnant women affected by COVID-19, particularly within local pregnant populations, remains under-explored.

Although CRP and D-dimer are established biomarkers of inflammation and coagulation and have been associated with disease severity in COVID-19, limited evidence exists regarding their specific relationship with maternal outcomes in pregnant women, particularly in local populations. This lack of context-specific data restricts early risk stratification and timely intervention for high-risk pregnancies affected by COVID-19. This study aims to investigate the relationship between these biomarkers and maternal health outcomes in pregnant women diagnosed with COVID-19.

METHODS

The prospective cohort study was carried out at the Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore, from July to September 2020. Ethical

approval was obtained from the ethical review committee of Fatima Jinnah Medical University, Lahore, vide reference no. 44-Res-Proposal/CERC dated 16-07-2020. Informed consent was taken from all participants. A total of 112 pregnant women, with symptoms of flu, body pains, cough, and fever, having a history of exposure to coronavirus patients, suspected of COVID-19, and hospitalized during the study period, were included by a non-probability purposive sampling technique. All those patients who had any potential source of elevated D-dimer, such as family or personal history of H/O venous thromboembolism, were excluded from the study. Similarly, patients with maternal age over 45 years, morbid obesity, patients with recurrent miscarriages, patients with DVT, patients with history of smoking, multiple pregnancies, coagulation disorders, patients on anticoagulant therapy, placental abruption, placenta, women with recent surgery and women with pre-eclampsia and eclampsia were also excluded from the study. All patients underwent detailed history and physical examination, and further management was done in collaboration with the Gynaecology and Medical Departments. A proforma was created to collect demographic information such as patient age, occupation, and education. The number of prenatal visits to the hospital, history of obstetric, perinatal, or postnatal obstetric complications or fetal complications such as preterm birth, intrauterine growth restriction (IUGR), or perinatal death were monitored. Blood specimen was drawn immediately after enrolment in the study to estimate D-dimer and CRP levels, and a nasopharyngeal swab for COVID-19 infection by PCR. Blood for D-dimer level estimation was collected in citrated vacutainers and processed on the same day. Coagulated and hemolyzed specimens were not processed for analysis. All blood specimens were centrifuged and subjected to quantitative estimation of D-dimer based on the chemiluminescence enzyme immunoassay by the PATHFAST [8]. A level of D-dimer ≥ 0.5 $\mu\text{g/mL}$ was taken as positive [9]. The quantitative estimation of CRP level was based on the immunoturbidimetric method by Human Diagnostics [10]. CRP values for pregnant women range from 7-9mg/l depending on gestational age [11]; therefore, CRP level ≥ 10 mg/L was considered positive. The real-time reverse transcriptase-polymerase chain reaction (RT-PCR) method was used for the detection of SARS-CoV-2 RNA in nasopharyngeal swabs by WHO guidelines [12]. All pregnant women were followed up for the incidence of adverse maternal outcomes, including ventilator requirement and mortality during hospitalization. Statistical Package for Social Sciences (SPSS) version 26.0 was used for data analysis. Mean $\pm$ SD was calculated for continuous variables. Frequency (percentage) was calculated for categorical variables, and the chi-square test was used to compare the frequency (percentage) between study groups. Crosstabs and binary logistic regression analyses were performed to calculate odds

ratios and adjusted odds ratios with 95% CI. p -value ≤ 0.05 was considered significant.

RESULTS

The age of the studied women ($n=112$) ranged from 20 to 40 years. Women aged ≤ 30 years, with a gestational age of 28–40 weeks and parity ≥ 2 , participated in greater numbers compared to their respective counterparts. Among 112 COVID-19 suspects, 58 (51.8%) were diagnosed as COVID-19 positive, 82 (73.2%) tested positive for CRP, and 19 (17.0%) were D-dimer positive. The overall mean D-dimer level was 0.68 ± 1.12 $\mu\text{g/mL}$, while the mean CRP level was 27.83 ± 32.04 mg/L . When participants were categorized into COVID-19 negative and positive groups and compared for D-dimer and CRP positive status, COVID-19 positive women had twice the rate of D-dimer positive cases (22.4% vs. 11.1%) and a slightly lower rate of CRP positive cases (70.7% vs. 75.9%). Similarly, COVID-19 positive women exhibited twice the mean D-dimer levels (0.92 ± 1.36 vs. 0.43 ± 0.70 $\mu\text{g/mL}$) and a slightly lower mean CRP level (26.47 ± 31.55 vs. 29.30 ± 32.79 mg/L) compared to the COVID-19 negative women (Table 1).

Table 1: Baseline Characteristics of Study Population

Baseline Characteristics		Total 112 (100.0%)	COVID 19 Negative 54 (48.2%)	COVID 19 Positive 58 (51.8%)
		n (%)		
Age (Years)	≤ 30	85 (75.9%)	40 (74.1%)	45 (77.6%)
	> 30	27 (24.1%)	14 (25.9%)	13 (22.4%)
Gestational Age (Weeks)	13–28	23 (20.5%)	12 (22.2%)	11 (19.0%)
	28–40	75 (67.0%)	35 (64.8%)	40 (69.0%)
	Postpartum	14 (12.5%)	7 (13.0%)	7 (12.1%)
Parity	≤ 1	34 (30.4%)	20 (37.0%)	14 (24.1%)
	2–4	55 (49.1%)	23 (42.6%)	32 (55.2%)
	≥ 5	23 (20.5%)	11 (20.4%)	12 (20.7%)

Table 2: Risk Factors of Adverse Maternal Outcomes by Cross-Tab Analyses

Variables		Ventilator Required				Maternal Death			
		No	Yes	OR (95% CI)	p-Value	No	Yes	OR (95% CI)	p-Value
CRP Status	Negative	96.7%	3.3%	Ref	0.008	96.7%	3.3%	Ref	0.014
	Positive	70.7%	29.3%	12.0 (1.5–93.1)		73.2%	26.8%	10.6 (1.3–82.8)	
D-dimer Status	Negative	81.7%	18.3%	Ref	0.034	82.8%	17.2%	Ref	0.066
	Positive	57.9%	42.1%	3.2 (1.1–9.3)		63.2%	36.8%	2.8 (0.9–8.2)	
COVID 19 Status	Negative	88.9%	11.1%	Ref	0.012	88.9%	11.1%	Ref	0.032
	Positive	67.2%	32.8%	3.8 (1.4–10.7)		70.7%	29.3%	3.3 (1.1–9.1)	

After adjustment, CRP positive status and COVID-19 positive showed statistically significant association and higher risk for ventilator requirement as well as maternal death. However, D-dimer positive status did not show any association with ventilator requirement and maternal death (Table 3).

Antenatal Clinic Registration	Yes	16 (14.3%)	9 (16.7%)	7 (12.1%)
	No	96 (85.7%)	45 (83.3%)	51 (87.9%)
CRP Status	Negative	30 (26.8%)	13 (24.1%)	17 (29.3%)
	Positive	82 (73.2%)	41 (75.9%)	41 (70.7%)
D-dimer Status	Negative	93 (83.0%)	48 (88.9%)	45 (77.6%)
	Positive	19 (17.0%)	6 (11.1%)	13 (22.4%)

Overall, 25 (22.3%) women required a ventilator, and 23 (20.5%) women did not survive. Ventilator requirement (32.8% vs. 11.1%) and maternal death rate (29.3% vs. 11.1%) were three times higher in COVID-19 positive cases as compared to the COVID-19 negative cases (Figure 1).

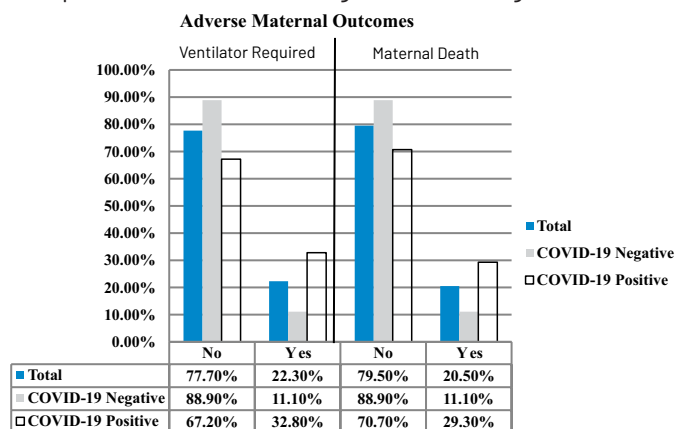


Figure 1: Incidence of Adverse Maternal Outcomes in Women with and without COVID-19

CRP positive status showed statistically significant association and higher risk for both ventilator requirement and maternal death. COVID-19 positive status also showed statistically significant association and higher risk for both ventilator requirement and maternal death. Whereas D-dimer positive status showed statistically significant association and higher risk only for ventilator requirement (Table 2).

Table 3: Risk Factors of Adverse Maternal Outcomes by Binary Logistic Regression Analyses

Variables	Ventilator Required		Maternal Death	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value
CRP Status (Negative/Positive)	13.7 (1.7-110.6)	0.014	11.7 (1.4-93.9)	0.020
D-dimer Status (Negative/Positive)	2.3 (0.7-7.3)	0.159	1.9 (0.6-6.3)	0.253
COVID-19 Status (Negative/Positive)	4.3 (1.4-12.5)	0.007	3.6 (1.2-10.4)	0.019

DISCUSSION

The body's ability to clot blood is impaired by both pregnancy and COVID-19 infection [13]. It is generally accepted that increased levels of D-dimer may be related to poor prognosis in COVID-19 disease, but this aspect is not studied comprehensively in pregnant patients [14, 15]. In current study, it was tried to establish an association between levels of D-dimer and CRP with the clinical condition of COVID-19 pregnant patients. As regards the maternal complications and maternal outcomes regarding CRP Status, D-dimer status and COVID status, it was observed that 96.7% of CRP Negative patients did not require a ventilator, and only 3.3% of these patients required a ventilator. On the contrary, 70.7% of CRP-positive patients did not require a ventilator, and only 29.3% of CRP patients required a ventilator, $p=0.008$. Similarly, when CRP status was correlated with maternal outcome (maternal death), the results showed that 96.7% of patients who were CRP Negative were alive at the end of follow-up, and only 3.3% of patients were dead. On the contrary, among CRP-positive patients, 73.2% were alive and 26.8% were dead. At the end of the follow-up and the results were statistically significant with $p=0.014$. So, CRP-positive patients had a poor prognosis in our study. When we review the literature regarding the association between CRP levels and the prognosis of COVID-19 pregnant patients, there exists a strong correlation. Khalil *et al.*, in their study of 105 pregnant women, quoted that the mean CRP level in these patients was 83.9 ± 103.9 mg/L, and most of the maternal and fetal complications were noted in the third trimester of pregnancy [16]. Another study of 50 COVID-19 pregnant patients documented that 22 (44%) patients showed elevated CRP levels, but no fetomaternal death was reported in this study, although 4 (8%) babies required ICU management and a few babies had physiological jaundice [17]. This may be because they included only mild cases of COVID-19 in pregnant patients in their study. Anter *et al.*, conducted a study between May 2020 and July 2021, including 65 pregnant women. COVID-19 disease was found in 83% of pregnant patients after roughly 5 months of pregnancy. The mean CRP level at admission was 28.86 ± 35.20 . Thrombolytic manifestations, decreased lymphocyte count, and CRP levels at admission predicted ICU admission. The CRP level in ICU-admitted patients was statistically significantly higher than in non-ICU-admitted patients ($p=0.001$) [18]. CRP levels were

elevated in 59% of patients in the early stage of disease in a study of 60 pregnant women. Increased CRP and D-dimer levels were associated with severe pneumonia. The median CRP level in admitted patients was 17.8 mg/L [19]. Maternal and fetal outcomes in pregnant women with COVID-19 were studied by enrolling 105 pregnant women and taking into account measurements such as hemoglobin, TLC, blood ferritin, CRP and blood creatinine. A significant proportion of patients (76.2%) had elevated D-dimer levels. Fetal and maternal complications were assessed in the first, second and third trimesters of pregnancy. The study clearly showed that the mothers faced a more serious problem in the third trimester, with more than 25% of patients requiring a ventilator and two-thirds of patients requiring oxygen therapy [16]. However, in our study, no statistically significant association was established between D-dimer levels and maternal outcome. Another prospective study examined 50 pregnant women who tested positive for COVID-19 at BJ Medical College and Government Hospital, Ahmedabad, between June and October 2020. Across multiple testing sites, D-dimer levels were slightly elevated in 19 (38%) patients. Of the 50 patients, 26 (52%) underwent C section and 23 (46%) were delivered vaginally. There were no maternal or fetal deaths [17]. In this study, fetal and maternal outcomes were favourable; this was probably because most patients had slightly elevated D-dimer, suggesting that D-dimer levels are directly related to fetal and maternal outcomes in pregnant women with COVID-19. A study in Spain, during the first 30 days of the pandemic, published medical records of the first 60 pregnant women infected with COVID-19 between March 14 and April 14, 2020, were reviewed. D-dimer levels were elevated in these patients and associated with severe pneumonia. SVD was detected in 18 women (30%) during the study period, and no maternal deaths were reported [19]. Similar to current's, a study in Iran included 106 pregnant women with COVID-19 in the study. The mean D-dimer value in COVID-19 patients was 852.14 ± 915.08 mg/L, and D-dimer was above the normal range (0-0.5 mg/L) in 79.2% of pregnant COVID-19 patients. The most common maternal complications in this study were Cesarean section (31.1%), miscarriage (5.7%) and preterm birth (3.8%) [20].

This study is limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings to broader populations. Additionally, the lack of longitudinal follow-up limits the ability to assess long-term maternal and fetal outcomes associated with CRP and D-dimer levels. Future multicenter, large-scale prospective studies with serial monitoring of inflammatory and coagulation markers are recommended to better clarify their prognostic value in pregnant COVID-19 patients.

CONCLUSIONS

It was concluded that COVID-19 positivity and CRP positivity in pregnant women are associated with adverse

maternal outcomes, including increased ventilator requirement and mortality. However, D-dimer positivity was not related to these adverse maternal outcomes. These findings highlight the importance of early medical intervention for pregnant women with COVID-19 and CRP positivity to prevent or minimize complications, while emphasizing that D-dimer alone may not be a reliable predictor of adverse maternal outcomes.

Authors' Contribution

Conceptualization: SA

Methodology: SA, ZK, UL

Formal analysis: SA, SR, SIM

Writing and Drafting: ZK, SH

Review and Editing: SA, ZK, SR, UL, SIM, SH

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 and Effects of Self-Medication Practice among Pharmacy Students: A Cross-Sectional Study in Karachi

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ABSTRACT

The prevalence of self-medication is notably high among medical students compared to the general population, which is primarily attributed to advanced knowledge of pharmacology and easier access to pharmaceuticals either through educational resources or hospital attachments, potentially underestimating the risks involved. **Objectives:** To determine the prevalence and effects of self-medication practice among pharmacy students: a cross-sectional study in Karachi. **Methods:** The study employed a cross-sectional descriptive design conducted on 283 pharmacy students using a structured, self-administered questionnaire developed specifically. The collected data were analyzed by SPSS-21 software. **Results:** The outcomes revealed the response rate of 92.93%, with the largest group of participants (23%) being first-year students, comprised mainly female respondents (72.24%), between the ages of 21-23. The relationship between both age and year of study with the usage of self-medication without consulting a doctor is found to be significant. Students were engaged in the use of self-medication occasionally. The commonly reported symptoms and conditions practiced were headaches (55.1%). However, a statistically significant relationship was observed between certain medical conditions, particularly fever, diarrhea, and nausea/vomiting, and gender. Further evaluated perceptions of the safety of self-medication, with statistical analysis highlighting significant associations with both age ($p=0.036$) and year of study ($p=0.014$). **Conclusions:** The Prevalence of self-medication among pharmacy students is high. It is needed to focus on developing and implementing programmes about the risks of self-medication, and to ensure self-practices along with a control system and monitoring of drug sales by health decision-makers and policymakers.

INTRODUCTION

Self-medication, or SM, is used for conditions diagnosed by the patient without professional healthcare guidance. Such practice involves procuring medications without a prescription, recycling leftover medications, and consultation from non-professional sources like family or the web [1-3]. Self-medication may seem the best convenience for many ailments, but it has its major health hazards, including misdiagnosis, inappropriate drug choices, and adverse reactions to the drugs taken [4]. Prevalence of SM varies in medical students from different countries in studies undertaken to ascertain the SM practice among medical students [5-7]. The practice is

especially more prevalent among medical students due to their advanced knowledge of pharmacology and easy access to medicines through educational resources [8, 9]. It is important to know the nature and the extent of self-medication practices among medical students because their habits become models for future patient care and public health [10, 11]. In Kermanshah, Iran, the prevalence is 89.6% due to easy access to medications and high stress [12]. In addition, peer influence, easy access to medications, and social factors have also been shown to serve as initiators of self-medication behaviour among the students [13, 14]. Medical students mostly possess



confidence in self-diagnosis, which can be dangerous as it results in underestimation of health risks due to their lack of proper medication use [9, 15]. Although numerous studies have been carried out on self-medication practices, very few studies investigate the long-term effects of self-medication practices and how to intervene in bringing such behaviours to an end among medical students. There are also a few studies comparing the self-medication practices of students through the various medical years and across cultures [16].

This study aims to fill those gaps by exploring prevalence and motivation, most used drugs, and adverse effects of self-medication in pharmacy students in a public sector university in Karachi. By studying this subgroup of pharmacy students, the purpose is to provide insight into the determinants of professional training and influencing self-medication behaviour. The findings can be useful in designing interventions for responsible self-care and medication use among future healthcare providers. In addition, empowering pharmacy students with the right attitude toward medication practices will help to promote safe and efficient use of medicines at home and in the workplace.

METHODS

A cross-sectional descriptive method to assess the prevalence and adverse consequences of self-medication among pharmacy students participating in a public sector university in Karachi was designed, which allows the collection of data from a defined population at a particular point in time for analysis of trends and patterns in self-medication. Participants for the study were students of the Department of Pharmacy of a Public sector University in Karachi. Students were selected using convenience sampling methodology, students (from first to final year) who were available promptly and willing to participate during the study period. Concerning the prevalence rate 89.6% for self-medication [12], a total 144 is sample size calculated at a 95% confidence level and $\pm 5\%$ margin of error, using the Open Epi sample size calculator, Version 3. Although the calculated sample size was 144 but the data was collected, almost double respondents. Sample size $n = [DEFF * Np(1-p)] / [(d^2 / Z_{1-\alpha/2}^2 * (N-1) + p(1-p))]$ (Table 1).

Table 1: Sample Size for Frequency in a Population

Variables	Values
Population size (for finite population correction factor or fpc)(N):	1000000
Hypothesized % frequency of outcome factors in the population (p):	89.6% $\pm$ 5
Confidence limits as % of 100 (absolute $\pm$ %)(d):	5%
Design effect (for cluster surveys-DEFF):	1
Confidence	Sample Size
95%	144
99%	248

The data were collected using a structured, self-administered questionnaire developed specifically for this study. The instrument consisted of three major components: demographic information (age, gender, academic year) and information on self-medication practices (type of drugs, frequency, reasons, sources of information and illnesses treated), and adverse effects (type, severity, and response). An objective pilot test of the questionnaire (as well as the feedback from the pilot test) was conducted with a small group of students (grades 6, 8, 9, 10, 11, 12, 14, 15), and subsequently revised and improved. A final version of the questionnaire was distributed both in the classroom during class sessions and online using Google Forms between July and September 2024, with instructions explaining that answers to the questionnaire must be honest and confidential. All responses were analyzed through SPSS version 21. Demographic characteristics, such as total number of students, gender, and self-medication frequency, were summarized by means and squared of the mean and standard deviations. To examine associations between demographic variables and self-medication patterns, inferential statistics were performed (chi-square test with $p \leq 0.05$ was considered statistically significant).

RESULTS

The study recruited 263 questionnaires out of 283 students approached, yielding a response rate of 92.93%. Most participants were first-year students (23%), and respondents were female (72.24%), between 21 and 23 years (54.7%), while male students accounted for 27% of the total respondents. Demographics, frequency and percentiles are mentioned. Participants used medication without consulting a doctor, 205 responded positively. The statistical analysis indicated a significant relationship between age, year of study and the usage of self-medication without consulting a doctor (Table 2).

Table 2: Detailed Demographics of Participants

Characteristics	n (%)
Age Group	
18-20	91 (34.6%)
21-23	144 (54.7%)
24-26	28 (10.6%)
Gender	
Female	190 (72.24%)
Male	73 (27%)
Marital Status	
Single	249 (94.6%)
Married	14 (5.3%)
Year of Study	
First Year	62 (23%)
Second Year	55 (20.9%)
Third Year	54 (20%)

Fourth Year	34 (12%)
Final Year	58 (22%)

The majority (n=106, 40.3%) indicated that they did so occasionally, a few times a year, while a substantial number (n=64, 24.3%) reported that they engaged in self-medication frequently, several times a month. In addition, few (n=78) reported self-medication used rarely once or twice a year (Figure 1).

Frequency of self Medication

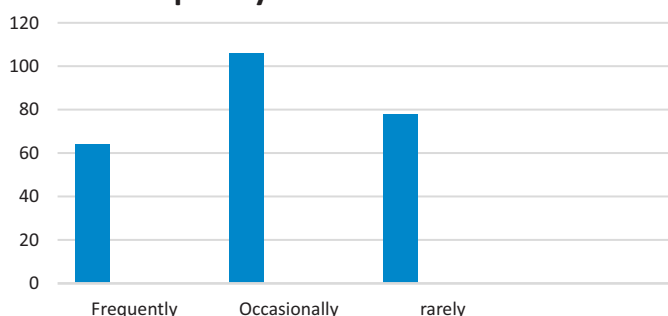


Figure 1: Self-medication Frequency Distribution

The commonly reported symptoms and conditions were headaches (55.1%, n=145), fever (36.1%, n=95), sore throat/cough (25.1%, n=66), diarrhea (12.2%, n=32), nausea and vomiting (15.6%, n=41), and allergies (20.2%, n=53). A statistically significant relationship was observed between certain medical conditions, particularly fever, diarrhea, and nausea/vomiting, and gender. Self-medication for these conditions was more prevalent among women, while the prevalence was significantly lower in men. Regarding age, none of the conditions showed a statistically significant association with self-medication. For gender, however, there was a significant relationship with fever ($\chi^2=7.623$, $p=0.006$), diarrhea ($\chi^2=6.641$, $p=0.010$), and nausea/vomiting ($\chi^2=10.706$, $p=0.001$), indicating higher self-medication rates for these conditions among women. In terms of year of study, fever ($\chi^2=10.934$, $p=0.027$), diarrhea ($\chi^2=11.271$, $p=0.024$), and nausea/vomiting ($\chi^2=11.491$, $p=0.022$) showed significant associations. Lastly, analysis by known illness did not reveal any statistically significant relationship with self-medication for headache, fever, sore throat/cough, diarrhea, nausea/vomiting, or allergies, suggesting that prior illness status did not influence the decision to self-medicate for these symptoms (Table 3).

Table 3: Statistical Relationship of Symptomatic Treatment Against Different Factors

Self-Medication Prevalence	Chi-Square Value	p-value	Decision
Age			
Fever	2.949	0.229	Non-Significant
Sore Throat/Cough	0.887	0.642	Non-Significant
Diarrhea	2.835	0.242	Non-Significant
Nausea and Vomiting	5.119	0.077	Non-Significant
Allergies	0.776	0.678	Non-Significant

Gender			
Headache	1.08	0.299	Non-Significant
Fever	7.623	0.006	Significant
Sore Throat/Cough	3.255	0.071	Non-Significant
Diarrhea	6.641	0.010	Significant
Nausea and Vomiting	10.706	0.001	Significant
Allergies	2.168	0.141	Non-Significant
Year of study			
Headache	7.361	0.118	Non-Significant
Fever	10.934	0.027	Significant
Sore Throat/Cough	8.839	0.065	Non-Significant
Diarrhea	11.271	0.024	Significant
Nausea and Vomiting	11.491	0.022	Significant
Allergies	3.741	0.442	Non-Significant
Known illness			
Headache	0.744	0.388	Non-Significant
Fever	0.262	0.609	Non-Significant
Sore Throat/Cough	0.486	0.486	Non-Significant
Diarrhea	0.099	0.753	Non-Significant
Nausea and Vomiting	0.301	0.583	Non-Significant
Allergies	0.16	0.689	Non-Significant

* $p \leq 0.050$ is statistically significant

The most commonly used medications were painkillers (n=171), fever reducers (n=71), cough syrups (n=61), antibiotics (n=38), multivitamins (n=44), herbal remedies (n=5), sleeping pills (n=8), antidepressants (n=54), and antiallergy medications (n=9). Statistical analysis revealed significant associations between certain types of medications and demographic factors, particularly age and year of study. For age, a statistically significant relationship was found with the usage of cough syrups ($\chi^2=7.046$, $p=0.030$), antibiotics ($\chi^2=6.858$, $p=0.032$), and sleeping pills ($\chi^2=6.104$, $p=0.047$), indicating that participants' age influenced their choice of these medications. Other medications did not show a significant relationship with age. Regarding gender, the only significant association was with the use of cough syrups ($\chi^2=3.920$, $p=0.048$). In terms of year of study, significant associations were observed for cough syrups ($\chi^2=13.780$, $p=0.008$), antibiotics ($\chi^2=12.191$, $p=0.016$), multivitamins ($\chi^2=14.955$, $p=0.005$), and sleeping pills ($\chi^2=12.083$, $p=0.017$), indicating that students' academic year influenced their self-medication choices for these drugs (Table 4).

Table 4: Association of Age, Gender and Year of Study with Different Classes of Drugs

Medications Commonly Used for SM	Chi-Square Value	p-value	Decision
Age			
Pain Killers	1.118	0.572	Non-Significant
Fever Reducers	1.356	0.508	Non-Significant
Cough Syrups	7.046	0.030	Significant
Antibiotics	6.858	0.032	Significant
Multivitamins	4.605	0.100	Non-Significant

Herbal Remedies	0.664	0.717	Non-Significant
Sleeping Pills	6.104	0.047	Significant
Anti-Depressants	1.858	0.395	Non-Significant
Anti-Allergy	2.356	0.308	Non-Significant
Gender			
Pain Killers	0.506	0.477	Non-Significant
Fever Reducers	17.001	<0.001	Significant
Cough Syrups	3.920	0.048	Significant
Antibiotics	0.324	0.569	Non-Significant
Multivitamins	0.435	0.510	Non-Significant
Herbal Remedies	2.643	0.104	Non-Significant
Sleeping Pills	2.036	0.154	Non-Significant
Anti-Depressants	2.919	0.088	Non-Significant
Anti-Allergy	1.294	0.255	Non-Significant
Year of Study			
Pain Killers	5.847	0.211	Non-Significant
Fever Reducers	6.450	0.168	Non-Significant
Cough Syrups	13.780	0.008	Significant
Antibiotics	12.191	0.016	Significant
Multivitamins	14.955	0.005	Significant
Herbal Remedies	3.639	0.457	Non-Significant
Sleeping Pills	12.083	0.017	Significant
Anti-Depressants	4.713	0.318	Non-Significant
Anti-Allergy	1.997	0.736	Non-Significant

* $p \leq 0.050$ is statistically significant

The most common reasons cited for engaging in self-medication were the convenience of treating minor ailments themselves ($n=138$) and the desire to avoid unnecessary tests or doctor visits ($n=112$). Other reasons included the urgency to save time ($n=79$) and cost-effectiveness ($n=54$) (Figure 2).

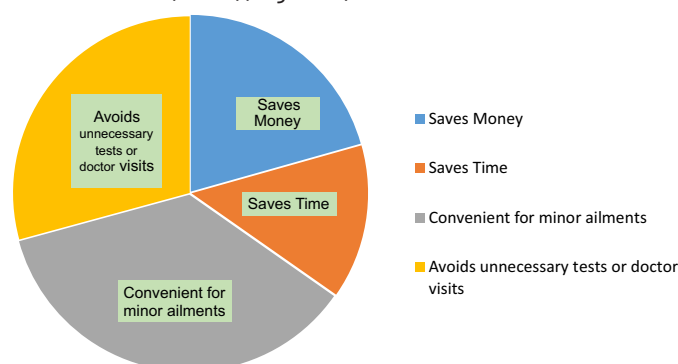


Figure 2: Dominant Features Attributed to Students Towards Self-Medication

Most commonly used dosage form was tablet ($n=232$), which is more prevalent in females ($n=168$) as compared to male ($n=64$), then syrups, which was ($n=19$) prevalent, along with a few using capsules ($n=09$) and ointment ($n=02$), as shown (Figure 3).

Type of dosage form commonly used as self-Medication

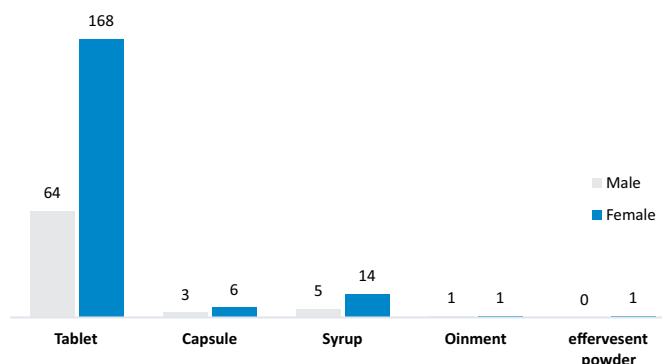


Figure 3: Commonly Used Formulations

Participants' understanding of self-medication, varied by age, gender, and year of study, showed that gender ($p=0.008$) and year of study ($p=0.022$) were significantly associated with understanding of self-medication. However, age did not show a statistically significant relationship with understanding SM. Perceptions of the safety of self-medication, highlighting significant associations with both age ($p=0.036$) and year of study ($p=0.014$). However, gender ($p=0.422$) was not significantly related to perceptions of self-medication safety. The side effects from self-medication were significantly associated with gender ($p=0.008$) and year of study ($p=0.008$). These results suggest that both gender and academic progression are linked to the likelihood of experiencing side effects from self-medication. However, age ($p=0.365$) did not show a significant association with the occurrence of side effects. Participants recommended self-medication to others, finding significant associations with gender ($p=0.611$) and year of study ($p=0.241$), while age ($p=0.466$) did not show a significant relationship. The awareness of the risks associated with self-medication includes the potential for incorrect diagnosis, adverse reactions, drug interactions, masking symptoms, incorrect dosage, dependence and abuse, resistance development, and worsening health conditions. The statistical analysis indicated a significant relationship only between age and awareness of adverse reactions, suggesting that age plays a role in participants' understanding of adverse reactions as a risk of self-medication. No other significant associations were found with age for the remaining risks. Additionally, there were no significant associations between gender and year of study with awareness of any specific risk (Table 5).

Table 5: Assessment of Possible Uncertainties with Self-Medications

Risks of Self-Medication	Chi-Square Value	p-value	Decision
Age			
Incorrect Diagnosis	1.799	0.407	Non-Significant
Adverse Reactions	7.173	0.028	Significant

Drug Interactions	0.861	0.650	Non-Significant
Masking Symptoms	0.428	0.807	Non-Significant
Incorrect Dosage	0.827	0.661	Non-Significant
Dependence And Abuse	0.124	0.940	Non-Significant
Resistance Development	0.805	0.668	Non-Significant
Worsening of Health Conditions	2.601	0.272	Non-Significant
Gender			
Incorrect Diagnosis	1.138	0.286	Non-Significant
Adverse Reactions	0.190	0.663	Non-Significant
Drug Interactions	0.037	0.848	Non-Significant
Masking Symptoms	0.062	0.804	Non-Significant
Incorrect Dosage	0.397	0.592	Non-Significant
Dependence And Abuse	1.451	0.228	Non-Significant
Resistance Development	0.219	0.640	Non-Significant
Worsening of Health Conditions	0.920	0.337	Non-Significant
Year of Study			
Incorrect Diagnosis	1.214	0.876	Non-Significant
Adverse Reactions	2.343	0.673	Non-Significant
Drug Interactions	5.051	0.282	Non-Significant
Masking Symptoms	2.185	0.702	Non-Significant
Incorrect Dosage	3.893	0.421	Non-Significant
Dependence And Abuse	2.132	0.711	Non-Significant
Resistance Development	1.610	0.807	Non-Significant
Worsening of Health Conditions	7.395	0.116	Non-Significant

* $p \leq 0.050$ is statistically significant

DISCUSSION

The current study on self-medication among pharmacy students brings significant findings that warrant attention for the implications that hold in healthcare contexts. With a high response rate from students, the study provides robust insights into the self-medication behaviours in the student population. The results indicate that a substantial majority, over 92.93%, engaged in self-medication to varying frequencies, reflecting a normalization of this practice among students who are future healthcare professionals [9]. This behaviour, while often rooted in convenience and perceived knowledge, carries implications for both patient care and public health, which might positive impact in their field. Key factors affecting self-medicine rehearses include age and year of study, with measurably huge connections noted. More youthful students and those in prior years could self-cure out of a longing to rapidly address medical problems without influencing their scholarly obligations [17]. On the other hand, the tendency to self-cure among more seasoned students and those in cutting-edge years probably comes from a developing trust in their clinical information, created through long stretches of study. These perceptions propose a developing pattern of independence as students progress through their scholastic process, possibly underrating the dangers

implied by unaided medication use. Among the circumstances treated with self-drug, migraines and fevers were prevalent, repeating discoveries from comparable investigations that distinguish these side effects as much of the time self-analyzed and treated without proficient discussion [18]. Alarmingly, the utilization of anti-microbials [19] without remedy was noticeable, with a huge relationship to specific age groups and study years. This abuse features the basic general wellbeing worry of anti-infection obstruction, accentuating the pressing requirement for training on the proper utilization of antimicrobials. The variety in prescription use, from pain relievers to antidepressants, highlights the expansive range of conditions students feel sure to treat autonomously, further reflecting holes in their ability to evaluate risks concerning tranquilizer associations and side effects. This hole in understanding mirrors an instructive setback, proposing that educational program improvements are important to foster a more thorough way to deal with pharmacological schooling [10]. A huge relationship between the time of study and mindfulness levels further shows that instructive meditations could be custom-fitted to various phases of clinical preparation, guaranteeing that students gain a more profound comprehension of safe prescription practices. Moreover, the cultural and monetary facilitators affecting self-medicine, for example, the accommodation and cost-adequacy of staying away from clinical interviews, align with the normal reasons referred to across writing [20]. This discernment presents possible dangers, as monetary considerations and the craving for convenience might eclipse the significance of expert medical services guidance. Accordingly, the discoveries from this study highlight the inescapable idea of self-medicine rehearses among pharmacy students, complementing both the dangers implied and the chance for educational change [16]. By tending to the distinguished instructional holes and emphasizing mindful prescription practices, colleges can more readily prepare students for jobs as promoters for safe medication use. This approach shields the singular strength of students as well as upgrades general wellbeing results by shortening the development of dangerous self-drug ways of behaving into future expert practices.

This study was limited by its self-reported questionnaire design, which may introduce recall and social desirability bias in reporting self-medication practices. Additionally, being a single-institution study restricts the generalizability of the findings to other pharmacy student populations. Future studies should include multi-institutional samples with observational or mixed-method approaches to better validate self-medication behaviours and reduce reporting bias.

CONCLUSIONS

The prevalence of self-medication practices in medical students is high which could lead to serious effects on health. It is urged to divert attention towards awareness and education regarding the strategies for easy accessibility implications of self medication, developing counter of medicines without prescription by pharmacies and strict policies over pharmaceutical advertising. Our research will provide a clear direction towards future research on self-medication usage in medical students.

Authors' Contribution

Conceptualization: LA

Methodology: LA, TRF, FI

Formal analysis: TRF

Writing and Drafting: LI, AK

Review and Editing: LA, TRF, FI, LI, AK

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

Conflicts of Interest

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Original Article



Association of Cutaneous Manifestations with Undiagnosed Diabetes Mellitus in Adults

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ABSTRACT

Diabetes mellitus (DM) remains underdiagnosed in resource-limited settings, where access to laboratory screening is constrained. Cutaneous manifestations may serve as visible, cost-effective indicators. **Objectives:** To determine the association between characteristic skin lesions (acanthosis nigricans, skin tags, xerosis) and undiagnosed diabetes in adults. **Methods:** A cross-sectional study involving 400 participants was conducted at a Teaching Hospital with adult patients without known diabetes (aged 18–70) attending dermatology and general medicine clinics. Detailed dermatological examinations documented predefined skin manifestations, while biochemical assessments (fasting plasma glucose, HbA1c, and oral glucose tolerance test) classified participants into normoglycemic, pre-diabetic (IFG/IGT), or diabetic groups per ADA criteria. Statistical analysis was done on SPSS version 26.0. **Results:** The prevalence of cutaneous markers was significantly higher in prediabetes and diabetes groups ($p < 0.001$). Acanthosis nigricans was present in 61.4% of cases, nearly eight times more prevalent than in normoglycemic individuals (8.1%). Similarly, multiple skin tags (≥ 5) affected 52.9% of diabetics compared to just 12.4% of controls, while xerosis showed a fourfold increase from 9.5% in normoglycemic subjects to 44.3% in diabetics. **Conclusions:** It was concluded that specific dermatological manifestations exhibit a robust correlation with undiagnosed diabetes and pre-diabetes. Incorporating cutaneous markers into routine clinical examinations may enhance early detection, particularly in resource-limited settings.

INTRODUCTION

Diabetes mellitus has become a major global health concern in the 21st century, with its prevalence escalating to epidemic levels worldwide. As per the International Diabetes Federation's 2021 data, 537 million adults globally were living with diabetes, a figure expected to rise to 783 million by 2045. In Pakistan alone, rates have increased dramatically, with estimates suggesting that nearly 26.7% of the adult population suffers from this metabolic disorder [1]. Almost half of all diabetes cases are unaware of their condition, in countries with limited healthcare resources

like Pakistan, where access to routine health screening is limited [2]. This diagnostic delay often leads to the development of serious complications, including neuropathy, retinopathy, nephropathy, and cardiovascular diseases before the condition is even recognized [3]. The economic burden of diabetes management and its complications places a substantial strain on healthcare systems, particularly in low-resource settings having limited access to specialized care [4]. The skin, being the largest organ of the human body, frequently manifests



visible signs of systemic diseases, including diabetes mellitus [5]. Numerous dermatological conditions have been strongly associated with insulin resistance and hyperglycemia. These cutaneous manifestations arise through several pathophysiological mechanisms [6]. Chronic hyperglycemia leads to the glycosylation of structural proteins in the skin, resulting in microvascular damage and impaired wound healing [7]. Insulin resistance triggers abnormal proliferation of keratinocytes and fibroblasts, leading to characteristic skin changes [8]. Additionally, the low-grade inflammatory state associated with diabetes contributes to skin barrier dysfunction and altered sebaceous gland activity [9]. Among the most well-documented cutaneous markers of diabetes are acanthosis nigricans (AN), characterized by velvety hyperpigmented plaques; skin tags (acrochordons), which are benign fibroepithelial polyps frequently observed in the neck and axillary regions; and xerosis, presenting as abnormally dry skin that often precedes other diabetic complications [10, 11]. These dermatological findings are particularly relevant in clinical settings, where they may serve as crucial visual clues for early diabetes detection [12]. Early identification of diabetes through cutaneous signs could substantially reduce healthcare costs by minimizing the need for expensive laboratory tests [13]. There is a paucity of data regarding the prevalence and diagnostic value of these cutaneous markers in the local population of Sargodha. Second, most existing studies have focused on patients with already diagnosed diabetes rather than investigating these signs in undiagnosed cases.

This study aims to determine the prevalence of characteristic skin manifestations in adults with undiagnosed diabetes or prediabetes to evaluate their diagnostic accuracy in identifying dysglycemia, and provide evidence for incorporating dermatological examinations into routine diabetes screening protocols in similar healthcare settings. Given the rising burden of diabetes in Pakistan, this research emphasizes the significance of fostering closer collaboration between dermatologists and primary care physicians in diabetes detection strategies.

METHODS

This cross-sectional study was done at the Department of Dermatology and Medicine, Niazi Welfare Foundation Teaching Hospital, Sargodha, from April 1, 2023, to March 31, 2024. The study gained ethical approval from the institutional review committee (Approval No: NM&DC-IRB-66 and Ref Letter No: IRB/NM&DC/203) and followed all ethical regulations during the entire study duration. A written informed consent, along with voluntary participation, was obtained from study participants. A sample size of 400 was calculated using Open Epi software

with an estimated prevalence of skin manifestation in diabetes of 23%, 95% confidence level, 4.12% margin of error [14]. Using a consecutive sampling technique, the study population included adults aged 18-70 years presenting to outpatient departments without known diabetes, excluding those with known diabetes mellitus, pregnancy, chronic steroid use, or severe systemic illnesses that could affect skin manifestations. Participants underwent a comprehensive dermatological examination by trained dermatologists under standardized lighting conditions. The examination focused on identifying specific cutaneous markers: acanthosis nigricans (defined as velvety hyperpigmented plaques in the neck, axillae, or groin), skin tags (≥ 5 lesions in characteristic locations), and xerosis (clinically significant dry skin with scaling). Each finding was documented using a standardized proforma with photographic documentation in suspicious cases. Anthropometric parameters such as body weight, stature, waist circumference, and blood pressure were systematically measured following the WHO STEPS protocol. Body mass index (BMI) was calculated and categorized according to Asian-specific cutoffs. For biochemical assessment, following an 8-hour overnight fast, venous blood samples were obtained. Fasting plasma glucose (FPG) levels were assessed, and HbA1c concentrations were quantified. Participants with FPG 100-125 mg/dL underwent a 75g oral glucose tolerance test (OGTT), measuring glucose levels two hours' post-load. Based on glycemic status, participants were categorized in diabetes (FPG ≥ 126 mg/dL, or HbA1c $\geq 6.5\%$, or 2-hour OGTT ≥ 200 mg/dL), prediabetes (FPG 100-125 mg/dL, or HbA1c 5.7-6.4%, or 2-hour OGTT 140-199 mg/dL) and normoglycemic (FPG <100 mg/dL and HbA1c <5.7%) groups. Data were analyzed using SPSS v26.0. Descriptive statistics (mean $\pm$ SD, frequencies) were computed. Chi-square tests are applied for categorical variables. Significance level was kept at p -value <0.05.

RESULTS

This study presents the demographic and clinical characteristics of 400 participants (mean age 45.2 ± 12.7 years, 58% female) stratified by glycemic status. Age, BMI, and waist circumference were significantly higher in prediabetes/diabetic groups ($p < 0.001$) (Table 1).

Table 1: Participant Profile According to Glycemic Status

Characteristic	Normoglycemic (n=210)	Prediabetes (n=120)	Diabetic (n=70)	p-value
Age (Years)	39.5 $\pm$ 10.2	47.8 $\pm$ 11.5	53.6 $\pm$ 9.8	<0.001*
Female Sex	58.1%	57.5%	58.6%	0.983
BMI (kg/m ²)	24.1 $\pm$ 3.2	27.8 $\pm$ 4.1	29.5 $\pm$ 4.6	<0.001*
Waist Circumference (cm)	84.5 $\pm$ 8.7	92.3 $\pm$ 9.5	96.8 $\pm$ 10.2	<0.001*
Family History of DM	18.6%	35.8%	44.3%	<0.001*

Among participants with confirmed diabetes, acanthosis nigricans was present in 61.4% of cases, nearly eight times more prevalent than in normoglycemic individuals (8.1%). Similarly, multiple skin tags (≥ 5) affected 52.9% of diabetics compared to just 12.4% of controls, while xerosis showed a fourfold increase from 9.5% in normoglycemic subjects to 44.3% in diabetics (all $p < 0.001$) (Table 2).

Table 2: Frequency and Percentage of Cutaneous Markers by Glycemic Status

Cutaneous Markers	Normoglycemic (n=210)	Prediabetes (n=120)	Diabetic (n=70)	p-value
Acanthosis Nigricans	17 (8.1%)	51 (42.5%)	43 (61.4%)	<0.001
Skin Tags (≥ 5)	26 (12.4%)	46 (38.3%)	37 (52.9%)	<0.001
Xerosis	20 (9.5%)	38 (31.7%)	31 (44.3%)	<0.001

DISCUSSION

This study highlights the significance of specific skin conditions—acanthosis nigricans, skin tags (acrochordons), and xerosis as early indicators of undiagnosed diabetes mellitus in Pakistani adults. A clear relationship was observed, with the prevalence of these dermatological manifestations increasing from normoglycemic individuals to those with prediabetes and diabetes. These findings are consistent with existing literature that underscores the role of cutaneous signs in the early detection of diabetes [15]. A pivotal finding of our study was the notably high prevalence of acanthosis nigricans (AN) observed at 61.4% among participants in the diabetes group. This prevalence was significantly higher compared to 42.5% in prediabetes individuals and 8.1% among those with normal glycemic levels. The findings support the pathophysiological understanding that AN develops as a cutaneous marker of hyperinsulinemia and insulin resistance. These results are consistent with other studies [16, 17] and particularly relevant for clinical practice in our setting, where AN is frequently observed but often overlooked as a cosmetic concern rather than a metabolic warning sign. Our findings reinforce the need for routine screening for dysglycemia in all patients presenting with AN, especially those with additional risk factors like obesity or a family history of diabetes. The study highlighted a significant association between the presence of multiple skin tags (≥ 5) and undiagnosed diabetes mellitus. This finding aligns with existing research suggesting that skin tags may serve as external indicators of underlying metabolic disturbances, particularly insulin resistance [18, 19]. Interestingly, our data showed significant concerns when skin tags co-occurred with AN, supporting the clinical practice of considering these markers in combination rather than isolation. This finding has particular relevance for primary care physicians in our region, who may encounter patients with skin tags but lack awareness of their potential metabolic significance. Xerosis was another common dermatological finding

among participants with undiagnosed diabetes, observed in 44.3% of individuals with newly diagnosed diabetes mellitus. This prevalence was notably higher compared to 31.7% in prediabetes participants and 9.5% among normoglycemic individuals. This finding aligns with existing literature indicating that xerosis is a common cutaneous manifestation in diabetic patients [20]. The clinical implications of our findings are substantial for healthcare providers as they support the incorporation of systematic skin examination into routine diabetes screening protocols, particularly in primary care, where resources for laboratory testing may be limited. Second, they highlight the importance of interdisciplinary collaboration between dermatologists and physicians in early diabetes detection. Third, they suggest that patient education about these cutaneous warning signs could improve community awareness and earlier healthcare seeking. We recommend that primary care physicians and dermatologists consider systematic screening for dysglycemia in all patients presenting with these cutaneous markers, particularly when multiple manifestations coexist.

This study is limited by its cross-sectional design, which prevents establishing a causal relationship between cutaneous markers and diabetes mellitus. Additionally, being conducted at a single center may limit the generalizability of the findings to broader populations across Pakistan. Future large-scale, multicenter longitudinal studies are recommended to validate these dermatological markers as predictive tools for early diabetes screening and to assess their role in disease progression over time.

CONCLUSIONS

Our findings establish a significant association between specific cutaneous manifestations, particularly acanthosis nigricans, multiple skin tags (≥ 5), and xerosis and undiagnosed diabetes mellitus in adults. The diagnostic utility of these markers is strongest when they co-occur, with the combination of ≥ 2 signs demonstrating high predictive value. These results underscore the clinical relevance of dermatological examination as a practical, non-invasive screening approach, particularly in resource-limited settings.

Authors' Contribution

Conceptualization: MZ

Methodology: MZ, ZP

Formal analysis: MKM

Writing and Drafting: AG, SN, AB

Review and Editing: MZ, AG, MKM, SN, ZP, AB

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



Caregiver-Reported Reasons and Outcomes of Treatment Default among Pediatric Oncology Patients at a Tertiary Care Hospital in Pakistan

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ABSTRACT

Despite the availability of free care, many children in Pakistan fail to complete cancer therapy, leading to poor outcomes and increased mortality. **Objective:** To determine reasons and outcomes of pediatric cancer patients defaulting treatment at tertiary care hospital in Pakistan. **Methods:** This descriptive cross-sectional study was conducted at Pediatric Hematology/Oncology unit of Children Hospital, Lahore. Total 82 pediatric oncology patients (<16 years) who started treatment but defaulted at any stage between 1st January and 30th June 2024 were included. Caregivers were interviewed regarding default reasons, and relevant clinical data were analyzed using SPSS version 27.0 for descriptive statistics. **Results:** Most frequently reported contributing factors were financial issues (100%), out-of-pocket expenses (98.8%), long travel distance (92.7%), and poor socioeconomic status (91.5%). Family-related challenges included other responsibilities (89%), parental job issues (84.1%), poor understanding of disease (81.7%), and lack of family support (63.4%). Additional reasons included large family size (72%) and family pressure to abandon treatment (29.3%). Patient-related causes were faith-based healing (50%), perceived long treatment duration (31.7%), consent withdrawal (25.6%), and fear of surgery (18.3%). System-related barriers included treatment unavailability (11%) and dissatisfaction with care (7.3%). Upon return, 54.3% were eligible only for palliative care, 25.6% resumed curative treatment, 14.8% expired, 3.7% were cured, and 2.5% were lost to follow-up. **Conclusion:** Treatment default in pediatric oncology is driven by financial, social, and systemic challenges. Overcoming these obstacles is essential to enhance treatment adherence and improve patient outcomes.

INTRODUCTION

Cancer is a leading cause of death among both adults and children globally [1]. Each year, approximately 400,000 new cases of cancer are diagnosed in children aged 0–19 years [2]. A significant proportion of these cases arise in Low- and Middle-Income Countries (LMICs), where outcomes are markedly poorer compared to High-Income Countries (HICs) [3]. The prognosis of childhood cancer varies significantly, often depending on geographical location [4]. While HICs report cure rates exceeding 80% due to advancements in diagnosis, treatment, and supportive care, LMICs lag behind with survival rates ranging from 20% to 70%, and in some regions, such as East Africa, as low as

10% [5]. This disparity is largely attributed to multiple systemic challenges in LMICs, including limited access to specialized pediatric oncology services, inadequate supportive care infrastructure, shortage of trained healthcare personnel, poor social support, late-stage presentation, and most critically, high rates of treatment abandonment [6, 7]. Treatment default is preventable but remains a significant cause of treatment failure, leading to increased morbidity and mortality due to uncontrolled disease progression [8]. Despite the availability of free treatment and specialized pediatric oncology centers in Pakistan, more than 20% of children with cancer still



discontinue therapy [9]. Globally, treatment default jeopardizes the survival of nearly one in every seven children with cancer each year [10]. Although issue of treatment default in pediatric oncology is well-recognized in LMICs, it remains significantly under-quantified and under-addressed, particularly in Pakistan. There is notable lack of local data regarding the specific reasons for treatment abandonment and the outcomes associated with defaulting therapy. Without such contextual evidence, efforts to design effective interventions remain hindered.

To reduce abandonment rates and improve survival outcomes at the centre, it is essential to generate baseline data and identify the social, economic, and healthcare-related risk factors contributing to treatment default. Therefore, this study conducted to determine the reasons and outcomes of pediatric cancer patients defaulting treatment at a tertiary care hospital in Pakistan. Addressing this gap would support the development of targeted strategies to enhance treatment adherence and overall pediatric cancer outcomes in resource-limited settings.

METHODS

This descriptive cross sectional study, conducted at Pediatric Hematology/Oncology unit, of Children's Hospital and University of Child Health Sciences Lahore, for duration of 6 months from April 2024 to September 2024. Ethical approval from IRB was taken before conducting this study [No.816/CH-UCHS]. The sample size of 82 patients was estimated based on a local study conducted in Karachi, which reported a 22% treatment default rate among pediatric cancer patients [11]. The unit of analysis was the patient, while the primary source of information regarding reasons for treatment default was the caregiver, who was interviewed at the time of return or follow-up. The sampling technique used was nonprobability purposive. It included all children diagnosed as having any pediatric malignancy with age range of 12 months to 16 years, who were treatment defaulted during any stage of management were included. Treatment default refers to failure of patient or caregiver to adhere to prescribed cancer treatment plan. This includes not starting the prescribed treatment, missing multiple appointments, or discontinuing treatment for prolonged period (typically more than 4 weeks) without medically valid reason. Children more than 16 years of age, treatment started/taken at other hospitals and those with consent withdrawal were excluded. Written informed consent was taken from parents/guardians before enrolment. Data collection was started with patients demographic (name, age, gender, address, underlying malignancy), and parents related characteristics (education, monthly income). The diagnosis of malignancy was confirmed from the hospital's medical records at the time of default and recorded in the proforma to ensure data consistency. Data were collected using a structured

questionnaire specifically developed for this study based on a review of relevant literature and expert consultation with pediatric oncology specialists. The questionnaire comprised approximately 30 questions covering multiple domains, including patient-related factors such as age, gender, type of malignancy, and treatment phase; family-related factors like parental education, occupation, family size, and support; socioeconomic aspects including monthly household income, financial constraints, out-of-pocket medical expenses, and travel distance to the hospital; as well as healthcare system factors such as treatment accessibility, satisfaction with hospital services, and medication availability. The reasons for treatment default were also explored, including refusal to start treatment, missed appointments, treatment discontinuation, fear of procedures, use of alternative therapies, and social or cultural pressures. Data collection was conducted through face-to-face interviews with the primary caregivers of the patients during their follow-up visits or return to the hospital. Trained research assistants administered the questionnaire to ensure consistency and completeness, and responses were recorded on paper forms before being entered into a digital database for analysis. These outcomes included treatment resumption, whether curative or palliative; disease progression as evaluated through clinical assessment and medical records; mortality, with cause of death documented when available; and loss to follow-up if patients did not return or could not be contacted. Outcome data were obtained from hospital records and caregiver interviews during follow-up visits. Patients were followed for 1 month to see outcomes. The collected data were entered and analyzed in SPSS version 27.0. Age was presented as median and range. Data regarding gender, education of parents, causes of treatment default, and outcomes were presented as frequency and percentage.

RESULTS

Among 82 patients included, median age found was 6 years (1-16 years). Fifty-two (63.4%) were male and thirty (36.6%) were females with male-to-female ratio of 1.7:1. Median duration of default was 16 weeks (Range 1-156). Forty-six (56.1%) patients were from the village and 36 (43.9%) from the city. Fathers were uneducated in 45 (54.9%) patients, mothers were uneducated in 43 (52.4%) patients. Seventy-five (91.5%) patients had monthly income <50,000 PKR/month, while only 7 (8.5%) patients had family income >50,000 PKR/month.

Table 1: Demographic of Patients and Parents Related Characteristics of Study Participants (n=82)

Patient Age: Median (Minimum -Maximum)	Categories	6 Years (1-16 Years) Frequency (%)
Gender	Male	52 (63.4)
	Female	30 (36.6)

Residence	Rural		46 (56.1)
	Urban		36 (43.9)
Malignancy	Hematological		47 (57.31)
	Sarcomas		8 (9.7)
	Neuroblastoma		2 (2.4)
	Retinoblastoma		3 (3.7)
	Wilms tumor		10 (12.2)
	CA colon		1 (1.2)
	Nasopharyngeal carcinoma		1 (1.2)
	Hepatoblastoma		3 (3.7)
	Germ cell tumour		7 (8.5)
Parents Educational status	Mother	Educated	-
		Uneducated	43 (52.4)
	Father	Educated	-
		Uneducated	45 (54.9)
Monthly income	<50,000 PKR/month		75 (91.5)
	> 50,000 PKR/month		7 (8.5)

The most frequently reported factors contributing to treatment default among pediatric oncology patients included financial issues (100%), poor socioeconomic status (91.5%), long travel distance to hospital (92.7%), and out-of-pocket expenses (98.8%). Family-related challenges were also prominent, with 89% citing other responsibilities, 84.1% facing parental job issues, 80.5% needing to borrow money, 81.7% having poor understanding of disease, and 63.4% lacking adequate family support. Additionally, large family size was noted in 72% of cases, while 29.3% experienced family pressure to abandon treatment. Among patient-related reasons, 50% turned to spiritual or faith-based healing, 31.7% cited long duration of therapy, 25.6% withdrew consent, 18.3% feared surgery, and 8.5% refused to initiate treatment. System-related issues were less common but included treatment unavailability (11%), overburdened healthcare services (9.8%), dissatisfaction with hospital care (7.3%), and witnessing death of other patients in the ward (2.4%). Language barriers were reported by 15.9% of families, and 11% of children came from broken families or had single parent.

Table 2: Factors Associated with Treatment Default

Factors Associated with Treatment Default		Frequency (%)
Patient-Based	Advanced disease	3 (3.7)
	Consent not given/withdrawal	21 (25.6)
	Refusal to start treatment	7 (8.5)
	Fear of surgery	15 (18.3)
	Long duration of therapy	26 (31.7)
	Healing through faith	41 (50)
Family-Based	Poor understanding of disease	67 (81.7)
	Other responsibilities	73 (89)
	Family pressure	24 (29.3)
	Family support NA	52 (63.4)
	Broken family/single parent	7 (11)
	Parental job issues	67 (84.1)

	Need to borrow money	66 (80.5)
	Death in family	11 (13.4)
	Illness of other member in family	15 (18.3)
System-Based	Treatment NA	7 (11)
	Overburden of patients	8 (9.8)
	Not satisfied	6 (7.3)
	Death of other patients in ward	2 (2.4)
Socioeconomic	Poor socioeconomic Status	73 (91.5)
	Financial issues	82 (100)
	Out of pocket expenses	81 (98.8)
	Language barrier	11 (15.9)
	Long Travel Distance	73 (92.7)
	Large family size	59 (72)

Out of 82 pediatric oncology patients who defaulted on treatment, majority (54.3%) were only eligible for palliative care upon their return, 21 patients (25.6%) were able to restart curative treatment, while 12 patients (14.8%) expired and only 3 patients (3.7%) achieved cure after resuming therapy. Two patients (2.5%) defaulted treatment again or were lost to follow-up, leaving their outcomes unknown.

Table 3: Outcome of Defaulted Patients

Outcomes	Frequency (%)
Expired	12 (14.8)
Palliative care	44 (54.3)
Treatment started	21 (25.60)
Cured after treatment	3 (3.7)
Unknown/Defaulted again	2 (2.5)
Total	82 (100)

DISCUSSION

It was observed in the current study that the most common malignancy found among treatment defaulters was hematological. This is in contrast with a previous study conducted in Ethiopia where most treatment defaulters were found to have bone sarcomas and brain tumours [12]. In the current study, the male gender was found to have a greater rate of treatment default. However, one review found that among treatment defaulter cancer children, no gender disparity was found [13]. Furthermore, in India, more treatment failure was noted among the female gender [14]. This study highlights treatment failure as a critical barrier to pediatric cancer care in Pakistan, reflecting trends seen across low- and middle-income countries. Financial constraints (100%) and low socioeconomic status (91.5%) were the most prominent factors. These findings are consistent with recent studies from Ethiopia (financial difficulty: 83%), Uganda (socioeconomic reasons: 78%), and India (poverty-related default: 28.6%), where cost of care was the leading cause of default [12, 15, 16]. Low socioeconomic status (91.5%) and out-of-pocket expenses (98.8%) further compounded the risk, as previously noted in similar LMIC settings, where

65% of parents were found to have borrowed money as a contributing factor to treatment failure [17, 18]. In contrast, one study found assumption of poor disease outcome as the most frequently found factor [19]. Parental illiteracy and poor disease understanding (81.7%) also played a major role, aligning with global reports that caregivers' misconceptions about cancer's curability often lead to treatment discontinuation [15, 19]. According to a study conducted in Karachi, the most commonly reported reason for treatment non-compliance among pediatric oncology patients was "perceived improvement in child's condition" (38.5%), followed by forgotten appointments (26.9%), school commitments (23.1%), and long travel distance to hospital (11.5%) [20]. The burden of long travel distance (92.7%) and out-of-pocket expenses (98.8%) mirrors data from studies where geographic and logistic barriers significantly influenced adherence [16]. Notably, similar patterns have been observed nationally; Tahirkheli *et al.*, in (2023) reduced abandonment to 6.7% at a Karachi center using call-back interventions and travel support [20]. In the current study, outcomes were poor 54.3% of patients returned only for palliative care, and 14.8% died emphasizing that abandonment leads to avoidable morbidity and mortality. These trends affirm previous findings that treatment default significantly lowers survival in LMICs and is a key contributor to global pediatric cancer disparities [6]. Furthermore, Farrag *et al.*, documented that 75% of patients have disease progression after treatment abandonment [21].

This study is limited by its single-center design and reliance on retrospective data, which may introduce selection and information bias. Additionally, lack of follow-up data on all defaulters restricts a comprehensive understanding of long-term survival outcomes. Future multicenter prospective studies incorporating follow-up tracking systems are recommended to better understand causes of treatment default and evaluate interventions aimed at improving adherence in pediatric oncology patients.

CONCLUSIONS

Treatment default in pediatric oncology is driven by financial, social, and systemic challenges. Overcoming these obstacles is essential to enhance treatment adherence and improve patient outcomes.

Authors' Contribution

Conceptualization: AG

Methodology: AG, SR, WM, LI, SG

Formal analysis: AG

Writing and Drafting: RUA, MF

Review and Editing: AG, RUA, MF, SR, WM, LI, SG

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



Beyond Weight Loss: Investigating Irritability and Mood Swings after Bariatric Surgery: A Prospective Study

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ABSTRACT

The physical changes after bariatric surgery are evident, but the significant changes in psychological and emotional effects are underscored and have not received much attention. **Objectives:** To determine the prevalence of Irritability and Mood Swings After Bariatric Surgery and its impact on hormonal and nutritional changes. **Methods:** This prospective observational study was conducted from February 2022 to January 2023. Patients undergoing any type of bariatric surgery with no existing psychiatric conditions that required medication were included. Structured questionnaires were distributed among the participants, and informed consent was also provided. **Results:** The study comprised 1,014 patients, with a mean age of 33 ± 13 years. According to the Profile of Mood States (POMS), 679 (67%) of participants had clinically severe mood abnormalities before surgery, which then increased to 844 (83%) at three months and then reduced to 355 (35%) at six months ($p < 0.001$). Compared to 740 (73%) before surgery, 902 (89%) of patients experienced moderate to severe irritation at three months ($p < 0.001$). After six months, this percentage dropped to 446 (44%). **Conclusions:** The research concluded notable changes in mood, irritability, and hormone levels after bariatric surgery, including increased irritability and mood disturbance at three months, with improvement at six months. Prevalent nutritional deficiencies of vitamins B12 and D regression were also found to be associated with increased mood and irritability. Multiple hormonal variations and nutritional deficiencies were found to result in postoperative mood variation significantly.

INTRODUCTION

Bariatric surgery has become a revolutionary treatment option and is considered a very viable alternative that can lead to substantial and long-lasting weight loss for those suffering from obesity [1]. This surgical strategy includes several operations that change the gastrointestinal tract's structure, which lowers food consumption and nutritional absorption [2]. Although the physical changes post-bariatric surgery is usually the main outcome of interest, the psychological and emotional changes following surgery are just as significant and yet are often overlooked, and research on the psychological effects of bariatric surgery has not received much attention [3]. Among the many psychological aspects of bariatric surgery, irritability and mood swings stand out as prevalent but little-known issues

that can have a big influence on a patient's long-term success [4]. Following surgery, certain patients exhibit a higher chance of experiencing negative mental health consequences [5]. High rates of preexisting depression, unfulfilled expectations about the transformative power of weight loss, and post-surgical changes in the hormonal and nutritional levels are some of the likely contributing factors leading to these adverse mental health outcomes, including mood changes and irritability [6]. After bariatric surgery, there are a variety of intricately linked physiological and psychological changes [7]. A key factor is the hormonal changes brought on by abrupt weight loss and changes in the gastrointestinal tract. RYBG and SG result in the enhancement of postprandial secretion of



satiety hormones, including glucagon-like peptide-1 (GLP-1) and oxyntomodulin (OXM), which contribute to a feeling of fullness and decrease hunger, resulting in the postoperative appetite regulation [8]. Following bariatric surgery, hormones including ghrelin, leptin, insulin Peptide YY (PYY) play a vital role in maintaining weight loss [9]. Ghrelin, a hunger hormone, also decreased after surgery due to the removal of ghrelin-secreting gastric tissue [10]. Leptin, produced by adipose tissue, sends feedback signals to the hypothalamus and regulates regular appetite and balances energy [11, 12]. The enteroendocrine changes brought on by sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB) have an impact on mental health, owing to the evidence now available, which indicates that several hormones and neuropeptides that regulate hunger have an impact on mood [13]. Similarly, a deficiency of vital minerals such as iron, magnesium, vitamin B12, and vitamin D can impair neurological function and lead to mood swings [14, 15]. Patients frequently struggle with adjusting to new eating habits and managing their altered body image, which can cause them to feel frustrated, anxious, or even depressed [16, 17]. Some people may encounter emotional challenges for the first time, while others may have pre-existing mental health disorders that are made worse. Emotional sensitivity can also be increased by the strain of adjusting to new lifestyle demands as well as the environmental and social factors connected to severe weight reduction [18, 19]. It's imperative to recognize and manage mood swings and irritability in bariatric patients since they can impact the patient's quality of life, long-term weight control success, and compliance with postoperative instructions, in addition to their mental health.

Although bariatric surgery is an effective intervention for long-term weight loss, limited attention has been given to its psychological consequences, particularly mood swings and irritability, which may significantly affect postoperative adjustment and outcomes. Existing literature largely focuses on physical outcomes, while evidence on emotional and behavioral changes, especially in relation to hormonal shifts, nutritional deficiencies, and psychosocial adaptation, remains insufficient. This study aims to determine the prevalence and contributing factors of irritability and mood swings in post-bariatric surgery patients.

METHODS

This prospective observational study was carried out in the International Metabolic and Bariatric Center, Afridi Medical Complex, Peshawar, over a year, from February 2022 to January 2023. Before enrolment, all subjects were given their informed permission, and the Institutional Review Board (IRB) granted ethical approval with reference no.234/DME/AMC/2022. A sample size of 1014 patients was

determined by using the WHO sample size calculator. The calculation was based on a 95% confidence interval (CI), 5% margin of error (d), population (50%), and estimated prevalence (p) of 85.8%. The sample size was calculated using the formula [20]: $n = Z^2 \times P \times (1-P) / d^2$. A non-probability consecutive sampling technique was applied in this study. Patients who had bariatric surgery procedures such as Sleeve gastrectomy, Roux-en-Y gastric bypass (RYGB), and micro gastric bypass were among the surgeries carried out. Patients between the ages of 18-65 years, of both genders, who had no history of drug abuse or had any psychiatric conditions that required medication were eligible. Patients who refused to participate in follow-up or had any unstable medical conditions were excluded. Further, patients below 18 and above 65 years were not included in the current study. Profile of Mood States (POMS), a 5-point Likert scale comprised of 65 65-item inventory with six different subscales, including tension-anxiety, depression-dejection, Anger-Hostility, Fatigue-Inertia, Confusion-Bewilderment and Vigour-Activity. The scoring of this scale ranges from ('0=not at all' to '4=very strong') and is widely used for the assessment of mood [21]. The Irritation Questionnaire (IRQ), a two 4-point Likert scale, was employed to assess the frequency and severity of irritation symptoms. For frequency, the score ranges from ('0=never' to '3=most of the time') and for severity of symptoms, the score ranges from ('0=not at all' to '3=very much so') [22]. The Postoperative Adaptation Questionnaire (PAQ), a 15-item questionnaire, is used to assess how well the patient has adapted to lifestyle modifications, including eating habits and body image. Each item is reported on a 5-point Likert scale ranging from (0=strongly disagree to 5=strongly agree). Further sleep disorders, which can be a factor in mood swings, were assessed through the Sleep Quality Index (SQI). SQI is an 8-item questionnaire with three categories weighted 0, 1, and 2 and scoring varied from 0-16 (23). Blood samples were collected after overnight fasting, centrifuged, and serum was stored at -80°C, at baseline (pre-operative), 3rd month, and 6th month. Vitamin B12 and D levels were measured using chemiluminescent immunoassays, a highly sensitive, specific and suitable laboratory technique for detecting low serum concentrations of these micronutrients. Serotonin, ghrelin, and leptin were evaluated using ELISA kits (Elabscience, USA) following the manufacturer's protocols. Clinical and Demographic Information that including Preoperative psychological history, age, gender, BMI, operation type, concomitant conditions, and other baseline variables, were taken from medical records. Before the surgery, patients were evaluated to determine baseline levels of hormones such as serotonin, ghrelin and leptin, which are associated with appetite regulation. Nutritional health was assessed via blood levels of vitamin B12 and vitamin D. Mood and irritability were evaluated through valid tools such as Profile of Mood States (POMS)

and Irritability Questionnaire (IRQ). Participants filled out the IRQ and POMS questionnaires at follow-up assessments that were held three and six months after surgery. To track variations in hormone and nutritional levels, blood samples were taken at regular intervals. Samples were then centrifuged to separate serum and then stored at -80°C for preservation. The PAQ and SQI were used to collect psychosocial and sleep-related data during follow-ups. SPSS version 26.0 was used to analyze the data. Demographic information and baseline traits were compiled using descriptive statistics. Categorical variables such as gender, nutritional deficiencies, and surgery type were represented in percentages and frequencies, while the data in numerical form, such as age, BMI, irritability, mood disturbances, and nutritional and hormonal changes, were illustrated in mean and standard deviation. Relationships between mood swings and dietary or hormonal factors were investigated using an independent sample t-test, and the impact on hormonal and nutritional changes was found by multiple regression, and $p \leq 0.05$ was chosen as the threshold for statistical significance.

RESULTS

The study comprised 1,014 patients, whose mean age was 33 ± 13 years. Of those who took part, 659 (65%) were men and 335 (35%) were women. Before surgery, the average BMI was $29 \pm \text{kg/m}^2$. The majority of individuals had mini gastric bypass 385 (38%), followed by sleeve gastrectomy 304 (32%) and Roux-en-Y gastric bypass (RYGB) 324 (30%). According to the Profile of Mood States (POMS), 679 (67%) of participants had clinically evident mood abnormalities before surgery, and 740 (73%) of participants experienced mild irritation. With 284 (28%) of patients lacking vitamin B12 and 730 (72%) lacking vitamin D, nutritional deficiencies were common (Table 1).

Table 1: Baseline Demographic and Clinical Characteristics

Variables	Categories	Mean $\pm$ SD	Frequency (%)
Mean Age (Years)	18-65	33 ± 13	—
Gender	Female	—	(335) 35%
	Male		659 (65%)
Mean BMI (kg/m^2)	—	29 ± 3	—
Surgery Type (%)	Sleeve Gastrectomy	—	385 (38%)
	Roux-en-Y Gastric		304 (30%)
	Mini Gastric Bypass		324 (32%)
Nutritional Deficiencies	Vitamin B12	—	284 (28%)
	Vitamin D		730 (72%)

Assessments conducted after surgery showed a marked rise in irritation. Compared to 740 (73%) before surgery, 902 (89%) of patients experienced moderate to severe irritation at three months ($p < 0.001$). After six months, this percentage dropped to 446 (44%). Increased frustration, trouble controlling emotions, and heightened

susceptibility to small stimuli were all signs of irritability. The percentage of patients reporting clinically significant mood disturbances increased from 679 (67%) before surgery to 844 (83%) at three months and 355 (35%) at six months ($p < 0.001$), indicating a significant worsening of mood swings following surgery a subsequent decrease after 6 months (Table 2).

Table 2: Changes in Mood and Irritability Scores Over Time

Measures	Baseline	3 rd Month	6 th Month	p-value
	n (%)			
Moderate to Severe Irritability	740 (73%)	902 (89%)	446 (44%)	<0.001
Mood Disturbances	679 (67%)	844 (83%)	355 (35%)	<0.001

After surgery, there were notable hormonal changes that were linked to mood swings and increased irritation. From $593 \pm 31 \text{ ng/L}$ before surgery to $258 \pm 18 \text{ ng/L}$ at six months, ghrelin levels significantly decreased ($p < 0.001$), and patients who saw larger decreases also reported higher irritation scores ($p < 0.001$). At six months, serotonin levels dropped dramatically from $120 \pm 20 \text{ ng/mL}$ to $80 \pm 15 \text{ ng/mL}$ ($p = 0.04$), which led to more frequent mood swings. A subgroup of patients continued to have nutritional deficiencies; at six months, 345 (34%) were still lacking in vitamin B12 and 588 (58%) in vitamin D. Increased irritability and mood disorders were highly associated with these inadequacies (respectively, $p < 0.003$) (Table 3).

Table 3: Hormonal and Nutritional Changes

Measures	Baseline	6 Months	p-value	95% CI (Confidence Interval)
Serotonin (ng/mL)	120 ± 20	80 ± 15	< 0.001	-12.7 to -8.3
Ghrelin (ng/L)	593 ± 31	258 ± 18	< 0.001	-352.0 to -282.0
Vitamin B12 (ng/mL)	284 (28%)	345 (34%)	< 0.003	0.12 to 0.25
Vitamin D (ng/mL)	730 (72%)	588 (58%)	< 0.003	0.10 to 0.23

A decline in Postoperative Adaptation Questionnaire (PAQ) scores suggested that 345 (34%) of patients had postoperative adaptation issues. These patients showed noticeably more mood swings and irritation ($p < 0.001$). At six months, 304 (30%) of patients reported sleep difficulties, as judged by the Sleep Quality Index (SQI), compared to 65% before surgery ($p < 0.01$) (Table 4).

Table 4: Postoperative Adaptation Issues

Parameters	Preoperative	6 Months Post-operative	p-value	95% CI
Adaptation Issues	—	345 (34%)	< 0.001	0.30 to 0.45
Mood Swings/Irritation	—	Increased	< 0.001	0.50 to 0.60
Sleep Difficulties	659 (65%)	304 (30%)	< 0.010	-0.25 to -0.15

DISCUSSION

The objectives of this study included the evaluation of the bariatric surgery candidates and post-surgical mood disorders, irritability, and postoperative adaptation over six months on a psychological, hormonal, and nutritional level.

Our results show alterations in mood and temper, which were at their worst at the three months following surgery and were relatively better at the six months. These changes are associated with a lower level of ghrelin and serotonin, and low levels of vitamin B12 and D remain low even many years postoperatively. Furthermore, only one-third of the patients responded that they did not have troubles with adaptation after surgery, and 304 (30%) reported persistent sleep disturbances. The results of this study, therefore, emphasize the importance of holistic care once the surgery is done. Our findings align with several previous studies, though with some differences in the magnitude and timing of changes. These changes of mood disturbances were described in bariatric patients by Loh et al., where 45 % of the patients had depressive symptoms and 58 % had anxiety symptoms before the surgery and changes which seem to increase in the first 3 months of the surgery, as it is seen in this study [24]. Ivezaj et al., also identified greater mood lability at three months after surgery, 13.1% of patients complained of irritability and depressive feelings. However, they noted that the resolution of these symptoms was slower, with 13 patients affected at 12 months in this study; only 44% of the patients still reported irritability at discharge at six months [25]. The changes in irritability and mood swings observed in bariatric surgery patients shortly after the surgery may be hormonal, nutritional, and psychosocial. One of the factors that aggravate such early mood disturbances is the hormonal change that follows surgery. Bariatric surgery results in a significant change in gut hormones, more specifically ghrelin, which is reported to fall swiftly after the operation. Ghrelin, which is also termed as the "hunger hormone", has some function in hunger as well as in the mood [26]. Hormonal fluctuation has been reported to affect brain reward and emotional centers, hence reducing or increasing irritability and poor emotional control [27]. In addition, serotonin, which plays a role in mood regulation, also decreases after surgery, making irritability and depressive-like symptoms worse [28]. Some of the changes also include the effects of nutritional deficiency, such as vitamin B12 and vitamin D deficiencies, which are usual after bariatric procedures, and worsen mood swings. These deficiencies may negatively affect the nervous system, which causes symptoms such as irritability, confusion, and fatigue [29]. Other aspects of the lifestyle change are expressed in psychosocial areas requiring interests, higher levels of stress, and changes in the parameters of the body, causing postoperative irritability [30]. Chronologically, these hormonal changes are balanced, nutritional deficiencies assuming a new diet, psychosocial adaptation is enhanced, and there is a decrease in mood disorders by six months after the surgery [31]. Therefore, the early postoperative period is a state of various physiological and psychological changes with relative amelioration of the process in the subsequent days

after surgery. The hormonal changes documented by Hamad et al., included a decrease in serotonin to an average of 54% of the preoperative levels, with a range of 36%–80% of the baseline value [32]. For that reason, Pasi et al., ascertained that 24.7% of persons who have undergone bariatric surgery experienced a decrease in serotonin levels, which are associated with increased irritability and mood swings, similar to our findings [33]. Our study observed that the percentage of patients who were deficient in vitamin B12 was 34% and those who were deficient in vitamin D was 58% at six months. These findings concur with those of Çalapkorur and Küçükkatirci, who reported that, among the bariatric surgery patients, 24.7% saw their levels of serotonin drop, which the authors attributed to increased irritability and mood swings, exactly as documented in this study [34]. Song and Fernstrom also observed that these vitamins were claimed to show some deficiency that is coupled with symptoms related to psychological side effects, such as irritation and depression [35]. In the present paper, we noted that 34% of patients experienced some problems with postoperative adjustment and reported more pronounced oscillations of mood and increased irritability. This is supported by Dalrymple et al., who observed that only 30% of bariatric patients had difficulties with emotional and psychological adjustment after the surgery. These difficulties were more pronounced in our poor sleep quality post-operative patients, who had 75% of them complaining of sleep disturbances at one-year follow-up, similar to our study, where 28% of the patients complained of sleep problems at six months follow-up [36]. Similarly, Lodewijks et al., also found that self-reported Sleep problems were still present in 30% of patients after six months of bariatric surgery and pointed out the probability of endocrine hormonal changes together with behavioural and lifestyle alterations [37]. Our assessment of sleep quality indicated that poor sleep quality changed from 65% before surgery to 30% at the six-month follow-up. By the above observation, Ab et al., reported that the patient had shown a 32% increase in sleep quality after surgery [38]. In a study by Sillo et al., they showed that 88.5% of bariatric patients had considerable clinical amendments in sleep apnea and other sleep disorders following weight loss, which is in agreement with our result of enhanced sleep quality; however, it also reveals that several patients continue to have some residual periods of sleep problem even after surgery [39]. This study is limited by its relatively short follow-up period of six months, which may not fully capture long-term psychological and nutritional outcomes after bariatric surgery. Additionally, being a single-center study may limit the generalizability of findings to broader bariatric populations. Future multicenter longitudinal studies with extended follow-up are recommended to better understand long-term psychological adaptation, hormonal

recovery, and nutritional deficiencies after bariatric surgery, and to develop structured post-operative mental health support programs.

CONCLUSIONS

The research found significant psychological and physiological changes after bariatric surgery. Mood disturbance and irritability status were increased at 3 months (83% and 89%, $p < 0.001$), and then improved by 6 months (35% and 44%, $p < 0.001$). Vitamins B12 and D deficiencies remained prevalent in 34% and 58% of patients throughout the 6-month follow-up, associated with increased irritability and mood issues ($p < 0.003$). Ghrelin and serotonin levels dropped significantly after surgery, contributing to mood changes ($p < 0.001$). Furthermore, Postoperative adaptation difficulties were observed in 34% of patients (PAQ), and sleep difficulties significantly reduced from 65% preoperatively to 30% at 6 months ($p < 0.010$).

Authors' Contribution

Conceptualization: MA¹

Methodology: MA¹, MA², WA

Formal analysis: MA², WA

Writing and Drafting: MA¹, MNDK, AHS

Review and Editing: MA¹, MA², WA, MNDK, AHS

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 Pregnant Women and Its Association with Musculoskeletal Pain: A Cross-Sectional Study

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ABSTRACT

Vitamin D deficiency is recognized as widespread public health issue especially prevalent in pregnant women, has been associated with negative maternal health consequences, including musculoskeletal pain. **Objective:** To assess vitamin D levels during pregnancy and explore their association with musculoskeletal pain in pregnant women **Methods:** A cross-sectional study was performed at a teaching hospital in Sargodha over a 16-month period (09/2023-12/2024). Biochemical assessment of vitamin D status was performed through serum 25(OH)D quantification, while musculoskeletal symptoms were documented using structured pain questionnaires. Statistical evaluation, including chi-square analysis of associations, was performed using SPSS Statistics version 26.0. **Results:** Out of 250 pregnant women, 72.4% (n=181) had deficiency of vitamin D (<20 ng/mL), while 18% (n=45) had insufficiency (20-30 ng/mL). The association revealed between vitamin D deficiency and musculoskeletal pain was significant as (p <0.001), moderate to severe pain was evident in 68.2% of deficient women compared to 31.8% in the sufficient group (≥30 ng/mL). **Conclusions:** Current evidence reveals alarmingly high rates of vitamin D deficiency among pregnant women and is significantly associated with musculoskeletal pain. Routine screening and supplementation should be considered to improve maternal health outcomes.

INTRODUCTION

The fat-soluble vitamin D plays an essential role in regulating calcium balance, promoting bone mineralization, and supporting musculoskeletal health. During pregnancy, the body's physiological requirement for vitamin D rises significantly to aid in the proper development of the fetal skeleton, yet deficiency remains alarmingly prevalent [1, 2]. Global epidemiological studies indicate that 40-90% of pregnant women in developing countries suffer from vitamin D deficiency, which is linked to negative maternal and fetal outcomes, such as

gestational diabetes mellitus, preeclampsia, preterm birth, and neonatal hypocalcemia [3, 4]. Pregnant women frequently encounter musculoskeletal problems as a result of hormonal, anatomical, physiological, and morphological changes. Common symptoms include muscle strain, cramping, pain, fatigue, and soreness. Prolonged changes in joint laxity can disrupt normal joint biomechanics, placing excessive stress on musculoskeletal tissues. Additionally, increased laxity may lead to abnormal or unevenly distributed stress on joint cartilage [5]. While



mechanical factors such as weight gain, postural changes, and ligamentous laxity due to relaxin hormone are well-documented contributors. Emerging evidence suggests that hypovitaminosis D may exacerbate musculoskeletal discomfort through multiple mechanisms [6]. Vitamin D Receptors (VDRs) are present in skeletal muscle, and deficiency has been linked to myopathy, muscle weakness, and increased inflammatory cytokine activity, which may predispose pregnant women to chronic pain syndromes [7]. Over the past decade, epidemiological research has increasingly highlighted the relationship of vitamin D deficiency during pregnancy with fatal outcomes for mothers, fetuses, and newborns. These adverse effects include pre-eclampsia, gestational diabetes mellitus, impaired fetal growth, low infant birth weight, impaired fetal skeletal development, and reduced bone mass [8]. Although increasing evidence associates vitamin D deficiency to musculoskeletal morbidity, routine screening for hypovitaminosis D in antenatal care is ignored, particularly in low-resource settings [9, 10]. Current guidelines from the Endocrine Society recommend a minimum serum 25(OH)D level of 30 ng/mL for optimal skeletal and extra skeletal health, yet many pregnant women fail to meet this threshold due to insufficient sun exposure, cultural practices favoring skin coverage, and diets low in vitamin D-rich foods [11, 12]. In Pakistan, where sunlight is abundant yet vitamin D deficiency paradoxically remains endemic due to sociocultural and dietary factors, there is a paucity of data on relationship between vitamin D deficiency and musculoskeletal pain in pregnancy [13, 14]. This study aimed to assess vitamin D levels during pregnancy and explore their association with musculoskeletal pain in pregnant women. Despite growing interest in this area, research on this specific population remains limited, indicating the need for further investigation to uncover unexplored aspects of this relationship. The findings of this study could help to initiate antenatal care policies regarding vitamin D screening and supplementation, potentially reducing the burden of preventable musculoskeletal morbidity in pregnancy.

METHODS

This cross-sectional study was done at Niazi Welfare Foundation Teaching Hospital, Sargodha, from September 1, 2023 to December 31, 2024. Study gained ethical approval from institutional review committee (Approval No: NM&DC-IRB-92 and Ref Letter No: IRB/NM&DC/408) and followed all ethical regulations during entire study duration. A written informed consent along with voluntary participation was taken from study participants. A sample size of 250 was calculated on open Epi software at 95% confidence level and 5.5% margin of error based on prevalence of vitamin D deficiency in Pakistan from a prior

study [3]. A total of 250 women aged 18–45 years with confirmed singleton pregnancies were included in the study via consecutive sampling. Exclusion criteria included: Chronic musculoskeletal disorders (e.g., rheumatoid arthritis, osteoarthritis), history of vitamin D supplementation in the past 6 months, medical disorders influencing vitamin D metabolism (such as chronic kidney disease, malabsorption syndromes), use of medications interfering with vitamin D metabolism (anticonvulsants, glucocorticoids). In data collection procedure, maternal age, gestational trimester, BMI, parity, sun exposure (≤ 30 minutes/day), and socioeconomic status were recorded. Under aseptic technique, venous blood was drawn and assessed for serum 25-hydroxyvitamin D [25(OH)D] concentrations. Vitamin D status was classified according to Endocrine Society guidelines as deficient (<20 ng/mL), insufficient (20–29 ng/mL), and sufficient (≥ 30 ng/mL) [15]. Musculoskeletal pain was assessed using a structured questionnaire and a Visual Analog Scale (VAS) ranging from 0 to 10, with pain considered present if the VAS score was 4 or higher [15, 16]. Participants reported pain location (e.g., lower back, pelvis, joints), duration, and intensity. Data were analyzed using SPSS version 26.0. Descriptive statistics (mean $\pm$ SD, frequencies) were computed. Chi-square tests applied for categorical variables and ANOVA for normally distributed continuous variables. Significance level was kept at p -value <0.050 .

RESULTS

Table 1 summarizes the maternal and gestational age in mean $\pm$ SD as 28.4 ± 5.2 and 24.6 ± 8.3 respectively. Out of 250 participants, majority were in their second trimester (42%) and had limited sun exposure (<30 min/day; 64%).

Table 1: Participants Demographic Profile

Variables	Mean $\pm$ SD	Frequency (%)
Age (Years)	28.4 ± 5.2	-
Gestational Age (Weeks)	24.6 ± 8.3	-
BMI (Kg/m ²)	26.8 ± 4.5	-
Trimester		
First	-	60 (24.0)
Second	-	105 (42.0)
Third	-	85 (34.0)
Parity		
Nulliparous	-	93 (37.2)
Multiparous	-	157 (62.8)
Sun Exposure		
<30 min/Day	-	160 (64.0)
≥ 30 min/Day	-	90 (36.0)

Table 2 revealed a high prevalence of deficiency (72.4%), with only 8.8% of women achieving sufficiency. Deficient women had significantly lower mean levels (14.2 ng/mL).

Table 2: Vitamin D Levels in Pregnant Women

Vitamin D Status	Frequency (%)	Mean $\pm$ SD 25-Hydroxy-vitamin D (ng/mL)
Deficient (< 20 ng/mL)	181 (72.4)	14.2 $\pm$ 3.8
Insufficient (20–30)	47 (18.8)	24.6 $\pm$ 2.1
Sufficient ($\geq$ 30)	22 (8.8)	36.4 $\pm$ 4.5

Table 3 demonstrated a dose-response relationship, with deficient women more likely to report moderate-to-severe pain (76.5%) compared to sufficient women (37.8%; $p < 0.001$).

Table 3: Vitamin D Status and Musculoskeletal Pain (n=250)

Pain Severity	Deficient Frequency (%)	Insufficient Frequency (%)	Sufficient Frequency (%)	p-Value
Mild (VAS 1–3)	43 (23.7)	21 (45)	14 (63.6)	<0.001
Moderate (4–7)	93 (51.4)	19 (40.4)	6 (27.2)	<0.001
Severe (8–10)	45 (24.8)	7 (14.8)	2 (9.2)	0.002

DISCUSSION

This study provided important insights exploring the link between vitamin D measures and musculoskeletal pain in 250 pregnant women with distinct demographic and lifestyle characteristics. The participant profile reveals several noteworthy findings that contextualize these results suggest directions for clinical practice. The mean age of participants (28.4 $\pm$ 5.2 years) reflects a typical reproductive-age population, while the trimester distribution (24.0% first, 42.0% second, 34.0% third) captures pregnancy stages when musculoskeletal complaints typically emerge and intensify. Of particular relevance, the majority of participants (62.8%) were multiparous, a factor associated with cumulative musculoskeletal stress from previous pregnancies [17]. The mean BMI of 26.8 $\pm$ 4.5 kg/m² indicates that nearly half of the cohort likely fell into overweight/obese categories according to WHO criteria, an important consideration given the established relationship between elevated BMI and both vitamin D deficiency and musculoskeletal pain [18]. This study found an alarmingly high rate of vitamin D deficiency (72.4%) in pregnant women, with only 9.2% achieving sufficient levels ($\geq$ 30 ng per mL). Mean vitamin D levels showed a clear gradation across categories: 14.2 $\pm$ 3.8 ng/mL in deficient, 24.6 $\pm$ 2.1 ng/mL in insufficient, and 36.4 $\pm$ 4.5 ng/mL in sufficient groups. These findings align with recent regional studies from Pakistan showing 61–75% deficiency rates but substantially exceed prevalence rates reported in European (19–45%) and Middle Eastern (52–68%) populations [2, 3, 19]. These results corroborate the growing body of evidence demonstrating that South Asian pregnant women experience highest deficiency rates globally linked to limited sunlight contact and diets low in fortified foods [20, 21]. This study revealed a strong inverse linkage between vitamin D measures and musculoskeletal pain severity in pregnant women, with deficient

participants (n=181) showing significantly higher pain burden (51.4% moderate, 24.8% severe) compared to sufficient women (n=22; 27.2% moderate, 9.2% severe; $p < 0.001$). These findings demonstrate a clear dose-response gradient, supporting biological plausibility, and align with but exceed effect sizes reported in Western studies, likely due to more extreme deficiency levels in the population (mean 25(OH)D 14.2 ng/mL in deficient group). The results are particularly concerning given that 76.2% of deficient women reported moderate-to-severe pain levels known to impair daily function, suggesting current vitamin D thresholds may need reevaluation for musculoskeletal health in pregnancy. These data reinforce emerging evidence from showing stronger vitamin D-pain associations possibly reflecting compounded effects of nutritional deficiency and pregnancy-related biomechanical stress while highlighting an under-addressed aspect of maternal morbidity that warrants urgent clinical attention through screening and targeted supplementation program [22, 23].

The study offers several strengths, such as a large sample of pregnant women, validated tools for assessing vitamin D levels and pain severity, and a clear dose-response relationship supporting potential causality. However, there are limitations too. The recall bias in self-reported pain and sun exposure metrics may affect accuracy. The cross-sectional design precludes causal inference, and single-center sampling limits generalizability. Longitudinal studies assessing pain resolution post-supplementation and cost-benefit analyses of screening programs are necessary. Future studies should explore vitamin D's role in pregnancy-related pain pathways to inform targeted intervention.

CONCLUSIONS

Deficiency of vitamin D is endemic in pregnancy and strongly correlates with musculoskeletal pain. Addressing this through targeted supplementation and sunlight exposure advocacy may enhance maternal well-being. Policymakers should prioritize prenatal vitamin D protocols in regions with high deficiency rates. Integrating routine vitamin D screening into antenatal care, coupled with WHO-recommended supplementation (400–600 IU/day), could mitigate deficiency and associated morbidity. Public health initiatives promoting dietary fortification and safe sun exposure are vital factors.

Authors' Contribution

Conceptualization: MUR

Methodology: MUR, SA

Formal analysis: MKM

Writing and Drafting: MZ, RAK, MZ, AW

Review and Editing: MUR, MZ, MKM, RAK, SA, MZ, AW

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 Between Anemia and Prevalence of Gestational Diabetes vs Non-Gestational Diabetes among Pregnant Women

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ABSTRACT

Gestational diabetes mellitus (GDM) affects a large number of pregnant women globally and generates significant health complications for both mothers and their newborns. **Objectives:** To establish anemia prevalence among pregnant women with and without gestational diabetes mellitus (GDM) by investigating how various demographic and clinical factors influence this relationship. **Methods:** A six-month comparative cross-sectional study was conducted at Khairpur Medical College, Khairpur Mir's. The study enrolled pregnant women n=200 between 18-40 years of age who had single child pregnancies during the gestational period of 24 to 28 weeks. The criteria established by WHO distinguished anemia while the diagnosis of GDM followed the OGTT results using a 75g Oral Glucose Tolerance Test (OGTT) as per WHO/ADA 2013 guidelines. Data were analyzed using descriptive statistics with chi-square tests and logistic regression. **Results:** The mean age of maternal individuals (29.8 years) along with body mass index (BMI 29.4 kg/m²) was higher in GDM group members than in non-GDM group individuals; p<0.001. GDM mothers had higher anemia prevalence at 78.3% compared to 57.1% in the other group (p=0.004), alongside lower average hemoglobin measurement results (9.8 g/dL compared to 10.5 g/dL, p=0.001). The analysis using logistic regression established both anemia along BMI and maternal age as independent risks for GDM diagnosis (OR: 2.35, p=0.006). **Conclusion:** It was concluded that anemia occurs more frequently in pregnant women with GDM, while remaining an independent GDM factor, which also correlates with elevated maternal age and BMI compared to non-GDM women.

INTRODUCTION

Gestational diabetes mellitus (GDM) represents a prevalent medical pregnancy complication because it causes glucose intolerance right after its first detection during pregnancy [1, 2]. The global prevalence of GDM continues to increase between 1% and 28% as maternal age and obesity and ethnicity, and lifestyle affect this rate [3]. GDM impacts maternal health while creating severe consequences for fetal development that result in macrosomia alongside preterm birth and cesarean section, together with long-term metabolic problems in both mother and child [4]. Pathological anemia impacts 40.5% of pregnant women worldwide and affects pregnant individuals most significantly in nations with limited or middle-income

status [5]. According to the World Health Organization (WHO), the diagnostic threshold for pregnant women anemia is when their hemoglobin measures below 11 g/dL, which leads to several complications, including exhaustion and hypertension and premature birth and reduced infant birthweight and maternal death [6]. Pregnancy requires increased blood volumes while simultaneously causing nutritional deficiency of iron, folate and vitamin B12, resulting in high occurrences of anemia [7]. The connection between GDM and anemia remains unclear, although new scientific evidence suggests they might be related to each other. Maternal anemia has been identified by studies as a factor which can modify glucose



metabolism through insulin resistance and oxidative stress, along with inflammation, which raises GDM development [8]. Multiple research studies have found that anemia does not impact GDM risk, and anemics sometimes show reduced GDM prevalence. The insufficient consensus across research studies reveals major knowledge gaps in this field, especially since anemia and gestational diabetes occur commonly among South Asian populations [9]. Maternal anemia and GDM burden remain high within Pakistan because of substandard nutrition, together with scarce prenatal care services, while maternal age increases and obesity rates continue to rise [10]. Few studies have investigated the joint occurrence of these healthcare conditions among pregnant women to determine their possible links. The relationship's comprehension is essential because it will affect procedures for antenatal screening and maternal nutritional plans, and healthcare treatment, which results in better pregnancy outcomes [11]. Pakistani women display high occurrence rates of both anemia and GDM, yet local research fails to establish their collective impact. Previous research examined these medical conditions separately without exploring their potential interconnectedness among Pakistani pregnant patients. The prevalence rates of anemia in patients with and without GDM require more detailed investigation to better understand their effects on prenatal outcomes.

This study aims to evaluate the presence of anemia among GDM and non-GDM pregnant women to analyze their relationship and examine related demographic and clinical characteristics. Also to investigate specific demographic characteristics and clinical variables associated with this relationship because these findings will enhance medical risk assessment methods while improving maternity health results.

METHODS

This comparative cross-sectional study was conducted in the Department of Medicine at Khairpur Medical College, Khairpur Mir's. over six months, from August 2024 to February 2025. Ethical approval for this study was obtained from the Institutional Review Board (IRB), Ref No. (KMC/RERC/122). All pregnant women who visited routine antenatal clinics, combined with those admitted to obstetric care during the research period, were included in the study population. Inclusion criteria: Pregnant women between 18-40 years old had singleton pregnancies at 24 to 28 weeks of gestation, which was verified through last menstrual period or early pregnancy ultrasound tests before consenting to participate in the study. Exclusion criteria: The study excluded pregnant women who had type 1 diabetes, type 2 diabetes, thalassemia or sickle cell anemia or systemic diseases or multiple pregnancies or blood transfusions during their current pregnancy. A

sample size calculation utilized the $n = Z^2 \times p \times q / d^2$ formula with Z set to 1.96 for 95% confidence, along with p representing pregnancy anemia prevalence (30%) and q (1-p), and d representing a tolerance of 7% error. A total of 200 pregnant women participated in the study after non-response adjustment, resulting in 60 GDM group participants alongside 140 participants in the non-GDM group. The researchers used non-probability consecutive sampling to select participants. The diagnosis of Gestational diabetes mellitus through a 75g Oral Glucose Tolerance Test (OGTT) occurred between weeks 24 to 28 of pregnancy. Blood samples were collected at the beginning of the test, followed by a second collection at one hour and a third at two hours after patients received glucose. GDM diagnosis followed the WHO/ADA criteria of 2013 for any fasting plasma glucose value above 92 mg/dL or one-hour plasma glucose above 180 mg/dL or two-hour plasma glucose above 153 mg/dL. Pregnant women displayed anemia according to WHO standards when their pregnancy hemoglobin levels fell below 11.0 g/dL. The clinical assessment divided anemia into mild (10.0-10.9 g/dL), moderate (7.0-9.9 g/dL) and severe (<7.0 g/dL) stages. A structured proforma collected demographic and clinical information from consenting participants who included age, pregnancy status, gestational period, BMI reading, social class, birth history, together with any family history of diabetes. The Complete Blood Count (CBC) analyzed patient hemoglobin levels for anemia grading and, alongside a 75g OGTT, evaluated patient glucose tolerance levels. The study participants were classified as GDM or non-GDM groups according to their OGTT results before researchers assessed and compared the extent and prevalence of anemia in both groups. The statistical analysis utilized SPSS version 26 for data entry and analysis. A statistical analysis of demographic and clinical variables produced mean values with standard deviations while reporting frequencies. A Chi-square test evaluated the frequency of anemia and its severity rates between patients with GDM and those without diagnosed GDM. Analysis for continuous variables included independent sample t-tests and Mann-Whitney U tests based on appropriate criteria. A logistic regression analysis determined independent anemia-related factors through an adjustment process which included age, BMI, and parity as potential confounders. The study considered statistical significance at $p < 0.05$.

RESULTS

The GDM group showed higher maternal age than the non-GDM group (29.8 vs. 27.6 years) according to statistical tests ($p = 0.008$). BMI levels among women with GDM reached 29.4 kg/m^2 while non-GDM women maintained 26.5 kg/m^2 ($p < 0.001$). The participant demographics were similar between groups, so either group received GDM pregnancy management or regular pregnancy

management. GDM patients showed lower hemoglobin levels than pregnant women without GDM at 9.8 g/dL compared to 10.5 g/dL ($p=0.001$). The prevalence of anemia in women with gestational diabetes mellitus (GDM) reached 78.3% while remaining at 57.1% in women without GDM based on significant statistical results ($p=0.004$). GDM women have higher BMI values while showing lower hemoglobin levels, which leads to increased prevalence of anemia (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants

Variables	GDM Group (n=60)	Non-GDM Group (n=140)	p-value
Maternal Age (Years)	29.8 ± 4.5	27.6 ± 4.2	0.008**
Gestational Age (Weeks)	26.3 ± 1.5	26.7 ± 1.8	0.112
BMI (kg/m ²)	29.4 ± 3.9	26.5 ± 3.7	<0.001**
Parity			
Primigravida	22 (36.7%)	63 (45%)	0.215
Multigravida	38 (63.3%)	77 (55%)	
Socioeconomic Status			
Low	18 (30%)	50 (35.7%)	0.360
Middle	29 (48.3%)	60 (42.9%)	
High	13 (21.7%)	30 (21.4%)	
Hemoglobin Level			
g/dL	9.8 ± 1.2	10.5 ± 1.4	0.001**
Anemia Status			
Anemic	47 (78.3%)	80 (57.1%)	0.004**
Non-anemic	13 (21.7%)	60 (42.9%)	

The GDM patients displayed a distinct hemoglobin concentration pattern because their results showed 9.8 ± 1.2 g/dL compared to 10.5 ± 1.4 g/dL in non-GDM patients ($p=0.001$). The study findings demonstrated poorer glucose tolerance in patients with GDM when comparing mean fasting, 1-hour and 2-hour OGTT values between groups ($p<0.001$ for each) (Table 2).

Table 2: Comparison of Mean Hemoglobin Levels and OGTT Values

Parameters	GDM Group (n=60)	Non-GDM Group (n=140)	p-value
Hemoglobin (g/dL)	9.8 ± 1.2	10.5 ± 1.4	0.001
Fasting Glucose (mg/dL)	102.3 ± 8.6	87.4 ± 7.9	<0.001
1-hour OGTT (mg/dL)	178.5 ± 24.7	132.2 ± 18.5	<0.001
2-hour OGTT (mg/dL)	152.7 ± 21.3	116.3 ± 16.7	<0.001

The logistic regression analysis demonstrated that anemia functioned as an independent factor for increased GDM odds because it produced an adjusted odds ratio of 2.35 (95% CI: 1.28–4.30, $p=0.006$). Both BMI and maternal age function as independent prognostic variables for GDM risk because the chances increase by 22% when BMI rises by one unit (OR: 1.22, $p<0.001$) and maternal age advances by one year (OR: 1.08, $p=0.048$). Parity status and socioeconomic standing did not establish a meaningful relationship with GDM (Table 3).

Table 3: Logistic Regression Analysis for Factors Associated with GDM

Variables	Adjusted OR (95% CI)	p-value
Anemia (Yes vs No)	2.35 (1.28–4.30)	0.006
BMI (per kg/m ² Increase)	1.22 (1.10–1.36)	<0.001
Maternal Age (Per Year)	1.08 (1.00–1.17)	0.048
Parity (Multigravida vs Primigravida)	1.35 (0.72–2.54)	0.340
Socioeconomic Status (Low vs High)	1.15 (0.60–2.22)	0.660

Women who had GDM (78.3%) showed an anemic condition more frequently than their non-GDM counterparts (17.9%), and the difference reached statistical significance at $p=0.021$ (Figure 1).

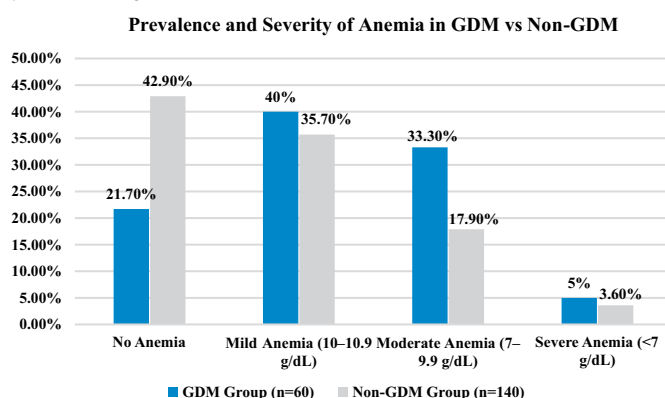


Figure 1: Prevalence and Severity of Anemia in GDM vs non-GDM

DISCUSSION

Current research confirmed that maternal age, together with BMI, served as important risk factors for GDM as demonstrated in existing literature. Maternal subjects diagnosed with GDM averaged 29.8 years old with a BMI measurement of 29.4 kg/m², which exceeded the values of non-GDM patients. Studies show that both increased BMI and older maternal age function as principal risk factors for GDM because elevated BMI causes insulin resistance, and maternal ageing diminishes pancreatic β -cell function in Table 1 [12]. Current research showed that parity status and socioeconomic background failed to establish any clear connection with developing GDM despite past research indicating otherwise. Women with reduced socioeconomic status exhibited elevated GDM risks according to Roustaei et al., because they had limited healthcare services and dietary access [13]. Our study results might show that socioeconomic characteristics within our research population maintained a similar distribution because this possibly explains the missing connection between these variables. Our findings about GDM risk factors relate to Gnanasambanthan et al., because we saw similar results that showed parity does not contribute to GDM development [14]. The GDM patient group demonstrated a statistically lower average hemoglobin level compared to the non-GDM group participants. Women with GDM experienced higher physiological stresses because their

insulin resistance potentially worsened their anemia condition [15]. The research from Guo *et al.*, matches our findings about anemia and GDM, but their work highlighted dietary habits and genetic background as elements affecting this connection [16]. Current study expands existing research by factoring in BMI and maternal age variables, which helps verify anemia as a standalone risk element for GDM [17]. Several research studies have backed our findings by demonstrating elevated anemia rates among pregnant women who have GDM. Anemia was detected in 72% of women with GDM based on the findings of Rasmussen *et al.*, and these findings are compatible with our study outcomes. The inflammatory and metabolic changes linked to GDM cause women with the condition to develop anemia at higher rates [18]. Our research investigated whether anemia exhibits any connection with gestational diabetes mellitus (GDM) prevalence during pregnancy in maternal patients in figure 1. Anemia produces a major connection with GDM, specifically in those cases of moderate anemia [19]. The prevalence of anemia among pregnant women with GDM at 78.3% exceeded the 57.1% rate observed in women without GDM, and moderate anemia commonly afflicted GDM patients. Pregnant women with GDM showed a statistically significant decrease in mean hemoglobin levels at 9.8 g/dL versus non-GDM group women who measured at 10.5 g/dL. The results of logistic regression validated anemia as an independent GDM risk factor with an adjusted OR of 2.35, together with BMI and maternal age being established predictors of GDM in Table 2 [20]. Some research findings fail to detect meaningful correlations between anemia and Gestational Diabetes Mellitus conditions. The research conducted by Santhakumar *et al.*, showed no clear connection between anemia and gestational diabetes within their study population. Another possible factor, including when anemia is detected and regional eating habits, potentially resulted in these contradictory findings. The methodological control adjustments in current study with confounding factors such as BMI, age and parity differ from their studies, which did not address these variables in Table 3 [21]. Current study establishes its diagnostic criteria for GDM and anemia through the WHO and ADA guidelines, thus proving the validity of its results. A 75g Oral Glucose Tolerance Test operated in our study served as a dependable GDM diagnostic method, which enables the results to match those from other worldwide research. This study is limited by its single-center design and relatively small sample size, which may affect the generalizability of the findings. Additionally, its cross-sectional nature restricts the ability to establish causal relationships between anemia and GDM. Future large-scale multicenter prospective studies are recommended to further explore the causal relationship between anemia

and GDM and to assess the impact of early correction of anemia on reducing GDM risk.

CONCLUSIONS

The results of this study indicate that pregnant women who have gestational diabetes mellitus demonstrate substantially higher rates of anemia in comparison to women without GDM. The study showed that moderate anemia establishes an independent link to the development of GDM among pregnant women. The study established higher maternal age and body mass index (BMI) as key elements in developing this condition. Early screening for anemia, along with glucose tolerance, must occur during antenatal care because it benefits all pregnant women who face GDM risk. The combination of anemia treatment with demographic and clinical factor management will create better results for mothers and their babies during pregnancy.

Authors' Contribution

Conceptualization: SAP

Methodology: SA, AHP, RKR

Formal analysis: SA, AA

Writing and Drafting: SAP, AHP, RKR, MAC

Review and Editing: SAP, SA, AHP, RKR, MAC, 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



Changes in Blood Pressure and Pulse Rate in Patients Following the Injection of Lidocaine with 2% Adrenaline in A Mandibular Nerve Block

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ABSTRACT

Local anaesthetic like lidocaine are commonly used in dental and maxillofacial procedures, but their systemic vasoconstrictive effects can cause physiological changes, especially in cardiovascular parameters. **Objectives:** To evaluate the blood pressure and pulse rate alterations in patients after administering a mandibular nerve block using 2% lidocaine with adrenaline. **Methods:** Three hundred patients aged 14-60 who came for extraction were selected through non-probability consecutive sampling. Clinical examinations were performed, and diastolic, systolic blood pressure, and pulse rate were recorded with an automatic digital blood pressure monitor in four stages (before local anesthesia (5 minutes' rest), before local anesthesia (sitting at chair), after local anesthesia (immediate) and after local anesthesia (10 minutes)). **Results:** A study of 300 mandibular nerve block patients found that male patients (69.3%) and female patients (30.7%) had a mean age of 32.95 ± 11.19 years. Blood pressure, pulse rate, and oxygen saturation significantly varied in all four stages. In the first stage, most patients had normal blood pressure (120/80 mmHg), while in stages 2-4, most had stage 1 blood pressure (139/89 mmHg). In stages 3 and 4, patients had stage 2 blood pressure (140/90 mmHg), and in stage 4, 1.3% experienced hypertensive crisis. In stages 1-4, most patients had normal pulse rate, followed by tachycardia and bradycardia. **Conclusions:** The study found significant differences in blood pressure and pulse rate among patients after administration of a mandibular nerve block using 2% lidocaine with adrenaline.

INTRODUCTION

Local anesthesia is a safe, effective, and economical method of reversibly blocking nerves at the application site without causing unconsciousness [1]. Anesthetic drugs block sodium ion entry via certain channels in neuronal membranes, preventing a nerve impulse from being sent [2]. Because the inferior alveolar nerve is a significant branch of the trigeminal nerve and passes through the jaw via the mandibular foramen, it is very important in dental

treatment. With an onset time of 10 minutes, this approach was claimed to have a 72% success rate. An inferior alveolar nerve block is the kind of dental anesthetic that is most often used by professionals to induce anesthesia in the posterior mandibular teeth and the soft tissues that surround them. Even in the case of a skilled physician, block failure may still happen due to anatomical, pathological, and psychological factors [3]. Today, a variety



of anesthetics with a strong safety and effectiveness record are available in dentistry to provide a comfortable procedure [4]. The fundamental molecular structure of this family of medications is composed of a positively charged amino terminus, an intermediate ester/amide chain, and a lipophilic aromatic ring. The potency, start time, and duration of action of anesthetic drugs are often taken into consideration while selecting them. However, dental practitioners should also take into account the substance's distribution, metabolism, excretion, and potential for toxicity [5]. Nowadays, the inferior alveolar nerve block is often treated using commercially accessible cartridges that include lidocaine and epinephrine [6]. A lipid-rich nerve and the interstitial tissues are easily penetrated by lidocaine, an amide-type anesthetic. Its duration of action is mild, and its start time is brief (3-5 minutes). Epinephrine is a well-known vasoconstrictor that is often used with lidocaine to lessen the likelihood of potential systemic toxicity [7]. To avoid difficulties and accomplish the desired aims, it is crucial to understand the pharmacokinetics and potential side effects of anesthetic medicines. It is fortunate that the symptoms of toxicity are only temporary and may be quickly reversed because of the short half-life of the substances [8]. When epinephrine is used with lidocaine, it may have unfavorable side effects, including hypertension, hypotension, chest discomfort, arrhythmias, tachycardia, and even cardiac arrest. However, there is a dose-dependent relationship between these cardiovascular adverse effects and the amount of anesthetic drugs in the blood. [9, 10].

This search aims to explore the effect of an injection of 2% lidocaine combined with epinephrine at a ratio of 1:80000 on cardiac parameters in people without systemic illnesses. Inconsistent findings and a lack of context-specific data, particularly in patients without underlying systemic conditions in our population, highlight a significant gap in the literature. This study shows the importance for dental professionals to assess the pharmacokinetics and pharmacodynamics of anesthetics, considering their diversity, potential side effects, and individual patient variability.

METHODS

This prospective cohort study with a non-probability consecutive sampling technique was performed at the Oral and Maxillofacial Surgery Department after the approval of the ethical committee (LUMHS/REC-127) of Liaquat University of Medical and Health Sciences from 1-8-2021 to 31-7-2022. Patients in the age range of 14-60 years of either gender, who reported for the extraction of mandibular 1st molar tooth, were included in the research. Patients suffering from high blood pressure, diabetes mellitus, cardiovascular disease, thyroid disease, pregnancy, or any known systemic illness, as well as those on medications

affecting cardiovascular parameters or with a history of allergy to local anesthetics, were excluded from the study. Written informed consent was taken from all the participants before the procedure. The sample size was calculated using the power package method in R for a paired t-test, with a significance level of 0.05 and a power of 80%. Based on the mean systolic blood pressure before injection (110.64 ± 4.14 mmHg) and after 60 minutes of injection (108.04 ± 3.24 mmHg), the estimated effect size yielded a minimum required sample size of 40 participants. However, we have included all available 300 cases in the study to enhance the robustness and generalizability of the findings [11]. Based on the American Society of Anesthesiologists Physical Status categorization Class, records of patients were reviewed to make sure none of them had any potential systemic diseases [12]. The measurement of cardiac indices was done in each instance while the patient was sitting upright and using the right hand. To determine the pulse rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP) in four distinct periods, an automated digital blood pressure monitor (HD-430M, Modigag) was utilized. First Stage (Stage 1) was before taking the subject's blood pressure and pulse rate during the first stage (Stage 1), they were instructed to relax for a minimum of five minutes. Second Stage (Stage 2) involved, before the local anaesthetic was injected, a second measurement was taken while the patient was sitting in the chair, and a dental syringe was prepared. Third Stage (Stage 3) involved, after that, each patient was given a typical inferior alveolar nerve block using a single cartridge of 2% lidocaine and 1:80000 epinephrine (Medicaine, manufactured in Korea). The final set of measurements was taken after the injection was correctly done and the dental syringe was removed. To avoid intravascular injection of the anesthetic solution, appropriate aspiration was carried out in each instance, and great care was taken to provide a painless injection. In Fourth Stage (Stage 4), ten minutes after the local anesthetic was administered, the last set of measurements was taken. To reduce the amount of variation in the results, a single operator performed all injections and measurements. After an inferior alveolar nerve block, each individual had dental operations depending on what was deemed required. Statistical analyses were performed using SPSS 22. All continuous variables were represented by means and standard deviations. The cardiac indicators were compared between the stages using a chi-square test/fisher exact test. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

The majority of the participants were male, 208 (69.3%), while female patients constituted 92 (30.7%). The mean age of the participants was 32.95 ± 11.19 years (Table 1).

Table 1: Age and Gender Distribution of the Participants Undergoing Mandibular Nerve Block (n=300)

Parameters	Variables	n (%)
Gender	Male	208 (69.3%)
	Female	92 (30.7%)
Age (Years)	Mean $\pm$ SD	32.95 (11.19%)

The distribution of patients' blood pressure across the four stages is presented. A statistically significant difference in blood pressure was observed across the stages ($p < 0.001$). Normal blood pressure (120/80 mmHg) was most commonly observed at Stage 1 (S1) in 158 patients (52.7%), which declined progressively in the subsequent stages. Elevated blood pressure (140/90 mmHg) was most prevalent in Stage 3 (S3), affecting 48 patients (16.0%), and remained high in Stage 4 (S4) (47 patients, 15.7%). Severe hypertension (180/120 mmHg) was only recorded in Stage 4 (S4) in 4 patients (1.3%), while no such cases were observed in the earlier stages (Table 2).

Table 2: Distribution of Blood Pressure of the Patients According to Four Stages of the Study (n=300)

BP (mmHg)	S1 (%)	S2 (%)	S3 (%)	S4 (%)	p-value
120/80	158 (52.7%)	29 (9.7%)	41 (13.7%)	35 (11.7%)	<0.001
129/80	74 (24.7%)	94 (31.3%)	77 (25.7%)	86 (28.7%)	
139/89	55 (18.3%)	152 (50.7%)	134 (44.6%)	128 (42.6%)	
140/90	13 (4.3%)	25 (8.3%)	48 (16.0%)	47 (15.7%)	
180/120	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (1.3%)	

*Fisher's exact test

The distribution of patients' pulse rates across the four stages is presented in Table 3. A statistically significant difference in pulse rate was observed across the stages ($p = 0.003$). Normal pulse rate (60–100 beats/min) was most frequently observed in Stage 1 (S1) in 216 patients (72.0%), which declined during Stage 2 (S2) (194 patients, 64.6%) and Stage 4 (S4) (196 patients, 65.4%). Tachycardia (>100 beats/min) increased from 63 (21.0%) in Stage 1 to 92 (30.7%) in Stage 2, with the highest prevalence in Stage 4 (32.3%, $n=97$). Bradycardia (<60 beats/min) was least common, with a gradual decline from 21 (7.0%) in Stage 1 to 7 (2.3%) in Stage 4 (Table 3).

Table 3: Patient's Pulse Rate Distribution According to Four Stages of Study (n=300)

Pulse Rate (beats /min)	S1 (%)	S2 (%)	S3 (%)	S4 (%)	p-value
60-100	216 (72.0%)	194 (64.6%)	209 (69.7%)	196 (65.4%)	0.003
>100	63 (21.0%)	92 (30.7%)	83 (27.6%)	97 (32.3%)	
<60	21 (7.0%)	14 (4.7%)	8 (2.7%)	7 (2.3%)	

*Chi-square test

DISCUSSION

Vasoconstrictive medications, which extend the duration and enhance clinical effectiveness of local anesthesia, are widely accessible and may be used with a variety of local

anesthetic agents. Adrenaline and lidocaine are most often used in different concentrations. Adrenaline-like medicines may produce a variety of cardiovascular problems, most of which are transient. However, in cases of pharmacologically induced ventricular arrhythmia, Ischemic myocardial necrosis, or cerebrovascular episodes, lasting harm or even death may result [13–16]. In this research, individuals who reported for the extraction of 1st molar teeth underwent mandibular nerve block, were male 208 (69.3%) and 92 (30.7%) were female, with a mean age of 32.95 ± 11.19 (14–60) years. A similar study by Gadve et al., reported the higher female patients 56.7% and 43.3% were male patients with a higher mean age of 37 years [10]. Deo et al., reported the higher male patients 60% and lower female patients 40% with a mean age of 24.93 years [17]. Most of the young patients were suffering from different tooth problems and underwent mandibular nerve block. In this study, blood pressure ($p < 0.001$) and pulse rate ($p = 0.003$) were significantly different in all four stages (before local anesthesia (5 minutes' rest), before local anesthesia (sitting at chair), after local anesthesia (immediate) and after local anesthesia (10 minutes)). A study by Gadve et al., also reported the significant changes in blood pressure and observed maximum blood pressure at the time of surgery. Four minutes after the local anesthetic injection, the heart rate reached its peak, and it fell to its lowest point once the tooth extraction was finished. throughout the course of the investigation, notable variations were seen in oxygen saturation, heart rate, and blood pressure [12]. Another study by Chowdhury et al., reported the difference in blood pressure preoperatively, whereas a significant increase in blood pressure intraoperatively and postoperatively [18]. Another study by Brkovic et al., reported a significantly decreased pulse rate 10 min after surgery [19]. All similar study findings show the effect of lidocaine with 2% adrenaline on cardiac indices such as increased blood pressure, tachycardia, bradycardia and hypoxemia during different stages, especially after injecting 2% lidocaine with epinephrine. according to research by Aliabadi et al., none of the patients had any signs of arterial hypertension, and both SBP and DBP were within the normal range at all phases (less than 130 and 80 mmHg, respectively). There were no indications of bradycardia or tachycardia, even though the pulse rate increased significantly at stages 2, 3, and 4 in comparison to stage 1 ($p < 0.050$) [20].

This study is limited by its relatively small sample size and single-center design, which may restrict generalizability to broader populations. In addition, the short observation period around the procedure limits assessment of delayed or rare cardiovascular complications associated with adrenaline-containing local anesthetics. Future multicenter studies with larger sample sizes and continuous intraoperative monitoring are recommended to better evaluate the cardiovascular effects of different concentrations of adrenaline in local anesthesia during dental procedures.

CONCLUSIONS

Following the administration of lidocaine and adrenaline at a concentration of 2% in mandibular nerve block, the researchers concluded that the patients' blood pressure and pulse rate were substantially different following each of the four phases of the procedure. Elevated blood pressure, stage 1 blood pressure, stage 2 blood pressure, tachycardia, bradycardia, low oxygen saturation and hypoxemia significantly increased from stage 1 to stage 4, especially after injecting 2% lidocaine with epinephrine. These findings show the importance of careful monitoring of hemodynamic parameters during dental procedures, especially in at-risk patients with underlying cardiovascular conditions.

Authors' Contribution

Conceptualization: M, SS

Methodology: M, FH

Formal analysis: SKP, AH

Writing and Editing: MAS, MO, MA

Review and Editing: M, AH, MAS, MO, SKP, FH, SS, MA

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



Assessing the Efficacy of Ultrasound-Guided Erector Spinae Plane Block in Pyelolithotomy or Nephrectomy Patients

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ABSTRACT

Nephrectomy and pyelolithotomy are invasive surgical procedures often associated with significant postoperative pain, necessitating effective analgesia for optimal recovery. **Objectives:** To evaluate the efficacy of ultrasound-guided erector spinae plane block (ESPB) in patients undergoing nephrectomy or pyelolithotomy, with a focus on pain relief, dermatome coverage, and duration of analgesia. **Method:** This quasi-experimental study was conducted over 12 months in the Anesthesia Department of Sharif Medical City Hospital, Lahore, enrolling 66 patients. After receiving ESPB, postoperative pain was assessed using the Visual Analogue Scale (VAS) at rest, where 0 indicated no pain and 10 indicated the worst possible pain. Dermatome coverage was evaluated via pinprick testing, and the time to first rescue analgesia was recorded. Data analysis was performed using SPSS version 25.0. **Results:** Out of the 66 patients, 47 were male and 19 female. VAS scores showed a significant reduction from 2.98 ± 1.31 at 24 hours to 0.87 ± 0.83 at 72 hours ($p=0.000$). Pain on movement significantly decreased ($p=0.000$), while sleep quality showed no significant improvement. The proportion of patients reporting adequate pain relief rose from 67.3% at 24 hours to 81.5% at 72 hours ($p=0.000$). Peak rescue analgesia demand occurred at 15-16 hours postoperatively (25 patients), indicating prolonged initial analgesia. **Conclusions:** It was concluded that the ultrasound-guided erector spinae plane block (ESPB) effectively manages pain, significantly reducing VAS scores over 72 hours. This method delivers high-quality analgesia with consistent dermatome coverage following pyelolithotomy and nephrectomy.

INTRODUCTION

Nephrectomy and pyelolithotomy are complex surgeries causing significant pain due to tissue manipulation, inflammation, and surgical trauma [1]. Postoperative pain intensity and duration vary due to surgical technique, patient factors, and comorbidities. Poor pain control reduces comfort, increases complications, prolongs hospital stay, and delays recovery. Additionally, in patients with existing or surgery-related renal impairment, careful analgesic selection and dosing are essential to avoid nephrotoxicity [2]. Normal clinical procedure for pain relief

after pyelolithotomy and nephrectomy involves instituting multimodal analgesia, which integrates both pharmacological and non-pharmacological interventions in an attempt to lower morbidity and mortality [3]. Morphine and hydromorphone provide pain relief but have side effects and tolerance issues, which peripheral nerve blocks and epidurals help reduce by lowering opioid use [4]. The erector spinae plane block (ESPB) has proven effective in decreasing opioid administration after surgery and is applicable in several surgical procedures, which include



thoracic, abdominal, and limb surgeries. [5]. ESPB is performed at lumbar or thoracic levels, where the erector spinae muscles are superficial, targeting the plane between these muscles and the vertebral transverse processes. Injection here blocks dorsal and ventral spinal nerves, providing relief for both visceral and somatic pain. [6]. Local anesthetic spread causes sympathetic blockade, leading to vasodilation and reduced pain signal transmission. ESPB effectively lowers pain scores and opioid use across surgeries, with analgesia duration varying by agent, dose, patient, and procedure [7]. ESPB provides prolonged analgesia lasting up to 24 hours and supports faster recovery through early mobilization, reduced hospital stay, and improved patient satisfaction. [8] Anatomical variations, such as erector spine muscle thickness and neurovascular proximity, can affect ESPB efficacy, highlighting the need for patient-specific planning [9]. Hematoma risk is a concern in coagulopathic or anticoagulated patients, warranting coagulation assessment and perioperative precautions. Improper spinal positioning may also hinder accurate needle placement and block success [10]. Though generally safe, ESPB carries risks of iatrogenic injury to neurovascular structures and pleura, especially at caudal thoracic levels; ultrasound guidance significantly reduces these risks by allowing real-time visualization [11, 12]. Complications like pneumothorax and systemic anesthetic toxicity, while rare, necessitate vigilance and adherence to dosing protocols, with readiness for interventions like lipid therapy [12]. Ultrasound aids in accurate needle placement, anesthetic spread, and avoidance of vital structures, improving safety and efficacy [13,14]. It also supports operator learning and standardization of technique, including in diverse clinical settings like Rawalpindi [15]. However, limitations remain regarding consistent evaluation of ESPB effectiveness and duration of postoperative analgesia [16]. Long-term follow-up is essential to assess the sustained effectiveness of ESP blocks, particularly after renal surgeries where dermatomal coverage remains unclear. Despite the effectiveness of multimodal analgesia in managing postoperative pain after nephrectomy and pyelolithotomy, opioid-related side effects and variability in pain control highlight the need for safer and more effective regional techniques such as the erector spinae plane block (ESPB). However, limited evidence exists regarding its analgesic efficacy, duration of action, and safety profile specifically in renal surgeries, particularly in local clinical settings. This study aims to evaluate ultrasound-guided ESP blocks in kidney procedures in Rawalpindi, focusing on analgesic efficacy, duration, and safety. Findings aim to refine block techniques and guide evidence-based perioperative pain management.

METHODS

A quasi-experimental study was done in the Anesthesia Department of Sharif Medical City Hospital from September 2022 to May 2023 after taking approval from the ethical review board of Sharif Medical City Hospital (IRB # 507-22). After informed consent, all the patients underwent open nephrectomy or pyelolithotomy under general anesthesia through flank incision. A specific criterion of inclusion and exclusion was designed. Inclusion criteria were patients aged between 20 and 65 years, either male or female and who came under the ASA II category. ASA Physical Status classification is a universally applied system to assess and communicate the pre-anaesthetic medical condition of the patient and related comorbidities. It contributes to the perioperative risk evaluation and makes the preoperative evaluation uniform. In the present study, only ASA II patients were analyzed, which means such individuals with mild and well-controlled systemic diseases that do not affect normal activity. Study excluded the patients who were operated on with any other incision, had a history of allergy to local anesthetics, any skin pathology at the site of needle insertion, bleeding disorders, diabetes, liver disease, psychiatric illness, or any other comorbidity. The sample size of 66 patients with open nephrectomy was estimated using the prevalence of open nephrectomy was 78% [17], at a 10% margin of error and 95% confidence level with the following formula: $n = Z^2_{\alpha/2} \cdot P(1-P)/d^2$. Patients were educated about the post-operative pain score preoperatively. All blocks were given in lateral decubitus position once the patient was given general anesthesia. We gave 0.25% bupivacaine at a dose of 1 ml/kg. After painting and draping, a 6-12 MHz linear ultrasound probe was placed parallel to the spine in a cephalocaudal orientation over the midline of the back between 10 to 12th thoracic vertebrae. The probe then slowly moves laterally until the transverse process of T11 is visible. Following this, the erector spinae is identified as being superficial to the transverse process. A 20-gauge spinal needle was advanced over the probe, in cephalad to caudal direction, using an in-plane approach. The needle is inserted until the tip touches the transverse process. Then the needle was withdrawn a little, and local anesthetic was injected. Before injecting the anesthetic, the plunger was withdrawn to confirm no intravascular injection was being given. The injection was then given slowly, and a separation of the plane between erector spinae and transverse process was observed, confirming the proper plane of injection. Postoperative pain at rest was evaluated using the Visual Analogue Scale (VAS) after the patient responded to verbal prompts and following the administration of the erector spinae plane (ESP) block. The VAS is a scale from 0 (no pain) to 10 (worst imaginable pain) [18]. Pain assessment was done at 24, 48, and 72 hours' post-surgery. To assess the degree of sensory blockade, the dermatomes were evaluated using the pinprick method

within 30 to 45 minutes after the block was given during the early postoperative period. Satisfaction with pain management was measured in addition to objective assessment of pain using the Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R) at 24, 48, and 72 hours postoperatively. This validated, multidimensional instrument captures multiple dimensions of pain care, including pain intensity, relief, interference, and communication with the healthcare provider. In addition, time to first rescue analgesic (in hours) was noted for each patient to assess the duration of effective analgesia [19]. Patients' baseline information like Age (years), Gender, BMI (kg/m²), Surgical side (R/L), ASA classification and Surgical Procedure (Open nephrectomy/pyelolithotomy) were collected on a pre-designed performa. All the data were entered and analyzed by SPSS version 25.0. Descriptive analysis was conducted by calculating Frequencies, percentages and mean $\pm$ SD for study variables. The comparison of mean pain score among different intervals was done by using one-way ANOVA after checking normality of data by Kolmogorov-Smirnov. Statistical significance was determined at p -value < 0.050 .

RESULTS

A total of 66 patients were included in this study. The average age reported in the current study was 46.2 ± 11.8 years. There were male (71.2%), while 28.7% were female. Regarding surgical laterality, 45 patients underwent surgery on the left side, while 21 had right-sided procedures. Based on the ASA classification, 56.0% of patients were categorized as ASA I, and 43.9% as ASA II. The most common surgical procedure performed was pyelolithotomy (59.0%), followed by open nephrectomy (40.9%) (Table 1).

Table 1: Patient Demographics and Baseline Information (n=66)

Parameters	n (%)
Age	
Years	46.2 ± 11.8
Gender	
Male	47 (71.2%)
Female	19 (28.7%)
BMI	
(kg/m ²)	24.3 ± 3.1
Surgical side (R/L)	21/45
ASA Classification	
ASA I	37 (56.0%)
ASA II	29 (43.9%)
Surgical Procedure	
Open nephrectomy	27 (40.9%)
Pyelolithotomy	39 (59.0%)

Post-procedure pain showed a significant reduction over time following the erector spinae block (ANOVA: $F=64.3$, $p<0.001$). The VAS score at 24 hours was 2.98 ± 1.31 ,

decreasing to 2.33 ± 1.07 at 48 hours, and further to 0.87 ± 0.83 at 72 hours. This progressive decline in pain scores indicates the sustained analgesic efficacy of the erector spinae block over three days postoperatively (Table 2).

Table 2: Comparison of Mean Pain Score and Different Time Interval among Patients

Post-Procedure Pain Levels (After the Erector Spinae Block)	Visual Analogue Score (Mean $\pm$ SD)	ANOVA (df), p-value
24 Hours	2.98 ± 1.31	$64.3(2)$, <0.001
48 Hours	2.33 ± 1.07	
72 Hours	0.87 ± 0.83	

The frequency of dermatome anesthesia achieved following the administration of the erector spinae block (ESB) was assessed across several levels. At the T8 level, anesthesia was observed in 17 participants (25.81%). At the T9 level, anesthesia was achieved in 57 patients, representing 87.09% of the total cohort. At the T10, T11, and T12 levels, complete anesthesia was observed in all 66 patients. At the lower levels, specifically at the L1 level, anesthesia was achieved in 43 patients, which accounted for 64.51% of the total participants (Table 3).

Table 3: Frequency of Each Dermatome Anesthetized

Dermatomes	Frequency (%)
T8	17 (25.81%)
T9	57 (87.09%)
T10	66 (100%)
T11	66 (100%)
T12	66 (100%)
L1	43 (64.51%)

Patient satisfaction with pain management, assessed over 72 hours, showed significant improvements in most parameters. Pain on movement in bed decreased from 2.95 ± 1.66 at 24 hours to 0.89 ± 0.80 at 72 hours (ANOVA: 38.21 , $p<0.001$), and pain during activity out of bed also declined significantly (ANOVA: 5.69 , $p=0.004$). In contrast, sleep-related parameters (falling asleep and staying asleep) showed no significant variation over time ($p=0.270$ and $p=0.954$, respectively), suggesting minimal impact of pain management on sleep disturbances. Pain relief from treatment increased steadily from 67.3% at 24 hours to 81.5% at 72 hours (ANOVA: 31.9 , $p<0.001$), indicating effective pain control over time. These findings highlight progressive pain relief and improved mobility, though sleep disturbances remained unchanged (Table 4).

Table 4: Comparison of Patients' Satisfaction Scores Among Different Time Intervals

Patient Satisfaction Scores	Response at 24 (Hour)	48 (Hour)	72 (Hour)	ANOVA (df), p-value
Pain on movement in the bed (0-10)	2.95 ± 1.66	2.18 ± 1.47	0.89 ± 0.80	$38.21(2)$, <0.001
Pain while doing an activity out of bed (0-10)	2.42 ± 1.72	1.98 ± 1.49	1.56 ± 1.12	$5.69(2)$, 0.004

Falling a sleep (0-10)	1.95 ± 1.41	2.27 ± 1.43	1.89 ± 1.46	1.31(2), 0.270
Staying a sleep (0-10)	2.46 ± 1.72	2.51 ± 1.72	2.42 ± 1.61	0.047(2), 0.954
Pain relief using pain treatment (0-100%)	67.3 ± 19.6	74.2 ± 15.6	81.5 ± 13.7	31.9(2), <0.001

One Way ANOVA, Score Interpretation: 0=no pain, 10= worst pain, (0% = no relief, 100% = complete relief).

Only 5 patients required rescue analgesia within 4 hours, indicating good initial pain control. The need gradually increased, peaking at 15–16 hours with 25 patients. After 16 hours, the demand slightly decreased but remained notable (16 patients), suggesting the block's effect wanes around 15–16 hours postoperatively (Figure 1).

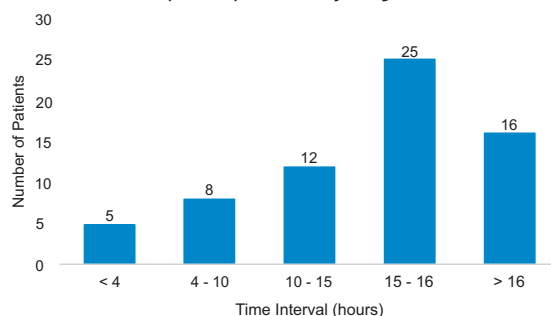


Figure 1: Distribution of Patients Based on the Time Interval Until Administration of Rescue Analgesia

DISCUSSION

Erector spinae block (ESB) has emerged as a promising alternative to traditional intravenous (IV) or inhalational anesthesia for pain management in open nephrectomy and pyelolithotomy. By directly targeting the nerves which transmit pain signals from the surgical site, ESB can provide effective pain management while minimizing systemic effects [20]. The study shows that ESB provides analgesic effects that are strong but also have a rapid onset; it reduces pain rapidly, which is helpful in clinical settings, for example, for acute trauma, emergency surgeries, or procedures requiring rapid pain relief. This immediate pain-relieving effect improves patient comfort, makes procedures easier to perform, and accelerates recovery after surgery. Moreover, ESB may help to decrease the systemic opioid consumption, together with the risks of respiratory depression and sedation. In addition, a randomized control trial by Elyazed showed that the ESB group (10 patients) had a lower rescue analgesia (pethidine) use compared to the control group (25 patients), with the requirement for rescue analgesia occurring after 12 hours and corresponding to 8 patients [21]. This aligns with the broader goal of continuous analgesia requirement, which aims to improve pain management by minimizing opioid exposure and related complications. Moreover, various studies have shown that erector spinae block provides a better analgesic effect than other types of block for renal surgeries. A randomized controlled trial has shown that erector spinae plane block provides non-inferior analgesia for pain at rest within 24

postoperative hours in comparison to thoracic paravertebral block for nephrectomy, which is consistent with the findings of this study [22]. An Indian study has also compared the post-operative analgesia of ultrasound-guided ESB with subcutaneous infiltration, showing that the first analgesia was given after 12 hours in ESB patients, while for the bupivacaine group first dose was needed after 30 minutes [23]. Ultrasound-guided ESPB reduces intravenous opioid consumption 24 hours after surgery, decreases postoperative analgesia requirements, and prolongs time to first rescue analgesia [24]. The erector spinae block (ESB) provides pain relief over several dermatomes, providing broader coverage than traditional nerve blocks or systemic analgesics. Research has shown 100% coverage in the T10, T11, and T12 dermatomes, 87.09% in T9, and 64.51% in L1, providing effective pain control distant from the site of incision. Such an extensive analgesic effect improves patient comfort during the postoperative period. Past studies indicate the efficacy of ultrasound-guided ESP blocks with 20 mL of 0.5% plain bupivacaine in the relief of pain in nine dermatomes with few complications [25]. With its efficacy and safety, the ESP block may prove to be a good choice for chest, abdominal, and limb surgery in Rawalpindi, which can decrease the requirement of strong opioids and enhance patient outcomes [26].

It is acknowledged that current research is limited by factors such as sample size and single-center study design. Nevertheless, existing data indicate that ESPB may serve as a safe and efficacious analgesic modality for lumbar surgical procedures. Future studies should include larger multi-center trials to confirm the safety and efficacy of ESPB in lumbar surgeries and optimize its clinical application.

CONCLUSIONS

Ultrasound-guided erector spinae plane block (ESPB) provides effective pain control, demonstrated by a significant decrease in VAS scores over 72 hours. Most patients required rescue analgesia only after 15 to 16 hours, indicating prolonged relief. This technique for managing perioperative pain in pyelolithotomy and nephrectomy offers high-quality, prolonged analgesia with consistent dermatome coverage and significantly reduced postoperative pain scores.

Authors' Contribution

Conceptualization: ST

Methodology: SN, AZ

Formal analysis: SN, MA

Writing and Drafting: ST, SA, HNA

Review and Editing: ST, SN, SA, AZ, HNA, MA

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



Barriers to the Implementation of Evidence-Based Practice in A Tertiary Care Hospital Mirpur, Azad Kashmir, Pakistan: A Cross-Sectional Study

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ABSTRACT

An approach to providing care to patients is based on problem-solving decisions on the greatest reliable and current data is known as Evidence-Based Practice (EBP). **Objective:** To assess the organizational and individual barriers to implementing Evidence-based practice among registered nurses in a tertiary care hospital in Mirpur, Azad Kashmir. **Methods:** A descriptive cross-sectional study was conducted from December 2023 to July 2024 at a tertiary care hospital in Mirpur, Azad Kashmir. Data were collected from 120 registered nurses from different departments with more than one year of clinical experience. The sample size was determined using the Yamane formula. Before starting the data collection process, the study protocol was approved by the Institutional Review Board, and written informed consent was obtained before data collection. A validated questionnaire comprises 24 statements on a five-point Likert scale from strongly disagree to strongly agree was used. **Results:** The most significant organizational barriers are lack of financial encouragement for using evidence-based practice ($M = 4.41$), inadequate resources at the workplace ($M = 4.25$), limited access to updated nursing journals ($M = 4.39$), and lack of human resources to implement EBP ($M = 4.24$). Resistance to adopting new strategies ($M = 4.22$) and limited autonomy in modifying procedures ($M = 4.15$) are the most common individual barriers. **Conclusions:** The study highlighted the prevalence of practical barriers that prevent nurses from implementing evidence-based practice and emphasizes the need for healthcare organizations to address them.

INTRODUCTION

Evidence-based practice is the process of transforming patients' informational needs into answerable questions, through the integration of clinical competence with patients' preferences and values, and the best available evidence [1]. Globally, health care must be grounded in the most recent scientific innovations, as emphasised by the WHO and the European Commission. Assessing the readiness of nurses before implementing Evidence-based practice is essential as it will demonstrate their effectiveness and knowledge [2]. The development of evidence-based guidelines and resources from specialised

organisations like Joanna Briggs Institute and Cochrane has resulted from the emphasis on Evidence-Based Practice (EBP) in nursing in countries like the United States, the United Kingdom, and Australia since the 1990s [3]. Nurses play a critical role in two major tasks: the care of the patient and the implementation of research findings into practice. This is because of their important roles in patient care and in putting research findings into practice [4]. Nurses are the most important healthcare professionals in providing healthcare services, according to study results for better patient outcomes. Rousseau et



al., explored the psychological factors influencing the implementation of evidence-based practice (EBP), highlighting how cognitive, social, and organizational dynamics affect its adoption in professional settings [5]. It is not adequate for nurses to provide care solely based on their textbook knowledge and experience; instead, they must deliver high-quality nursing care based on research findings. This is because society today has higher expectations for high-quality nursing care [6]. EBP has many advantages for nurses, such as strengthening their capacity to serve patients with safe and valid practices, developing their leadership abilities, and increasing their critical thinking skills [7]. Although the usage of the findings in the healthcare setting is important, there is still a knowledge gap regarding the practical application of these findings [8]. EBP implementation is hindered worldwide by many challenges, including staffing shortages, education, technology, time restrictions, and financial assistance [9]. Given its foundation in the relationship between clinical practice and research evidence, evidence-based nursing has gained widespread acceptance among healthcare providers. Many solid barriers and attitudes impact how EBP is understood and applied [10]. The concept of evidence-based practice is not well-known to many nurses, and several barriers prevent its application in the nursing profession [11]. A few of the things that can significantly affect a nurse's performance are heavy workloads, a lack of technological support, skills and competencies, confidence and communication skills, commitment, a high standard of work-life balance, stress at work, and motivation. It's interesting to note that the majority of these elements fall within the leadership management category [12]. A narrative review done by the Nursing department at the University of Ibadan, Nigeria, discoursed that evidence-based practice is relatively young in Africa when compared to other developing countries. Major variables that impact the adoption of EBP in these regions include a lack of time, a high burden of disease-limited resources, and poor support from the government, organisations, and professional leaders [13]. Some major barriers regarding EBP adoption were identified in a study undertaken at public hospitals in Ethiopia. Barriers to the implementation of EBP, mostly mentioned by study participants, were the lack of official EBP frameworks, poor facility infrastructure, difficulty in accessing the guidelines, and insufficient training for medical staff [14]. Although there are many researchers conducted related to evidence-based practice and its benefits on an international level, there is limited research available on this topic in the specific region of Azad Jammu Kashmir (AJK). Therefore, the study aimed to determine the organisational and individual barriers to the implementation of EBP among registered nurses in the

tertiary care hospital in Mirpur, Azad Jammu and Kashmir. The contribution of this study is to fill the existing gap. It can also provide valuable insights into healthcare practices related to the implementation of EBP after identifying and eradicating those factors that are hindrances in the way of implementing EBP within the nursing culture of Pakistan. EBP has historically focused on questioning, reading, and analysing the evidence, but it has had difficulty putting the evidence into practice. Sackett's model mainly depends on considering patient values and preferences together with clinical skills utilising the best available evidence. Every aspect of healthcare has adopted and changed this model as a result of its effect [15]. Each of the components of Evidence-Based Practice (EBP) has little value by itself; it becomes significant when combined with adjacent elements. Finding, evaluating, and using the best external clinical data that is available is the first step. Numerous sources, such as case reports, different scientific designs including qualitative and descriptive research, and randomised controlled trials, can provide this data. The second component is clinical expertise, encompassing the competence and awareness that doctors acquire during their clinical practice. The application of external evidence to specific patients is determined by the clinician's skill, not by the external evidence itself, even while it offers insightful information that cannot replace clinical experience. The last step is to take the values and preferences of the patients into account, which is crucial for choosing the right course of treatment. Patients' perceptions must be taken into account when making decisions about their care since even excellent external evidence may not apply to every patient [16, 17]. Using the Sackett Model of EBP, the researcher tried to explore the concept of using evidence-based practice in this study. The researcher thinks that this model will provide the theoretical support necessary to direct appropriate and successful treatment in light of major contextual challenges (Figure 1).

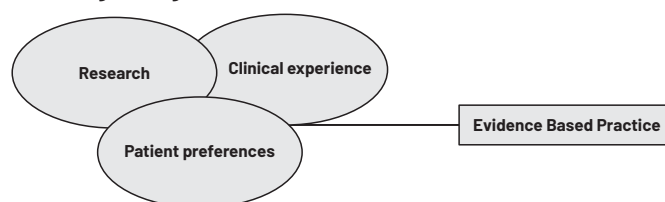


Figure 1: Evidence Based Practice Model (Sackett, 1992) [16]

Despite the global emphasis on Evidence-Based Practice and its proven benefits in improving patient outcomes, its practical implementation among nurses remains limited due to multiple organizational and individual barriers. In regions like Azad Jammu and Kashmir, there is a significant lack of context-specific evidence exploring these challenges, highlighting a clear research gap. Therefore,

this study aims to identify and assess the key barriers affecting the adoption of EBP among registered nurses in a tertiary care hospital in Mirpur, with the goal of informing strategies to enhance evidence-based nursing practices in Pakistan.

METHODS

This study was conducted at a tertiary care hospital in Mirpur, AJK, because it's a teaching hospital with a nursing college offering various nursing degrees and specialties. The hospital has different departments that require evidence-based practice. A total of 173 registered nurses were identified as the study population, and a sample of 120 nurses was selected using simple random sampling through the lottery method. The sample size was calculated using the Yamane formula with a 5% margin of error, resulting in a sample size of 120.

Yamane formula $n = N / 1 + N(e)^2$

Where n sample size

N= total population=173

E= margin of error

$n = 173 / 1 + 173(0.05)^2 = 120$

The calculated sample size was 120 nurses registered by the Pakistan Nursing and Midwifery Council with over one year of experience and specific educational backgrounds (BSN/Post RN and general nursing diploma). These nurses were chosen due to their direct involvement in patient care and awareness of organizational activities. Nurses not present during data collection, and those unwilling to participate were excluded. A questionnaire regarding barriers to the implementation of EBP was used by Khamarnia in 2014 in Iran, which consists of two parts: individual barriers and organizational barriers has been used in this study. It consists of 24 statements with a Likert scale from strongly disagree to strongly agree, and respondents were asked to score according to these statements. Scoring Key: 1) SD = strongly disagree 2) D = Disagree 3) N = Neutral 4) A= Agree 5) SA = strongly agree. Demographic data about age, education and work experience was also gathered. The permission was obtained from the author via email for the tool's adaptation and use. The questionnaire's validity was confirmed by a panel of experts, and pilot testing showed it was clear and feasible. The tool's reliability was confirmed with a Cronbach's alpha score of 0.81. Before starting the data collection process, ethical approval and official permission were obtained for data collection from the Institutional Review Board committee of the tertiary care hospital Mirpur, Azad Kashmir. (REF.NO.05/ACADEMICS BLOCK TRAUMA CENTRE/SURGERY/2024). Data were collected in February 2024. To protect the data, strict measures were taken to ensure its security and confidentiality. These measures included storing electronic data on password-protected devices and securely storing hard copies in

locked facilities. The study duration was from December 2023 to June 2024. Before data collection, each participant was given written informed consent and an information sheet. A forty-minute conversation was held with participants to provide a clear explanation of the questionnaire. Voluntary participation was ensured as participants had the freedom to refuse or withdraw at any time without being penalised. In addition, they were ensured in terms of confidentiality by protecting data from access by unauthorized persons. Also, participants' anonymity was ensured by assigning different codes instead of using their names. The statistical package for the social sciences (SPSS), version 24.0, for data entry and analysis was used. The study used descriptive statistics, including frequency and percentage for demographic data, and mean and standard deviation to assess individual and organizational barriers to Evidence-Based Practice implementation.

RESULTS

The study sample was 120 nurses; the maximum number of nurses (60%) is in the 22–32 age range, which suggests that the participants are mostly younger. The next largest age group is 33–43 (27.5%), followed by those 43 and over (12.5%), also shown in figure 2.

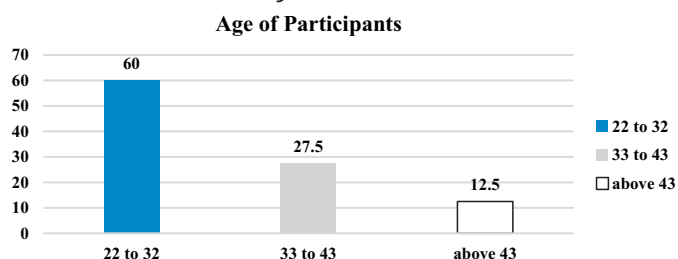


Figure 2: Percentages of Participants' Age Groups

The majority (71.7%) held a diploma in general nursing, while 28.3% had a post-RN/BSN degree, also shown in figure 3.

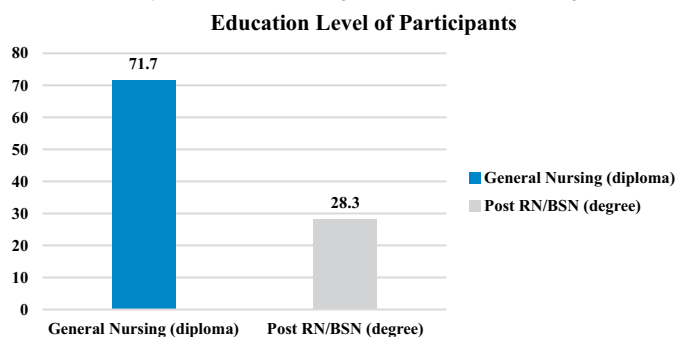
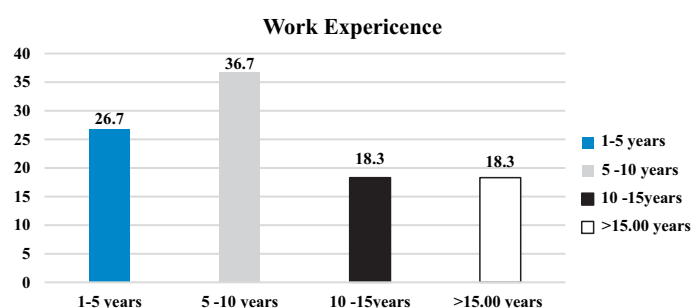


Figure 3: Education Level of the Respondent

Work experience was diverse, with the largest group (36.7%) having 5–10 years of experience, followed by 1–5 years (26.7%), 10–15 years (18.3%), and >15 years (18.3%), also shown in figure 4.

**Figure 4:** Job Experience of the Respondent

The most significant barriers to implementing Evidence-Based Practice (EBP) are resource-related that are revealed in Table 1. Specifically, the top barriers include: lack of financial encouragement for using evidence-based care ($M = 4.41 \pm 0.93$), inadequate resources at the workplace ($M = 4.25$), limited access to updated nursing journals (mean = 4.39), and lack of relevant literature ($M = 4.15$) lack of human resources to implement EBP ($M = 4.24$) highlights the need for adequate staffing (Table 1).

Table 1: Organizational Barriers to Implementing EBP (n=120)

S. No.	Questions	SD	D	N	A	SA	Mean $\pm$ SD
1	Lack of knowledge among nurse managers about Evidence-Based Practice (EBP)	4.2	10	25.8	44.2	15.8	3.57 $\pm$ 1.00
2	Lack of interest in EBP by nurse managers	5.0	10.0	22.5	43.3	19.2	3.61 $\pm$ 1.06
3	The new ideas do not apply to nursing care	11.7	23.3	12.5	27.5	25	3.30 $\pm$ 1.37
4	The results of the research are not applicable in the clinical setting	13.3	20.8	11.7	31.7	22.5	3.29 $\pm$ 1.37
5	Lack of financial encouragement for nurses who use EBP	1.7	6.7	8.3	45.0	38.3	4.41 $\pm$ 0.93
6	The nurse managers do not have sufficient time to evaluate evidence-based nursing care	5.8	15.0	5.8	40.8	32.5	3.83 $\pm$ 1.23
7	No cooperation and participation by physicians in using EBP	5.8	18.3	7.5	26.7	41.7	3.85 $\pm$ 1.31
8	No appreciation by managers to implement EBP in patient care	7.5	29.2	12.5	25.0	25.8	3.32 $\pm$ 1.33
9	Insufficient attention by managers to the use of research in the performance of EBP	1.7	12.5	10	42.5	33.3	3.93 $\pm$ 1.04
10	No conference or workshop on the importance of the implementation of EBP by the administration for nurses	5.0	5.0	5.8	40.0	44.2	4.13 $\pm$ 1.06
11	Lack of trained (expert) staff on how to use the results of research studies in clinical practice	1.7	17.5	10.8	45.0	25.0	3.74 $\pm$ 1.07

12	Insufficient resources at the workplace	0	4.2	18.3	26.7	50.8	4.25 $\pm$ 0.89
13	Access to an updated library with nursing journals is limited	0	4.2	5.0	38.3	52.5	4.39 $\pm$ 0.77
14	Lack of relevant literature about EBP, such as Journals	1.7	5	8.3	46.7	38.3	4.15 $\pm$ 0.89
15	Lack of human resources to implement EBP	0	5.8	8.3	41.7	44.2	4.24 $\pm$ 0.84

*(SD=Strongly Disagree, D= Disagree, N=Neutral, A= Agree, SA= Strongly Agree,)

Table 2 presented a comprehensive analysis of barriers to evidence-based practice (EBP) among nurses. Key problems include insufficient knowledge of EBP ($M = 3.36$), resistance to adopting new strategies ($M = 4.22$), limited autonomy in modifying procedures ($M = 4.15$), and a skills gap despite valuing colleagues' recommendations ($M = 3.74$). Additional barriers are a lack of interest in EBP ($M = 2.94$), limited English proficiency ($M = 3.39$), insufficient computer skills ($M = 3.24$), and a shortage of time for literature review ($M = 3.92$).

Table 2: Individual Barriers to Implementing EBP (n=120)

S. No.	Questions	SD	D	N	A	SA	Mean $\pm$ SD
1	Lack of knowledge of the implementation of EBP by nurses	9.2	19.2	7.5	54.2	10	3.36 $\pm$ 1.17
2	Difficulty in using new techniques instead of traditional methods	0.8	2.5	5.8	55.0	35.8	4.22 $\pm$ 0.73
3	Lack of autonomy to change the clinical practice of nurses for the patients	0.8	3.3	5.0	61.7	29.2	4.15 $\pm$ 0.72
4	The best information resource is the experience and recommendations of colleagues	7.5	5	15.8	49.2	22.5	3.74 $\pm$ 1.09
5	Lack of skills to implement EBP by nurses	5	21.7	24.2	31.7	17.5	3.35 $\pm$ 1.14
6	Lack of interest in EBP by nurses	13.3	40.0	9.2	14.2	23.3	2.94 $\pm$ 1.42
7	Insufficient proficiency in the English language	4.2	20.8	19.2	43.3	12.5	3.39 $\pm$ 1.07
8	Lack of ability to work with a computer	1.7	40.0	10.8	27.5	20.0	3.24 $\pm$ 1.22
9	Shortage of time to read literature (Lack of time to search strategies or practice related to EBP)	0	7.5	10.8	63.3	18.3	3.92 $\pm$ 0.76

*(SD=strongly disagree, D= Disagree, N=Neutral, A= Agree, SA= strongly agree,)

DISCUSSION

The study highlighted key barriers to implementing Evidence-Based Practice (EBP) in nursing, including organisational factors such as lack of resources (equipment and internet access), limited availability of current nursing literature, high workload, and inadequate internet access at workplaces. Individual-level barriers

include resistance to change, limited autonomy to modify clinical procedures, reliance on observed rather than evidence-based knowledge, poor EBP skills, and time constraints for literature review. The findings of this study align with some studies. For instance, research in Saudi Arabia identified non-generalizability of research findings and lack of facility support as major barriers [18]. The findings of a study in Cyprus also support this study's results, highlighting barriers like limited authority to modify procedures, time constraints, and lack of cooperation from healthcare staff [19]. The study conducted by Zeb (2018) found issues such as time constraints, lack of access to research materials, and limitations in modifying patient care due to inadequate facilities, which also show similarity with the findings of this study. These consistent challenges point to a broader pattern faced by nurses in implementing Evidence-Based Practice (EBP) [6]. The study's findings are also congruent with research conducted in Indonesia by Rahmayanti (2020), which identified similar barriers to translating research into clinical practice, including time constraints for literature review and limited resources. These parallels highlight the common challenges nurses face in implementing evidence-based practice across different settings [20]. All of these studies together point to common challenges facing nurses in the implementation of EBP and underscore the idea that strategies targeting improvements at both organisational and individual levels are necessary to increase EBP implementation and bring about better nursing practice outcomes.

This study had some limitations, including a single-hospital sample in Mirpur, which may affect generalizability, and a small, homogeneous sample that may not represent all barriers. Future research should expand to multiple healthcare settings and geographies to enhance generalizability and recruit larger, more diverse samples to provide a richer view of EBP barriers and representative findings. The study highlights the importance of addressing both the individual and organisational barriers through targeted interventions that advocate for a supportive environment that is conducive to evidence-based decision-making among nurses. The findings support healthcare systems having a culture that enables the implementation of EBP to help increase the EBP competencies of nurses to improve patient outcomes. Probably, nursing managers would wish to think of how best to prepare them through education.

CONCLUSIONS

The study concluded that barriers to implementing Evidence-Based Practice (EBP) are both organizational and individual. Organizational challenges include inadequate resources such as equipment and internet

access, as well as limited availability of up-to-date nursing literature. These issues are compounded by high workloads, time constraints for literature review, and insufficient internet connectivity. On the individual level, barriers include resistance to adopting new practices, restricted clinical autonomy, and reliance on experiential knowledge over evidence-based approaches, limited proficiency in EBP methodologies, and a lack of time for engaging in research activities. To overcome these challenges, it is recommended to implement targeted training programs that focus on building EBP skills, improving access to resources, and offering ongoing staff support.

Authors' Contribution

Conceptualization: SN

Methodology: SN, KE, ZK, TK, RT

Formal analysis: FF, KE

Writing and Drafting: SN, FF, KE, SK, TK, RT

Review and Editing: SN, FF, KE, SK, ZK, TK, RT

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



Labor Augmentation in Primigravida: A Comparative Evaluation of Drotaverine and Tramadol

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ABSTRACT

Prolonged labor increases maternal and fetal risks. Pharmacological agents such as Drotaverine hydrochloride and Tramadol have been utilized to shorten the duration of labor by facilitating cervical dilation and uterine activity. However, comparative evidence regarding their efficacy and safety remains limited. **Objective:** To compare the effectiveness of Drotaverine hydrochloride and Tramadol in reducing the duration of active labor in primigravida women, and to assess associated maternal and neonatal outcomes. **Methods:** This quasi-experimental study was conducted at the Department of Obstetrics and Gynecology, Niazi Medical and Dental College, Sargodha. A total of 146 primigravida women in active labor were divided into two groups (n=73 each) using non-probability consecutive sampling. Group A received intravenous Drotaverine hydrochloride (40 mg every 2 hours, up to 3 doses), while Group B received intramuscular Tramadol (100 mg, single dose). Duration of labor stages, cervical dilation rate, maternal side effects, and neonatal outcomes were recorded and analyzed using SPSS version 20.0. A p-value ≤ 0.05 was considered significant. **Results:** The first stage of labor was significantly shorter in the Drotaverine group (208.7 ± 38.5 min) compared to the Tramadol group (228.9 ± 42.3 min, $p = 0.001$). Drotaverine also showed a significantly higher cervical dilation rate and fewer maternal side effects such as nausea and dizziness. Neonatal outcomes were comparable between both groups. **Conclusion:** Drotaverine hydrochloride was more effective than Tramadol in shortening the first stage of labor with fewer maternal side effects, making it a preferable agent in primigravida labor management.

INTRODUCTION

The process of labor places significant strain on both the mother and fetus. According to a World Health Organization (WHO) analysis, 9.4% of maternal deaths in Ethiopia are attributed to obstructed labor [1]. Additionally, the neonatal mortality rate increases sharply when the first stage of labor exceeds 20 hours and the second stage extends beyond 2 hours [2]. The cervix consists of smooth muscle and connective tissue, which is innervated by the parasympathetic nervous system. Antispasmodic agents help relieve smooth muscle spasms through musculotropic or neurotropic effects, promoting cervical dilation. Among these agents, Drotaverine has been found to enhance cervical dilation, potentially leading to a shorter

and more efficient labor process [3]. A shorter labor duration is also associated with lower cesarean section rates [4]. Spasmolytics work by reducing cervical spasm, thereby facilitating the progression of labor [5]. A study found that women receiving Phloroglucinol experienced a 34% reduction in the duration of the first stage of labor and a 23% reduction in the second stage, compared to the control group [6]. Furthermore, research confirms that antispasmodics can effectively shorten labor duration without causing toxicity to either the mother or fetus and do not lead to uterine atony [7]. Two independent studies by Tantengco & Menon, and Aziz, observed that Tramadol was associated with a longer first stage of labor compared



to Drotaverine, which showed a noticeable reduction in labor duration [3, 8]. Similarly, research conducted in Rawalpindi reported that Phloroglucinol was effective in shortening the active phase of labor, supporting the role of antispasmodic agents in facilitating labor progression [8]. Tramadol is classified as a centrally acting analgesic from the latest generation of synthetic opioid analgesics, with a low affinity for opioid receptors. Research has indicated that the mean duration of labor in the Tramadol group is approximately 2 hours [9]. A study conducted in India in 2014 reported that the average rate of cervical dilation with Tramadol was 1.71 cm/hr in primigravida and 2.1 cm/hr in multigravida. The drug increased the rate of cervical dilation by 0.51 cm/hr in primigravida and 0.62 cm/hr in multigravida. In the Drotaverine group, the mean cervical dilation rate was 1.70 cm/hr in primipara, increasing by 0.50 cm/hr, while in multipara, the rate increased by 0.52 cm/hr. Both Tramadol and Drotaverine significantly improved cervical dilation compared to the control group [10]. Although multiple studies have compared spasmolytics and Tramadol, variations exist in the meantime reduction of the first stage of labor. It was hypothesized that there would be a difference between mean duration of first stage of labour among the primigravida by Drotaverin verses Tramadol. Therefore, the purpose of this study is to compare the mean duration of the first stage of labor among primigravida women administered Drotaverine versus Tramadol for labor augmentation. The findings of this research will contribute to enhancing maternal and fetal health by effectively reducing labor duration.

METHODS

This study was a quasi-experimental study conducted from 1st Feb, 2024 to 31st July, 2024 at the Department of Obstetrics and Gynecology, Niazi Medical and Dental College, Sargodha. Ethical approval was obtained from the Niazi Welfare Foundation Teaching Hospital, Sargodha, with ERC Reference No: ERC/NWFTH-ERC/08-24. The sample size was calculated using the OpenEpi sample size calculator (mean difference), based on the mean duration of active labor (first phase) for Tramadol (21.28 ± 2.42 minutes) and Drotaverine Hydrochloride (23.42 ± 6.02 minutes), with a 95% confidence interval and 80% power [8]. A total of 146 primigravida women were included, with 73 participants allocated to each group. Participants were enrolled through non-probability consecutive sampling. Group A received 40 mg of Drotaverine Hydrochloride intravenously every two hours, up to a maximum of three doses. Group B received 100 mg of Tramadol intramuscularly as a single dose during active labor. Eligible participants were primigravida women aged between 20 to 40 years with term gestation (37–41 weeks) confirmed by a first-trimester ultrasound and cephalic

fetal presentation. Women with known uterine anomalies, prior cesarean section, comorbid conditions (including respiratory disease, hypertension, diabetes, epilepsy, or psychiatric illness), or those who declined consent were excluded from the study. After obtaining ethical approval and written informed consent, data regarding age, weight, height, Body Mass Index (BMI), gestational age at the time of delivery, mean duration of the first, second, and third stages of labor, total duration of labor, and the mean cervical dilation rate, mode of delivery, maternal side effects and neonatal outcomes, were collected using a pre-coded and validated questionnaire. The questionnaire was reviewed by a panel of experts in obstetrics and gynecology to ensure face and content validity. Women in the active phase of labor—defined as having more than three uterine contractions in ten minutes lasting at least 30 seconds, with cervical dilation greater than 4 cm were included. The stages of labor were determined based on criteria set by WHO. The first stage extended from the onset of regular uterine contractions to full cervical dilatation (10 cm), subdivided into a latent phase (0–4/6 cm) and an active phase (4/6–10 cm). The second stage spanned from full dilation to delivery of the baby, while the third stage covered the period from delivery of the baby to expulsion of the placenta. The onset of active labor was recorded, and the duration until full cervical dilatation (10 cm) was noted. Cervical dilation was monitored hourly to calculate the dilation rate. Adverse effects were observed and recorded throughout labor, with most noted during the first stage. Maternal vitals, fetal heart rate, and any side effects were monitored throughout labor and for 24 hours postpartum. Neonatal outcomes were assessed immediately after birth through Apgar scores, birth weight, and NICU admission. Treatment effectiveness was determined using primary outcomes such as the duration of the first stage of labor and cervical dilation rate. Secondary outcomes included maternal side effects and neonatal outcomes (Apgar scores, birth weight, and NICU admissions). Data were analyzed using SPSS version 20.0. Means and standard deviations were calculated for continuous variables such as age, BMI, gestational age, and duration of the first stage of labor. Normality of quantitative data was assessed, and appropriate tests were applied: independent t-test for continuous variables, and Chi-square test for categorical variables. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 146 primigravida women were included, evenly divided into two groups: Drotaverine ($n=73$) and Tramadol ($n=73$). The demographic characteristics were comparable between the two groups. The mean age in the Drotaverine group was 24.8 ± 3.2 years, while in the Tramadol group it

was 25.1 ± 3.5 years. Both groups had similar mean BMI (26.1 ± 2.1 vs. 26.2 ± 2.3 kg/m²) and gestational age at delivery (39.0 ± 1.1 vs. 38.9 ± 1.3 weeks). Mode of delivery was predominantly normal vaginal in both groups, with slightly higher rates in the Drotaverine group (86.3%) than the Tramadol group (80.8%). Rates of assisted delivery and cesarean section were also slightly lower in the Drotaverine group (Table 1).

Table 1: Demographic Characteristics of Both Groups (n=146)

Variables	Drotaverine Mean $\pm$ SD / (%)	Tramadol Mean $\pm$ SD / (%)
Age (Years)	24.8 $\pm$ 3.2	25.1 $\pm$ 3.5
Weight (Kg)	65.4 $\pm$ 6.3	66.1 $\pm$ 5.8
Height (cm)	158.2 $\pm$ 5.6	159.1 $\pm$ 6.2
BMI (Kg/m ²)	26.1 $\pm$ 2.1	26.2 $\pm$ 2.3
Gestational Age (Weeks)	39.0 $\pm$ 1.1	38.9 $\pm$ 1.3
Mode of Delivery		
Normal Vaginal	86.3%	80.8%
Assisted (Forceps/Vacuum)	8.2%	11.0%
Cesarean Section	5.5%	8.2%

Regarding labor outcomes, the Drotaverine group demonstrated a significantly shorter mean duration of the first stage of labor (208.7 ± 38.5 minutes) compared to the Tramadol group (228.9 ± 42.3 minutes) with a p-value of 0.001. Although the second and third stages of labor showed no statistically significant differences between groups ($p = 0.580$ and $p = 0.160$, respectively), the total duration of labor was shorter in the Drotaverine group (6.22 ± 2.41 hours) than in the Tramadol group (8.33 ± 3.56 hours), though this difference did not reach statistical significance ($p = 0.061$). Notably, the mean cervical dilation rate was significantly higher in the Drotaverine group (1.68 ± 1.02 cm/hr) compared to the Tramadol group (1.06 ± 0.53 cm/hr) ($p < 0.010$) (Table 2).

Table 2: Comparison of Duration of Labor and Its Stages (n=146)

Variables	Drotaverine Mean $\pm$ SD	Tramadol Mean $\pm$ SD	p-Value
Mean duration of 1 st stage (min)	208.7 $\pm$ 38.5	228.9 $\pm$ 42.3	0.001
Mean duration of Second Stage (min)	45.6 $\pm$ 10.2	46.3 $\pm$ 11.1	0.580
Mean duration of Third Stage (min)	10.2 $\pm$ 2.1	10.4 $\pm$ 2.3	0.160
Total labor duration (Hours)	6.22 $\pm$ 2.41	8.33 $\pm$ 3.56	0.061
Mean cervical dilation rate (cm/hr)	1.68 $\pm$ 1.02	1.06 $\pm$ 0.53	<0.010

In terms of maternal side effects, nausea and dizziness were significantly more frequent in the Tramadol group (15.1% and 9.6%, respectively) compared to the Drotaverine group (5.5% and 2.7%), with p-values of 0.042 and 0.045, respectively. No significant differences were observed for flushing, hypotension, or respiratory depression. A significantly higher proportion of patients in the Drotaverine group experienced no side effects (84.9% vs. 65.8%, $p = 0.012$). Neonatal outcomes were similar across both groups. Mean birth weights were nearly identical (2.62

± 1.2 kg vs. 2.64 ± 1.2 kg), and there were no statistically significant differences in Apgar scores or NICU admission rates (Table 3).

Table 3: Comparison of Maternal and Fetal Adverse Effects (n=146)

Maternal Side Effect	Group A (Drotaverine) Frequency (%) / Mean $\pm$ SD	Group B (Tramadol) Frequency (%) / Mean $\pm$ SD	p-Value
Nausea	4 (5.5)	11 (15.1)	0.042
Dizziness	2 (2.7)	7 (9.6)	0.045
Flushing	3 (4.1)	2 (2.7)	0.650
Hypotension	2 (2.7)	3 (4.1)	0.650
Respiratory Depression	0 (0)	2 (2.7)	0.150
None	62 (84.9)	48 (65.8)	0.012
Neonatal Outcomes			
Mean Birth Weight (Kg)	2.62 $\pm$ 1.2	2.64 $\pm$ 1.2	0.900
Apgar Score <7 at 1 min	4 (5.5)	2 (2.7)	0.680
Apgar Score <7 at 5 min	1 (1.4)	0 (0)	0.500
NICU Admissions	6 (8.2)	5 (6.8)	0.760

DISCUSSION

The present study revealed that Drotaverine hydrochloride significantly reduces the duration of the first stage of labor in primigravida women compared to Tramadol, without adversely affecting maternal or neonatal outcomes. These findings reinforce the role of Drotaverine as an effective and safe labor-augmenting agent. In this study, the mean duration of the first stage of labor was significantly shorter in the Drotaverine group (208.7 ± 38.5 minutes) compared to the Tramadol group (228.9 ± 42.3 minutes) ($p = 0.001$). This finding aligns with a study by Jogi, who reported that Drotaverine significantly shortened active labor duration in primigravida women compared to placebo (6.22 ± 2.41 hours vs. 8.33 ± 3.56 hours, $p < 0.001$) [11]. Similarly, Mandal and Molla, observed a mean duration of 123.12 ± 37.82 minutes in the Drotaverine group, significantly less than 156.30 ± 45.10 minutes in the Valetamate group ($p < 0.001$) [12]. Our study also demonstrated a significantly higher rate of cervical dilatation in the Drotaverine group (1.68 ± 1.02 cm/hour) than the Tramadol group (1.06 ± 0.53 cm/hour, $p < 0.001$). This is consistent with a trial conducted in Nepal, which showed that the cervical dilatation rate was significantly higher in women who received Drotaverine compared to controls (2.26 cm/hr vs. 1.67 cm/hr, $p < 0.05$) [13]. Total labor duration was also significantly reduced in the Drotaverine group (6.22 ± 2.41 hours) compared to the Tramadol group (8.33 ± 3.56 hours, $p < 0.001$), which corroborates the findings from a study in India that reported total labor duration as 164 minutes in the Drotaverine group and 296 minutes in the control group ($p < 0.001$) [14]. Regarding maternal side effects, both groups were well-tolerated with no significant differences. Minor adverse effects such as nausea and headache were noted

in both groups, which aligns with earlier findings on the tolerability of Drotaverine in obstetric populations [15]. Tramadol, while providing analgesic benefits, is associated with nausea, dizziness, and vomiting, as seen in multiple studies [16, 17]. Neonatal outcomes such as Apgar scores and NICU admissions were similar in both groups, indicating that Drotaverine is safe for the fetus. These findings echo those of Sharma et al., who found no significant differences in neonatal Apgar scores between women receiving Drotaverine and those in the control group [18]. In addition to efficacy, Drotaverine has a faster onset of action compared to Tramadol and does not interfere with uterine contractility or fetal monitoring. Recent pharmacological reviews note that Drotaverine selectively inhibits phosphodiesterase-4 (PDE4), thereby enhancing smooth muscle relaxation without causing sedation or respiratory depression [19, 20]. The clinical implication of the study is that Drotaverine hydrochloride should be preferred for labor augmentation in primigravida women, particularly in low-resource settings where reducing labor duration could improve maternal and neonatal care outcomes [21]. Its proven safety, faster action, and effectiveness make it a valuable pharmacological tool in obstetrics.

However, this study had some limitations. It was a single-center trial with a modest sample size and excluded multigravida patients. Future studies with larger and more diverse populations, possibly in multicenter settings, would be valuable to further validate these results [22].

CONCLUSIONS

Drotaverine hydrochloride is significantly more effective than Tramadol in reducing the duration of the first stage of labor and increasing cervical dilatation rate, without compromising maternal or neonatal safety. These findings support its broader clinical application in labor augmentation protocols.

Authors' Contribution

Conceptualization: MT

Methodology: MT

Formal analysis: MT, BFM

Writing and Drafting: MT, BFM, DS

Review and Editing: MT, BFM, DS

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 Pressure Support versus T-Piece Trial for Weaning from Mechanical Ventilation

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ABSTRACT

Post-operative patients are particularly vulnerable to hazardous effects of prolonged ventilation owing to their limited reserves, catabolic state and acute injury related to surgical incision and dissection. Thus, early weaning protocols are required for better outcome in this population. **Objective:** To compare PSV versus T-Piece trial for weaning from Mechanical Ventilation. **Methods:** The quasi experimental study was conducted at ICU of Mayo Hospital Lahore from 28-05-2021 to 28-11-2021. Total 60 patients undergoing elective post-operative mechanical ventilation were selected after taking written informed consent. Patients were divided in two groups, Group A: Pressure support ventilation and Group B: T piece ventilation. Frequency and percentage of successful extubation were recorded in both groups. Data were analysed with SPSS version 26.0. Frequency of successful extubation was compared using chi square test taking p-value ≤ 0.05 as significant. **Results:** In Group A, 93.33% (n=28) of patients had successful extubation, while only 66.66% (n=20) patients in Group B had successful extubation, p-value=0.009. **Conclusion:** This study indicated that PSV results in successful extubation and liberation from mechanical ventilation than T piece trial.

INTRODUCTION

In the ICU setting, making the decision to extubate a patient is a crucial moment, as failed extubation followed by reintubation is associated with a high risk of mortality [1]. On average, reintubation occurs in about 10% of planned extubations, but this rate can surpass among patients with increased risk factors [2]. Successfully weaning patients off mechanical ventilation is among the most complex challenges for ICU clinicians. Early recognition of patients who are ready to breathe independently can help reduce the duration of ventilator use and decrease the likelihood of associated complications [3]. Typically, when a patient is

considered ready for spontaneous breathing, a screening tool known as the Spontaneous Breathing Trial (SBT) is performed; however, evidence on its effectiveness remains mixed [4]. Various strategies are employed for weaning [5]. Pressure Support Ventilation (PSV) is a spontaneous mode of ventilation in which a constant pressure level is maintained, and the ventilator delivers support whenever the patient initiates a breath [6]. In T-piece mode, the Endotracheal Tube (ETT) is disconnected from the ventilator and attached to a T-shaped tube which provides oxygen therapy to the patient; in this mode,



patient satisfaction may be better than in pressure mode [7]. Studies comparing T-piece trials and PSV have shown mixed results. In some trials, PSV was associated with a higher rate of successful extubation than the T-piece [8]. PSV has also shown superiority in terms of respiratory parameters such as respiratory rate and tidal volume, and in some cases, shorter weaning durations [9]. Despite this, other studies found no significant difference between the T-piece and PSV in terms of extubation success. In certain patient populations, switching to spontaneous breathing can negatively impact left ventricular function and may increase the risk of SBT failure, particularly with the T-piece due to higher respiratory muscle workload and potential cardiogenic pulmonary edema [10].

This study aimed to add clinical evidence regarding use of T-piece versus pressure support to discontinue the mechanical ventilation in patients admitted in the local ICU setup. No conclusive evidence regarding use of either t-piece or pressure support for weaning from mechanical ventilation. So, this study would add clinical evidence and implementation of this study will help to reduce the duration of hospital stay of patient. In this way financial burden can be reduced in the health care system.

METHODS

This Quasi experimental trial was conducted at ICU of Mayo Hospital, Lahore, from September 28, 2020, to March 28, 2021, following approval IRB [762/RC/KEMU]. Total 60 patients were enrolled using non-probability consecutive sampling. Sample size was calculated with 5% level of significance, 80% power of test, using expected percentage of successful extubation as 81.54% in T-piece group and 61.15% in pressure support group [11]. Sample size was calculated using WHO sample size calculator. Patients were divided into two groups using lottery method. Eligible participants included post-operative patients aged 18–50 years of either gender who were electively ventilated for more than 12 hours in surgical ICU. Patients were excluded if they had anemia (hemoglobin <8g/dl), intractable hypotension (BP <90/60 mmHg or MAP <60 mmHg despite adequate resuscitation), ventilator dependence due to chronic respiratory disease, heart failure with ejection fraction <30%, myocardial infarction (based on ECG changes and elevated troponin >100 mIU), or known neuromuscular or CNS disorder. After obtaining written informed consent, baseline demographic data including name, age, gender, history of diabetes (random blood sugar >200 mg/dl), smoking (>5 pack-years), hypertension (BP >140/90 mmHg). In pressure support group (Group A), patients were given inspiratory pressure of 5–7 cmH₂O, PEEP 5 cmH₂O, FiO₂ 0.4, and expiration was triggered at 25% of peak inspiratory flow rate. In T-piece group (Group B), mechanical ventilation was stopped and ETT was connected to T-piece circuit transporting oxygen

at 10–15 L/min. Twelve hours after surgery, patients were evaluated for readiness to wean using criteria: RR<30 breaths/min, SpO₂>90%, HR <120 bpm, systolic BP 90–160 mmHg, alert, and rapid shallow breathing index <105. Patients who fulfilled these criteria were extubated and monitored [12]. Successful extubation was defined as no need for re-intubation, while re-intubation was performed if patients developed HR >120/min, RR >30/min, or SpO₂<90%. The dataset was analyzed utilizing IBM SPSS version 26.0. For continuous variables, descriptive statistics such as means and standard deviations were calculated. Categorical variables were summarized using frequencies and percentages. To account for potential effect modifiers, data stratification was performed. Comparative analysis of successful extubation rates between different groups was conducted using chi-square test, p-value of 0.05 or less was considered indicative of statistical significance.

RESULTS

In Group A mean age of patients is 39.5 ± 1.50 years which is comparable to mean age of 39.0 ± 2.00 in Group B, p=0.277. In Group A, 11 (36.66%) patients had diabetes, 16 (53.33%) patients were smokers, and 12 (40.0%) patients had hypertension. In Group B, 13 (43.37%) patients had diabetes, 17 (56.66%) patients were smokers, and 13 (36.66%) patients had hypertension.

Table 1: Comparison of Demographic Characteristics of Study Groups (n=30)

Variables	Group A Mean ± SD / Frequency (%)	Group B Mean ± SD / Frequency (%)	p-Value
Age (Years)	39.5 ± 1.50	39.0 ± 2.00	0.277
Gender	Male	16 (40)	0.600
	Female	14 (60)	
Diabetics	11 (36.66)	13 (43.37)	0.598
Active Smokers	16 (53.33)	17 (56.66)	0.795
Hypertensive	12 (40.0)	13 (36.66)	0.790

In Group A, 93.33% (n=28) of patients had successful extubation vs 66.66% (n=20) in Group B p-value=0.009, as shown in figure 1.

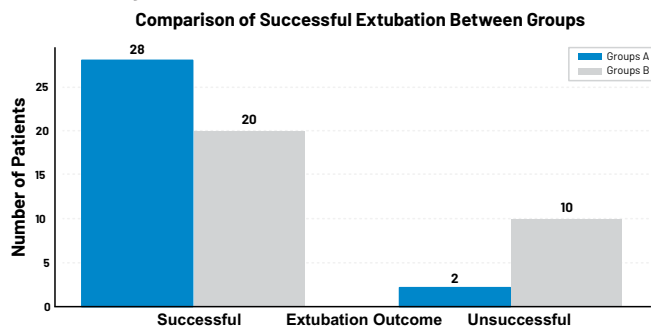


Figure 1: Comparison of Successful Extubation between Groups

As shown in table 2 successful extubation was higher in Group A across all age brackets, (p > 0.05 not statistically significant). Statistically significant difference was observed in males (p = 0.012), with Group A showing notably

higher success rate. No significant difference was seen among females ($p = 0.217$). No significant difference in extubation success between groups for both diabetic ($p = 0.977$) and non-diabetic patients ($p = 0.522$), hypertensive and non-hypertensive patients, ($p = 0.428$ and 0.612 , respectively). Among non-smokers, Group A had a significantly higher success rate ($p = 0.020$). Among smokers, this difference was not statistically significant ($p = 0.166$).

Table 2: Stratification of Successful Extubation between Groups by Various Factors

Variables	Subgroup	Group	Successful Extubation Yes (n)	Successful Extubation No (n)	p-Value
Age (Years)	18-30	A	05	00	0.104
		B	04	03	
	31-40	A	11	01	0.104
		B	07	04	
	41-50	A	12	01	0.238
		B	09	03	
Gender	Male	A	15	01	0.012
		B	07	06	
	Female	A	13	01	0.217
		B	13	04	
Diabetes	Yes	A	10	01	0.977
		B	08	05	
	No	A	18	01	0.522
		B	12	05	
Hypertension	Yes	A	11	01	0.428
		B	06	05	
	No	A	17	01	0.612
		B	12	05	
Smoking	Yes	A	15	01	0.166
		B	13	04	
	No	A	13	01	0.020
		B	07	06	

DISCUSSION

Extubation is critical step in the management of mechanically ventilated patients, marking the transition from artificial to spontaneous breathing [13]. Its success is vital to patient recovery, as failed extubation is associated with increased morbidity, prolonged ICU stay, and higher healthcare costs [14]. In this trial, the Pressure Support Ventilation (PSV) group had a significantly higher percentage of successful extubation compared to the group using the T-piece method (93.33% vs. 66.66%, $p = 0.009$). Similarly, Chittawatanarat et al., suggested that PSV may lead to lower reintubation rates 10% in PSV versus 14.6% in T-piece [11]. Another meta-analysis also found a significant advantage for PSV over T-piece in terms of successful extubation ($p < 0.001$) [15]. PSV appears to facilitate shorter weaning processes, with a higher proportion of patients achieving successful weaning more quickly [16]. In contrast, Li et al., reported no significant

difference in successful extubation rates between T-piece and PSV ($p = 0.27$) [17]. Yekefallah et al., supported a superior role of the T-piece in successful extubation as compared to PSV [18]. Thille et al., also found the reintubation rate to be lower in the T-piece group compared to PSV (13.6% vs. 14.9%, $p = 0.024$) [18, 19]. However, Azouz et al., concluded that the T-piece, instead of aiding in weaning, may lead to prolonged weaning intervals and associated complications [20]. It is also supported that while both T-piece and PSV are effective for extubation, PSV may be preferable in patients with difficult weaning due to its potential to reduce reintubation rates and shorten the weaning duration. However, the choice of method should be tailored to individual patient needs and clinical scenarios, as some studies indicate no significant differences in mortality or length of stay between the two methods [21].

This study has certain limitations that should be considered. Foremost, sample size was comparatively small. Although calculation was performed to ensure adequate power larger sample size would have increased the generalizability of the results. Secondly, study was conducted on a homogeneous group of elective post-operative patients in surgical ICU, which limits the generalizability of findings to other patient populations such as those with medical conditions, emergency surgeries, or complex weaning scenarios (sepsis, trauma, or neuromuscular diseases). Inclusion of broader range of patients and comparison across different clinical settings may yield more comprehensive and generalizable results. This study did not evaluate long-term outcomes such as morbidity, mortality, or the reintubation requirement beyond the immediate post-extubation period. Future studies should include larger, multicenter populations with severity stratification and combined hematological markers to improve diagnostic performance.

CONCLUSIONS

In conclusion, this study demonstrated that pressure support ventilation had high incidence of effective extubation versus T-piece ventilation in patients requiring mechanical ventilation. These findings suggest that PSV is preferable strategy for facilitating successful extubation in this patient population.

Authors' Contribution

Conceptualization: SB

Methodology: SB, MR, AQ, FM, MSA, MUS

Formal analysis: SB

Writing and Drafting: AQ, AB

Review and Editing: SB, MR, AQ, AB, FM, MSA, MUS

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

Comparing Probiotics Plus Lactulose with Lactulose Alone in Treatment of Overt Hepatic Encephalopathy

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ABSTRACT

A neuropsychiatric condition known as hepatic encephalopathy (HE) is brought on by liver malfunction, which accumulates poisons like ammonia and impairs brain activity. **Objectives:** To compare the viability of combining probiotics with lactulose versus utilizing lactulose alone within the treatment of obvious hepatic encephalopathy. **Methods:** This quasi-experimental study took place in the Gastroenterology and Hepatology Department at the Pakistan Institute of Medical Sciences in Islamabad from August 2019 to January 2020. A total of 160 patients diagnosed with overt HE were included and divided into two groups. Group A received a combination of probiotics and lactulose, while Group B received lactulose alone. Treatment outcomes were evaluated over six months based on improvement in HE symptoms, Model for End-Stage Liver Disease (MELD) scores, length of hospital stay, and potential precipitating factors. **Results:** The mean age of participants was 44.08 ± 11.31 years. Group A comprised 64 males (80%) and 16 females (20%), while Group B had 30 male (37.5%) and 50 female (62.5%). The MELD scores were comparable between groups ($p=0.648$). However, the mean hospital stay was significantly shorter in Group A (2.34 ± 0.56 days) than in Group B (2.42 ± 0.63 days; $p<0.05$), indicating enhanced recovery in the combination therapy group. **Conclusions:** The addition of probiotics to lactulose significantly improves clinical outcomes in patients with overt hepatic encephalopathy by reducing hospital stay and enhancing treatment efficacy.

INTRODUCTION

Hepatic Encephalopathy (HE) is a complicated brain problem that happens mainly because the liver is not working well. It happens because the liver can't clear toxins from the blood, causing harmful substances, especially ammonia, to build up and affect the brain [1]. Hepatic encephalopathy (HE) is commonly observed in individuals with advanced liver disease, such as cirrhosis, but it can also occur in other conditions, including certain genetic

disorders, chronic liver dysfunction, and altered hepatic blood flow [2]. A mild form of HE occurs in 20-80% of people with cirrhosis, and it can lead to a lower quality of life and more car accidents [3]. The signs of HE can vary from mild thinking problems that can only be found with special tests to severe unconsciousness. The severity of the condition can be measured using different systems, many of which rely on research and brain wave tests (EEG). The



most widely used classification system divides hepatic encephalopathy (HE) into stages based on the patient's level of consciousness, cognitive function, neurological signs, and electroencephalogram (EEG) findings [4]. People with cirrhosis are very likely to develop hepatic encephalopathy (HE), with 50-70% showing clear symptoms. But many people might only show slight issues with thinking skills, which can only be noticed through special tests. It's very important to notice the early signs of hepatic encephalopathy (HE) because getting medical help quickly can greatly help patients [5]. While ammonia is known to be the main cause of HE, other factors may also play a part. These include changes in how the brain uses energy, a decrease in the function of a specific pump in the brain cells, an increase in misleading chemicals that act like neurotransmitters, and the activation of certain brain receptors such as gamma-aminobutyric acid (GABA) receptors, and manganese (Mn) deposition in the basal ganglia [6]. A zinc deficiency can exacerbate the situation by disrupting the urea cycle, resulting in increased ammonia levels [7]. Probiotics and lactulose are becoming more popular as a possible way to improve treatment results. Probiotics are live germs that can help improve health by affecting the good bacteria in our stomachs. This is important for reducing harmful substances like ammonia [8]. Probiotics can help reduce the production and absorption of ammonia, which may ease symptoms in people undergoing hemodialysis by bringing back a healthy balance of bacteria in the gut. Probiotics and lactulose together may work better than using lactulose alone to help manage hepatic encephalopathy (HE), especially for patients who have ongoing problems or don't respond well to just lactulose [9].

Despite several studies exploring the role of probiotics in hepatic encephalopathy, limited research exists on the comparative effectiveness of combining probiotics with lactulose versus using lactulose alone, particularly in resource-limited settings such as Pakistan. This study aims to address this gap by evaluating whether adjunct probiotic therapy offers superior clinical outcomes compared to standard lactulose therapy alone.

METHODS

This quasi-experimental study took place in the Gastroenterology and Hepatology Department at the Pakistan Institute of Medical Sciences in Islamabad after approval of the Ethical Committee of the University with Reference No. F.2-11/SZABMU/AS&-RB/2018 from August 2019 to January 2020. It uses a non-equivalent control group design with patients allocated by lottery into two groups for outcome comparison. The number of samples needed was calculated using the World Health Organization's calculator (openepi.com) for an 80% chance of detecting a true effect and a 5% chance of error, based

on expected frequencies were 76% in the lactulose plus rifaximin group and 50.8% in the lactulose-only group. Based on these calculations, a total of 160 patients were enrolled in the study, with 80 patients assigned to each group [10]. Using the formula for comparing two proportions: $n = (Z_{1-\alpha/2} + Z_{1-\beta})^2 \cdot [P_1(1-P_1) + P_2(1-P_2)] / (P_1 - P_2)^2$. Where: $P_1 = 0.76$ (probiotic + lactulose group), $P_2 = 0.508$ (lactulose only group), $Z_{1-\alpha/2} = 1.96$ for 95% confidence, and $Z_{1-\beta} = 0.84$ for 80% power. Inclusion criteria consisted of patients aged 18 to 80 years, of both genders, diagnosed with liver cirrhosis and overt hepatic encephalopathy based on the West Haven criteria. Individuals with hepatocellular carcinoma, degenerative central nervous system disease, serious psychiatric illness, active alcohol consumption within four weeks before the current episode, and creatinine levels more than 1.5 mg/dL upon admission were excluded from the study. A written informed consent was taken from all the study participants. The lottery method was used as a simple randomization technique where patients picked sealed, opaque envelopes containing group assignments to ensure allocation concealment and prevent selection bias. Patients in Group A were given lactulose together with probiotics. The probiotics were given as a daily oral supplement that contained 10 billion mixed-strain colony-forming units (CFU), which included *Bifidobacterium* and *Lactobacilli*. A dose of 30-60 mL of lactulose was given daily. Patients in Group B were given lactulose alone, similarly tailored to produce the desired bowel movement, at a dose of 30-60 mL per day. Age, gender, aetiology of liver disease (hepatitis B, hepatitis C, alcohol-related), Child-Pugh classification, grades of HE, Model for End-Stage Liver Disease (MELD) score, and length of hospital stay were among the demographic, clinical, and biochemical factors on which data were gathered. Electrolyte abnormalities, pneumonia, UTIs, spontaneous bacterial peritonitis (SBP), constipation, gastrointestinal bleeding, and UTIs are other causes that might result in hepatic encephalopathy (HE). The effectiveness of the treatment was evaluated using the improved scores on the West Haven criteria, which demonstrate the resolution of liver-brain disease symptoms. People whose severity of HE improved by at least one level were called "responders. Those whose symptoms didn't change or got worse were called "non-responders. They also checked for improvements in thinking and mental health to see if the treatment worked. Collected data were analyzed using IBM SPSS, version 27.0. Using independent t-tests, we examined variables such as age, MELD score, and length of hospital stay. Using Chi-square tests, we examined categorical variables such as gender, Child-Pugh class, HE grades, and causes. Data were organized by gender, Child-Pugh score, grades of HE, causes, and drug effectiveness to make sure we could compare the two groups fairly. A p-value less than 0.05 was seen as important.

RESULTS

The mean age of patients in both groups was 44.08 ± 11.31 years. Group B, which only received lactulose, had 30 males (37.5%) and 50 females (62.5%). Group A, which received probiotics along with lactulose, had 64 male (80%) and 16 female (20%). Hepatitis C was the leading reason for liver disease in both groups. It made up 68.75% of cases in Group A and 78.75% of cases in Group B, based on the analysis of the causes. With 23 patients (28.75%) in Group A

and 13 patients (16.25%) in Group B, hepatitis B was less common. Two patients (2.5%) in Group A and four patients (5%) in Group B had alcohol-related cirrhosis. Class C comprised the majority of patients according to the Child-Pugh classification, with 54 (67.5%) in Group B and 55 (68.75%) in Group A. Class B was seen in 23 (28.75%) of Group A and 24 (30%) of Group B, while Class A had 2 patients (2.5%) in each group (Table 1).

Table 1: Demographic, Etiology, and Child-Pugh Class Distribution

Variables	Category	Group A (Probiotics + Lactulose)	Group B (Lactulose Only)	Total (n=160)
Age	Mean $\pm$ SD	44.08 $\pm$ 11.31		
Gender	Male	64 (80%)	30 (37.5%)	94 (58.8%)
	Female	16 (20%)	50 (62.5%)	66 (41.2%)
Etiology	Hepatitis B	23 (28.75%)	13 (16.25%)	36 (22.5%)
	Hepatitis C	55 (68.75%)	63 (78.75%)	118 (73.75%)
	Alcohol	2 (2.5%)	4 (5%)	6 (3.75%)
Child-Pugh Class	A	2 (2.5%)	2 (2.5%)	4 (2.5%)
	B	23 (28.75%)	24 (30%)	47 (29.38%)
	C	55 (68.75%)	54 (67.5%)	109 (68.12%)

Group A and Group B had similar average MELD scores. Group A's average was 23.24, while Group B's average was 22.36. The MELD scores of the groups were pretty much the same, with a p-value of 0.648 showing no important difference. However, the mean duration of hospital stay was significantly different, with Group A having a shorter stay (2.34 ± 0.56 days) compared to Group B (2.42 ± 0.63 days), and the p-value of 0.000 indicated a significant difference in hospital stay duration (Table 2).

Table 2: MELD Score and Hospital Stay Duration in Both Treatment Groups

Variables	Group A (Probiotics + Lactulose)	Group B (Lactulose Only)	p-value
MELD Score	23.24 $\pm$ 2.15	22.36 $\pm$ 1.98	0.648
Hospital Stay	2.34 $\pm$ 0.56	2.42 $\pm$ 0.63	p < 0.001

Independent t-test showed no significance for MELD scores (p=0.648) but was significant for hospital stay (p<0.05).

Constipation was the most common precipitating factor in both groups, affecting 44 patients (55%) in Group A and 43 patients (53.75%) in Group B. Other factors included spontaneous bacterial peritonitis (SBP) in 9 patients

(11.25%) in Group A and 15 patients (18.75%) in Group B, urinary tract infections (UTIs) in 7 (8.75%) of Group A and 5 (6.25%) of Group B, pneumonia in 8 (10%) of Group A and 4 (5%) of Group B, gastrointestinal (GI) bleeding in 9 (11.25%) of Group A and 12 (15%) of Group B, and serum electrolyte imbalance in 3 (3.75%) of Group A and 1 (1.25%) of Group B (Table 3).

Table 3: Distribution of Precipitating Factors in Both Treatment Groups and Percentage for Both Groups

Precipitating Factors	Group A (Probiotics + Lactulose)	Group B (Lactulose Only)	Total (n=160)
SBP	9 (11.25%)	15 (18.75%)	24 (15%)
UTI	7 (8.75%)	5 (6.25%)	12 (7.5%)
Pneumonia	8 (10%)	4 (5%)	12 (7.5%)
GI Bleed	9 (11.25%)	12 (15%)	21 (13.13%)
Constipation	44 (55%)	43 (53.75%)	87 (54.38%)
S/E Imbalance	3 (3.75%)	1 (1.25%)	4 (2.5%)
Total	80 (100%)	80 (100%)	160 (100%)

The efficacy of the treatment was significantly different between the two groups, with 21 patients (26.25%) in Group A showing improvement, compared to 63 patients (78.75%) in Group B. In contrast, 59 patients (73.75%) in Group A did not respond to treatment, compared to 17 patients (21.25%) in Group B. The p-value of 0.0321 indicated a statistically significant difference in drug efficacy between the two groups (Table 4).

Table 4: Efficacy of Drugs in Both Treatment Groups

Efficacy of Drugs	Group A (Probiotics + Lactulose)	Group B (Lactulose Only)	Total (n=160)	p-value
Yes	21 (26.25%)	63 (78.75%)	84 (52.5%)	0.032
No	59 (73.75%)	17 (21.25%)	76 (47.5%)	
Total	80 (100%)	80 (100%)	160 (100%)	

Chi-square test showed a statistically significant difference in drug efficacy between the two groups ($p=0.032$)

To adjust for the significant gender imbalance between groups, binary logistic regression was performed with gender as a covariate. The treatment group (probiotics + lactulose) remained a significant independent predictor of efficacy (adjusted OR=2.45, $p=0.013$), while gender was not statistically significant ($p=0.174$) (Table 5).

Table 5: Binary Logistic Regression Analysis for Drug Efficacy Adjusted for Gender (Covariate)

Variable	Adjusted Odds Ratio (OR)	95% Confidence Interval	p-value
Treatment Group (A vs. B)	2.45	1.21–4.97	0.013
Gender (Male vs. Female)	1.58	0.83–2.99	0.174

DISCUSSION

Hepatic encephalopathy (HE) is a mental condition often seen in people with liver disease, especially those with cirrhosis. It happens when harmful substances, usually ammonia, build up in the body because the liver can't handle them properly. This causes problems with thinking and movement. A common treatment for HE is lactulose, which helps remove ammonia from the body through the intestines, reducing ammonia levels. Probiotics are being looked at as a possible additional treatment because they may change the bacteria in the gut and reduce ammonia levels [11]. This study is trying to find out if using probiotics along with other treatments helps patients feel better. The average age of the patients in our study was 44.08 ± 11.31 years, which is quite similar to the results of Pervaiz et al., who found that the average age was 44.92 ± 11.36 years. The gender distribution in our study differed slightly from that of Pervaiz et al., Group A (Probiotics + Lactulose) in our study had 64 male (80%) and 16 female (20%), while Group B (Lactulose Only) had 30 male (37.5%) and 50 female (62.5%). Conversely, Pervaiz et al., reported that Group A had 31 male (68.89%) and 14 female (31.14%). Group B had 35 male (77.78%) and 10 female (22.22%). Both studies had more male than female overall. However, our study found that Group A had more males, while Group B had a more equal number of males and females. These minor discrepancies in the male-to-female count might result from the way the studies were carried out or from variations among the populations. However, they show similar patterns in the characteristics of patients with liver-related brain problems in both studies [12]. The findings of our study revealed that administering probiotics alongside lactulose provided considerable assistance to patients suffering from severe hepatic encephalopathy (HE). In Group A, 84.4% of the patients improved, while only 53.3% of patients in Group B improved ($p=0.032$). These results match what other studies have shown about the benefits of using

different treatments together for managing HE. They also show new ways that probiotics can help using lactulose. When looking at it with Peeyush and Pradhan. In 2023, it was reported that 54.54% of patients felt better after taking probiotics with lactulose. We observed an even higher rate of improvement in our study. The observed variation may be attributed to the patient population or the particular strains of probiotics utilized, which may have had a greater effect on altering the gut microbiota in our investigation [13]. In our study, the mean hospital stays for Group A (Probiotics + Lactulose) was significantly shorter at 2.34 ± 0.56 days compared to 2.42 ± 0.63 days in Group B ($p<0.001$), a finding that aligns with Wang et al., who also reported faster recovery rates in patients receiving combination therapies. Wang et al., reported recovery rates of 58.8% in patients receiving probiotics and lactulose, which, while lower than our 84.4%, still supports the overall benefit of probiotics in HE management. The higher rate of improvement in our study could be due to more effective probiotic dosing or a better-controlled clinical environment [14]. Similarly, our findings resonate with those of Shavakhi et al., where PHES scores improved significantly with combination therapy. In our trial, the significant reduction in hospital stay further suggests that probiotics, when combined with lactulose, may accelerate recovery by modulating gut flora and reducing systemic ammonia levels more effectively [15]. Abd-El Salam et al., demonstrated that the NTZ (Nitazoxanide) group had significantly better outcomes than the lactulose and placebo group, with a reduction in CHESS score from 4.15 ± 2.09 to 0.00 ± 0.00 (NTZ group), compared to 4.96 ± 2.29 to 1.28 ± 0.91 in the lactulose and placebo group ($p<0.001$). While our study did not use NTZ, the principle of combining lactulose with another therapeutic agent, in our case probiotics, produced similarly significant results [16]. Contrary to Butt et al., who found no significant difference between lactulose alone and lactulose combined with rifaximin ($p=0.276$), our study demonstrated a clear and statistically significant difference in favor of probiotics ($p=0.032$). This suggests that probiotics may offer superior benefits compared to rifaximin as an adjunct to lactulose, particularly in reducing the severity of HE symptoms and shortening hospital stays [17]. However, research conducted in 2023 by Rehman and his group, as well as by

Riaz and his team, has shown different results. In 2022, researchers found big differences in blood ammonia levels and how well treatments worked. This means that for people with HE, using different types of therapy together might help prevent the illness from coming back and make them feel better overall [17, 18]. Also, Riaz and others discussed this too. A 2022 analysis demonstrated that combining therapies led to higher success rates, with Group A demonstrating 72% effectiveness. 58% of people in Group B showed improvement, with a significance level of $p=0.01$. This is similar to our results, where 84.4% of patients in the combination therapy group improved. The similar results in different studies support the idea that additional treatments, like probiotics or rifaximin, can greatly improve how well lactulose works for treating HE (hepatic encephalopathy). Additionally, both our study and Riaz *et al.*, report underline the importance of combination therapy in improving clinical outcomes in HE [19]. Although Hussain *et al.*, focused on mortality rates, their finding that combination therapy significantly reduced mortality with a p -value of 0.02 parallels the positive outcomes we observed in symptom reduction [20]. While current study did not report mortality, the significant improvement in HE grades and hospital stay reduction suggests that probiotics may have a broader impact on overall HE management, which warrants further investigation. Present findings are similar to those of Sattar *et al.* In 2022, some researchers found that patients who took both lactulose and rifaximin had better results (72.6%) than those who only took lactulose (51.6%) [21]. In contrast, studies such as Rehman *et al.*, and Riaz *et al.*, reported significant differences in serum ammonia levels and outcomes, suggesting that combination therapies might reduce recurrence rates and improve clinical outcomes in HE management [17, 18]. Moreover, Riaz *et al.*, reported that combination therapy led to higher efficacy rates (72% in Group A vs. 58% in Group B, $p=0.01$), which aligns with our findings, where 84.4% of patients in the combination therapy group showed improvement. This consistency across studies reinforces the idea that adjunct therapies, whether probiotics or rifaximin, can significantly enhance the efficacy of lactulose in treating HE. Additionally, both our study and Riaz *et al.*, report underline the importance of combination therapy in improving clinical outcomes in HE [19]. Although Hussain *et al.*, focused on mortality rates, their finding that combination therapy significantly reduced mortality with a p -value of 0.02 parallels the positive outcomes we observed in symptom reduction [20]. While our study did not report mortality, the significant improvement in HE grades and hospital stay reduction suggests that probiotics may have a broader impact on overall HE management, which warrants further investigation. Our findings are similar to those of Hussain *et al.* In 2022, some researchers found that patients who took both lactulose and rifaximin had better results (72.6%) than

those who only took lactulose (51.6%) [21]. The main strength of our study is its enormous improvement in health results, and shorter hospital stays show that probiotics are as important as a helpful extra treatment. This study was limited by a relatively small sample size and short follow-up duration, which may restrict the generalizability and long-term applicability of the findings. Additionally, variations in probiotic strains and lack of control over potential confounders (e.g., disease severity, diet, and concurrent treatments) may have influenced the outcomes. Future studies should involve larger, multi-center trials with standardized probiotic regimens and longer follow-up to better assess long-term efficacy and clinical outcomes in hepatic encephalopathy.

CONCLUSIONS

When probiotics and lactulose were taken together, patients with liver-related brain problems had better health, stayed in the hospital for less time, and had more successful treatment compared to when they only took lactulose. These results suggest that probiotics could help treating overt hepatic encephalopathy.

Authors' Contribution

Conceptualization: OHAA

Methodology: OHAA, AA¹, AA², MT, SM, SM, MA

Formal analysis: AH

Writing and Drafting: AA¹

Review and Editing: OHAA, AH, AA¹, AA², MT, SM, SM, MA

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



Detection of Intrauterine Growth Retardation in 2nd And 3rd Trimester with Fetal Parameters and Umbilical Artery Doppler

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ABSTRACT

Intrauterine Growth Restriction (IUGR) occurs when a fetus fails to reach its growth potential. Ultrasound plays a key role in diagnosis by assessing fetal biometry, and estimated weight. Umbilical artery Doppler studies evaluate placental function, with abnormal findings like increased resistance or absent/reversed end-diastolic flow. **Objective:** To detect Intrauterine growth retardation in 2nd and 3rd trimester with fetal parameters and umbilical artery doppler.

Methods: This descriptive cross-sectional research took place at Diagnostic centre, Combined Military Hospital, Lahore from September to December 2024. All eligible 130 females in 2nd and 3rd trimester had recruited excluding females with Polyhydromnias. The examination involved the use of a curvilinear transducer (3-5MHz). Non probability convenient technique was employed for data collection. IBM (SPSS) version 26.0 was used for data analysis. For inferential statistics, Chi square test was employed. Statistical p-value <0.05 was considered as a significant value.

Results: The study involved 130 pregnant women (mean age 28.82 ± 4.64), with 29.2% in the 2nd and 70.8% in the 3rd trimester. IUGR history (25.4%), gestational hypertension (50.8%), and diabetes (19.2%) were noted. IUGR was diagnosed in 52 cases with 3-6week growth delays. Abnormal PI values in all cases confirmed PI as a reliable marker. **Conclusions:** In conclusion, fetal biometric parameters (BPD, HC, AC, FL) below the 10th percentile indicated IUGR in over one-third of 2nd and 3rd trimester pregnancies, with growth lags of 15-43 days. Abnormal umbilical artery Doppler PI was present in all IUGR cases, highlighting PI as a consistent and reliable detection marker.

INTRODUCTION

Intrauterine Growth Restriction (IUGR) is a clinical definition applied to neonates born with clinical features of malnutrition and in-utero growth retardation irrespective of their birth weight percentile [1]. A Doppler ultrasound is a non-invasive technique utilized to approximate blood flow within blood vessels. This is achieved by leading high-frequency sound waves (ultrasound) toward flowing red blood cells and analyzing the resultant echoes [2]. A standard ultrasound examination includes sizes of Biparietal Diameter (BPD), Head Circumference (HC), Abdominal Circumference (AC), Femur Length (FL), Estimated Fetal Weight (EFW), assessment of Amniotic Fluid Index (AFI) [3]. The fetal Umbilical Artery (UA) provides

a site of velocimetric studies as Doppler indices Pulsatility Index (PI), resistive index, and Systolic/Diastolic (S/D) ratio evaluates the impedance to the flow through them. An abnormal UA Doppler is therefore an indicator of fetal peripheral vasoconstriction, hence reduced fetal oxygenation. UA Doppler study therefore helps in identifying a compromised fetus, thus reducing adverse perinatal outcomes including mortality [4]. Similar characteristics are shown in figure 1. The incidence is around 3-9% in higher socioeconomic group, whereas the rate is as high as 30% in low socioeconomic group. Almost 20-50% stillborns are growth retarded. After prematurity, this is the second commonest cause for perinatal mortality



[5]. Intra-uterine growth restriction is frequently a sequel of hypertensive disorders of pregnancy and the frequency of IUGR in patients with PIH was found to be 65% [6]. Occurrence of IUGR is notably lower in developed nations, ranging from 4% to 8%, compared to the higher rates observed in developing countries, which range from 6% to 30%. On average, approximately 8% of the general population experiences IUGR [7]. Intrauterine Growth Restriction (IUGR) is classified into symmetrical, asymmetrical, and mixed types. Symmetrical IUGR involves proportional reductions in weight, length, and head circumference, with a head-to-chest circumference difference of less than 3 cm and a Pulsatility Index (PI) greater than 2. It reflects early developmental issues, often linked to genetic factors or early pregnancy complications. Asymmetrical IUGR typically appears in the late second or third trimester due to placental insufficiency, which reduces nutrient supply. While cell numbers remain normal, cell size decreases due to limited glycogen and fat storage. A key marker is a PI less than 2. Mixed IUGR combines characteristics of both symmetrical and asymmetrical IUGR, causing reductions in both cell number and size. This type reflects more complex underlying issues, making diagnosis and management challenging. Understanding the type of IUGR is essential for tailoring prenatal care and improving fetal outcomes through targeted interventions [8]. Maternal, fetal, and placental/adnexal parameters are among the many risk factors for intrauterine growth restriction the primary risk elements are broken down below. Maternal Aspects: A lower socioeconomic status raises the risk of intrauterine growth retard Weight: IUGR may be caused by a very low or exceptionally elevated (BMI). Smoking: it is a major risk factor for IUGR during pregnancy. Recreational Drug Use: Using drugs recreationally while pregnant may harm the development of the fetus. Advanced Maternal Age: the possibility of IUGR is increased for women over 35. Women who become pregnant for the first time are more vulnerable to nulliparity. Overview of Gestational Hypertension: intrauterine growth restriction may result from this condition's limitation in the fetus's blood supply. Family History: The risk gets higher if there is a family history of IUGR or if there have been prior IUGR pregnancies [9]. The prenatal TCD in IUGR babies was less impacted than the fetal HC, indicating that cerebellar growth has been preserved preferentially over other cranial structures. In order to identify aberrant fetal growth, the TCD/AC ratio proved useful. Since this ratio is GA independent, it may be used even when the GA is unclear [10]. Common causes of LBW are restricted intrauterine fetal growth or Intrauterine Growth Retardation (IUGR), Small for Gestational Age (SGA), fetal malnutrition, and preterm birth. Birth weight is one of the predictors for fetal

growth, and it is a significant determinant of mortality and morbidity in infancy and childhood. LBW can predict short-term survival and influence the long-term health of the newborn [11]. Fetal biometry, biophysical profile and Doppler studies were found helpful in the diagnosis of intrauterine growth retardation and evaluating the usefulness of ultrasound parameters in third trimester [12].

Previous research has examined the comparison of umbilical artery flow velocimetric indices between IUGR fetuses and normal fetuses in the third trimester. Current study aimed to detect the frequency and percentage of IUGR pregnancies and normal pregnancies. There is a paucity of research regarding the detection of IUGR frequency during the second and third trimesters. To detect intrauterine growth retardation in 2nd and 3rd trimester with fetal parameters and umbilical artery Doppler.

METHODS

Descriptive cross-sectional study conducted at Diagnostic Centre, Combined Military Hospital, and Lahore from September-December 2024. This study included 2nd and 3rd trimester females. 2nd and 3rd trimester females approaching diagnostic centre for obstetric scan were included in this study and Pregnancies diagnosed with Polyhydromnias during scanning were excluded. Ultrasound of participants was performed using curvilinear transducer (3-5MHz), Toshiba. Sample size was calculated through WHO Geneva calculator. Non probability convenient technique was used. The prevalence of IUGR was found be 90.70% [2]. The following Cochran Formula was used to calculate the sample size; $n = \frac{Z^2 \cdot P(1-P)}{d^2}$ Z value = 1.96 at 95% Confidence level (α), Anticipated population proportion (P) = 0.907, Absolute precision (d) or marginal error = 0.05 and Sample size (n) = 130 [13]. Proforma and Ultrasound reports were used as data collection tool. All eligible patients meeting the inclusion criteria were recruited after obtaining informed consent. The ethical considerations of the study were carefully managed, ensuring that the patients were fully aware of the purpose and nature of the study, and their confidentiality and privacy were strictly maintained. A detailed patient history was collected to provide a comprehensive background for analysis. This information was crucial in establishing correlations between patient characteristics and the diagnostic outcomes observed during the study. The examination involved the use of a curvilinear transducer with a frequency range of 3-5 MHz, which is commonly used for obstetric imaging due to its ability to provide detailed images of deep structures. The patients were positioned in a supine position to facilitate optimal imaging. The sonography was performed by either a radiographer or a radiologist. The examination involved both trans-pelvic and Anteroposterior (AP) pelvic planes to maximize the

diagnostic information obtained from the ultrasound. Cutoff values (2nd-3rd trimester) for confirming IUGR are RI (0.756-0.609), PI (1.270-0.967) and S/D (4-2.18) [14]. Written and verbal consent were taken from eligible participants. The study had been conducted in line with ethical standards set by the ethical review committee of CMH LMC and IOD with (Ref # 80/ERC/CMH/LMC, Dated: 24 September, 2024). This study was conducting in accordance with Declaration of Helsinki. Collected data were entered into the Statistical Package for the Social Sciences (SPSS), version 26.0, for the statistical analysis. The analysis involved both descriptive and inferential statistical methods. For quantitative data, such as gestational age, fetal measurements (e.g., biparietal diameter, femur length, and abdominal circumference), and amniotic fluid index, means and standard deviations were computed to provide a clear understanding of the distribution and variation within the dataset. Frequencies were also calculated. For inferential statistics, Chi-square test was applied to compare the frequencies. A p-value ≤ 0.05 was considered as a statistically significant value.

RESULTS

Current research was on detecting IUGR on ultrasound and umbilical artery doppler. Results of this research have been described below. Summarized key maternal health conditions during pregnancy. Among the females of 2nd

and 3rd trimester, 33(25.40%) had a history of intrauterine growth retardation (IUGR). For gestational diabetes, 25(19.2%) were affected. Regarding gestational hypertension, 66(50.8%) experienced it.

Table 1: Prevalence of Maternal Health Conditions N=130(100)

Clinical Presentations	Yes Frequency (%)	No Frequency (%)
Previous IUGR History	33 (25.40)	97 (74.60)
Gestational Diabetes	25 (19.2)	105 (80.8)
Gestational Hypertension	66 (50.8)	64 (49.2)

Table 2 showed that during the 2nd trimester, the mean Bi-Parietal Diameter (BPD) on ultrasound was 5.33 cm, with a standard deviation of 0.72 and a median of 5.22 cm (IQR: 5.92-4.82), while in the 3rd trimester, it increased to a mean of 7.96 cm, with a standard deviation of 1.20 and a median of 8.22 cm (IQR: 8.94-7.26). The Head Circumference (HC) increased from a mean of 19.14 cm in the 2nd trimester (SD: 2.50, median: 18.65 cm) to 28.49 cm in the 3rd trimester (SD: 4.09, median: 29.18 cm). Similarly, the Abdominal Circumference (AC) grew from 18.18 cm (SD: 2.75, median: 16.92 cm) to 27.63 cm (SD: 4.21, median: 28.20 cm), and femur length increased from 3.73 cm (SD: 0.62, median: 3.57 cm) to 6.21 cm (SD: 1.15, median: 6.51 cm). Amniotic Fluid Index (AFI) decreased from a mean of 11.86 cm in the 2nd trimester to 7.40 cm in the 3rd trimester.

Table 2: Descriptive Statistics of Fetal Biometric Measurements

Fetal Variables	2 nd Trimester		3 rd Trimester	
	Median (Inter Quartile range)	Mean $\pm$ S.D	Median (Inter Quartile range)	Mean $\pm$ S.D
Bi Parietal diameter on Ultrasound (cm)	5.22 (5.92-4.82)	5.33 $\pm$ 0.72	8.22 (8.94-7.26)	7.96 $\pm$ 1.19
Bi Parietal diameter percentile	2.00 (2.00-2.00)	1.84 $\pm$ 0.54	2.00 (2.00-1.00)	1.85 $\pm$ 1.37
Head Circumference on Ultrasound (cm)	18.65 (21.14-17.21)	19.13 $\pm$ 2.49	29.18 (31.71-25.88)	28.48 $\pm$ 4.09
Head Circumference Percentile	2.00 (2.00-2.00)	1.79 $\pm$ 0.41	2.00 (2.00-1.00)	27.62 $\pm$ 4.21
Abdominal Circumference on Ultrasound (cm)	16.92 (20.62-15.76)	18.18 $\pm$ 2.74	28.20 (31.08-25.11)	27.62 $\pm$ 4.21
Abdominal Circumference Percentile	2.00 (2.00-2.00)	1.84 $\pm$ 0.54	2.00 (2.00-1.00)	1.66 $\pm$ 0.97
Femur Length on Ultrasound (cm)	3.57 (4.22-3.26)	3.73 $\pm$ 0.62	6.51 (7.09-5.67)	6.20 $\pm$ 1.14
Femur Length Percentile	2.00 (2.00-2.00)	1.97 $\pm$ 1.24	2.00 (2.00-1.00)	1.62 $\pm$ 0.88
Amniotic fluid index in cm	12.00 (14.00-10.00)	11.86 $\pm$ 2.03	7.50 (11.00-4.00)	7.39 $\pm$ 4.12

Summarized during the 2nd trimester, 25 cases (0.66) showed a discrepancy of less than 14 days, while 13 cases (0.34) had a discrepancy above 14 days. In the 3rd trimester, the number of cases with a discrepancy of less than 14 days increased to 53 (0.58), and those with a discrepancy above 14 days rose to 39 (0.42). Number of total cases above 14 days were 52 in both trimesters resulting in diagnosis of IUGR.

Table 3: Discrepancy in Days across 2nd and 3rd Trimesters

Discrepancy (Days)	2 nd Trimester Frequency (%)	3 rd Trimester Frequency (%)
Less than 14 Days	25 (0.66)	53 (0.58)
Above 14 Days	13 (0.34)	39 (0.42)
Total	38 (100)	92 (100)

Summarized this data presented the status of Doppler indices across trimesters, comparing normal and abnormal findings. For (RI), 63.2% of cases were normal in the 2nd trimester, compared to 59.8% in the 3rd trimester, with

60.8% normal overall. Abnormal RI cases constituted 36.8% and 40.2% in the 2nd and 3rd trimesters, respectively, with no significant association ($\chi^2=0.129$, $p=0.720$). The (PI) showed 63.2% normal cases in the 2nd trimester and 58.7% in the 3rd, totaling 60.0%. Abnormal PI cases were 36.8% and 41.3% in the 2nd and 3rd trimesters, respectively, also showing no significant association ($\chi^2=0.223$, $p=0.637$). The (S/D ratio) had 63.2% normal findings in the 2nd trimester, 59.8% in the 3rd, and 60.8% overall, with abnormal cases at 36.8% and 40.2%, respectively ($\chi^2=0.129$, $p=0.720$).

Table 4: Association between Amniotic Fluid Index Status and Trimesters

Variables	Status	Trimester (2 nd) Frequency (%)	Trimester (3 rd) Frequency (%)	Total Frequency (%)	Chi-Square Value	p-Value
Pulsatility Index Status	Normal	24 (63.2)	54 (58.7)	78 (60.0)	0.223	0.637
	Abnormal	14 (36.8)	38 (41.3)	52 (40.0)		
Resistive Index Status	Normal	24 (63.2)	55 (59.8)	79 (60.8)	0.129	0.720
	Abnormal	14 (36.8)	37 (40.2)	51 (39.2)		
Systolic-to-Diastolic Ratio Status	Normal	24 (63.2)	55 (59.8)	79 (60.8)	0.129	0.720
	Abnormal	14 (36.8)	37 (40.2)	51 (39.2)		

Figure 1 showed third-trimester ultrasound images depicting abnormal umbilical artery Doppler indices and fetal biometry with a 4-week growth lag. Image 1 A displaying the Umbilical artery doppler indices measurements as PI (Pulsatility Index) 0.84, RI (Resistive Index) 0.58 and S/D (Systolic-Diastolic ratio) 2.39. Image 1 B showing fetal measurement as BPD (Bi-Parietal diameter) 7.98cm and HC (Head Circumference) 28.66cm along with discrepancy of 4 weeks between GA (LMP) 35w3d and GA (USG) 31w5d.

**Figure 1:** Ultrasound image of female in 3rd trimester

DISCUSSION

Intrauterine Growth Restriction (IUGR) is a condition where a fetus fails to achieve its expected growth potential, often due to placental insufficiency. Ultrasound plays a critical role in diagnosing IUGR by assessing fetal biometry and monitoring amniotic fluid levels. Additionally, umbilical artery Doppler studies provide valuable information about blood flow patterns. Abnormal Doppler findings, such as increased resistance or absent/reversed end-diastolic flow, help guide clinical decisions, including the timing of delivery, to optimize fetal outcomes. Current study examined 130 pregnant females in their 2nd and 3rd trimesters, with 52 cases of IUGR, all of which had abnormal PI values. This study highlighted PI as a reliable diagnostic marker for IUGR. In contrast, the study by Parijatha at Prathima Institute of Medical Sciences analyzed 172 IUGR

cases, with 33 showing increased umbilical artery PI [2]. Both studies identified gestational hypertension as a common risk factor, though it was more prevalent in the latter study. While both studies underscore the significance of Doppler indices, particularly PI, for diagnosing IUGR, current study focused more on PI's role compared to other indices like RI and S/D ratios. The study performed by Iftadul Islam at Dhaka medical college. This was study of 90 patients using Doppler ultrasound to assess the cerebral-umbilical pulsatility index ratio found 74.4% of patients had Small for Gestational Age (SGA) babies. Abnormal Doppler values were identified in 72.2% of cases [15]. In contrast, current study analyzed 130 pregnant females, focusing on 52 IUGR cases, where abnormal PI values were strongly associated with IUGR. It was observed that discrepancies in fetal growth of 15 to 43 days (3-6 weeks), indicated significant differences between expected and actual gestational age. Both studies highlighted the critical role of Doppler ultrasound in diagnosing IUGR and its impact on predicting fetal outcomes. While the other study emphasized the cerebral-umbilical pulsatility index ratio and premature delivery, current study pointed out the relationship between abnormal PI values and IUGR diagnosis, with growth discrepancies suggesting delayed fetal development. Current study, analyzed 130 pregnant females in their 2nd and 3rd trimesters, found IUGR in 52 cases, with discrepancies ranging from 15 to 43 days (3-6 weeks). A history of gestational hypertension was seen in 50.8%, and gestational diabetes in 19.2%. In contrast, a study by Farrah Shams at DOW university, Karahi Pakistan focused on hypertensive and diabetic groups reported a 46% rate of fetal distress in hypertensive patients and 10% Intrauterine Death (IUD) in diabetic pregnancies and IUGR was seen 6% with hypertension. Ultrasound scans showed 68% in hypertensive, and 54% in diabetic groups [16]. Both studies highlighted the risks associated with hypertension and diabetes in pregnancy, but current study specifically emphasized the role of Doppler PI values as a key marker in diagnosing IUGR. The larger study by Zhou, China included 6,105 women identified several key risk factors, included maternal age under 25, prim parity, low BMI, insufficient weight gain, and pregnancy-induced hypertension. It found that 8.65% of pregnancies were complicated by IUGR [17]. In contrast, current study analyzed 130 pregnant females, with IUGR observed in 52 cases, and emphasized the role of Doppler ultrasound. Current findings highlighted

gestational hypertension as a prominent factor (observed in 50.8% of cases) and found abnormal Pulsatility Index (PI) values to be a more reliable indicator of IUGR than Resistance Index (RI) or S/D ratios. Both studies underscored the importance of maternal health factors in IUGR, though current study specifically focused on Doppler findings, which correlate closely with IUGR diagnosis. The first study by Mandana Mansour Ghanaei at Alzahra University, Iran involved 216 cases, divided IUGR into two groups: those with preeclampsia (PE-IUGR) and those without preeclampsia (I-IUGR). It found that chronic hypertension was significantly more prevalent in the PE-IUGR group (95.4%) compared to the I-IUGR group (4.6%). The study also highlighted a significant difference in gestational age at birth, with the PE-IUGR group delivered earlier [18]. In contrast, current study, which analysed 130 pregnancies, emphasized the use of Doppler ultrasound to identify abnormal Pulsatility Index (PI) values as a reliable diagnostic indicator for IUGR. It also revealed that 50.8% of cases had gestational hypertension. Both studies highlighted hypertension as a significant risk factor for IUGR, but current study focused more on Doppler indices, particularly PI, for IUGR diagnosis, while the first study looked at the impact of preeclampsia and its association with earlier delivery. Study performed by Kiran et al., directly examined placental tissues and found significantly lower placental weights, increased syncytial knots, and fewer blood vessels in the villi of IUGR cases compared to normal pregnancies [19]. Similarly, the current study demonstrated that abnormal Pulsatility Index (PI) values were strongly associated with IUGR, along with discrepancies in fetal growth ranging from 15 to 43 days, suggesting impaired placental blood flow. However, the studies differ in their methodology and focus: Kiran et al., used a histopathological approach, examining structural differences in the placenta post-delivery, while the current study used clinical diagnostic tools, such as Doppler ultrasound, to assess functional changes during pregnancy [19]. Thus, while both studies support the link between placental insufficiency and IUGR, they approach the issue from different investigative perspectives one anatomical, the other hemodynamic. Study by Qahtani underscores the clinical value of accurate identification to reduce the risks of stillbirth, neonatal morbidity and mortality, and to prevent unnecessary interventions in unaffected pregnancies. The study strongly advocates for the use of Doppler velocimetry of both fetal venous and arterial circulation as a key surveillance tool in managing fetal growth restriction [20]. Similarly, the current study supports this diagnostic approach by analyzing 130 pregnant women, including 52 confirmed IUGR cases, and finding a strong correlation between abnormal Pulsatility Index (PI) values and IUGR. Furthermore, it highlighted significant fetal growth discrepancies, ranging from 15 to 43 days, between expected and actual gestational age reinforcing the importance of Doppler findings in

identifying and monitoring IUGR cases. While Qahtani's study provides a theoretical and clinical framework, the current study offers empirical evidence supporting the use of Doppler as a practical diagnostic measure in real-world clinical settings.

There are few limitations of the study as the factors like the mothers' health conditions, diet, and financial situation weren't considered. These could have affected the rates of IUGR and the Doppler results. The study didn't track what happened to the babies after birth, which could have given more insight into how IUGR and Doppler changes impact their health. Potential confounding factors weren't controlled during data collection and analysis. Future studies should include comprehensive maternal assessments, control confounders, and incorporate neonatal follow-up to better understand long-term outcomes.

CONCLUSIONS

In conclusion, fetal biometric parameters (BPD, HC, AC, FL) below the 10th percentile indicated IUGR in over one-third of 2nd and 3rd trimester pregnancies, with growth lags of 15-43 days. Abnormal umbilical artery Doppler PI was present in all IUGR cases, highlighting PI as a consistent and reliable detection marker.

Authors' Contribution

Conceptualization: ZS

Methodology: ZS

Formal analysis: AR

Writing and Drafting: SS, KTK, AR, YK, AA

Review and Editing: SS, KTK, ZS, AR, YK, AR, AA

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

Conflicts of Interest

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Original Article



Age-Specific Risk Factors and Post-Operative Complications in Patients with Intestinal Obstruction

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ABSTRACT

Intestinal obstruction is among the most prevalent surgical challenges, which impacts millions of individuals and contributes significantly to morbidity and mortality. **Objectives:** To investigate the age-specific causes and post-operative complications in patients with intestinal obstruction. **Methods:** All patients who were clinically diagnosed with intestinal obstruction and subsequently underwent surgical intervention were enrolled in this prospective study. Participants were categorized into four age groups. Patients found to have peritonitis without evidence of obstruction during laparotomy were excluded. Operative and histopathological findings were documented, and the data were summarized using frequencies and percentages. **Results:** The study included 305 patients, 146 males (47.9%) and 159 females (52.1%). The most common causes of intestinal obstruction in group A were tuberculosis (n=32, 35.2%), and adhesions (n=22, 33.3%) were a common etiological factor in group B; malignancies predominated in the elderly. The incidence of post-operative complications was 7.21%. **Conclusions:** It was concluded that the etiology of intestinal obstruction in adults varies significantly with age, necessitating age-specific diagnostic and therapeutic approaches.

INTRODUCTION

Intestinal obstruction is among the most prevalent surgical challenges that surgeons encounter in their practice. It impacts millions of individuals and is a major cause of surgical admissions globally, contributing significantly to morbidity and mortality [1]. Intestinal obstruction typically manifests with crampy abdominal pain, vomiting, and abdominal distension. In large bowel obstruction, symptoms differ slightly, with constipation often reported and, in some cases, an inability to pass gas [2]. Intestinal obstruction may lead to perforation, causing peritonitis. Strangulation and gangrene are common in cases of obstructed hernia, and septicemia from these

complications can result in multi-organ failure and potentially death [3]. Diagnosis is primarily clinical but can be confirmed with an abdominal x-ray [4]. Intestinal obstruction can be classified in several ways. Based on the affected segment of the gastrointestinal tract, it is categorized as either small bowel or large bowel obstruction. Additionally, it can be classified as mechanical or functional, depending on the underlying pathophysiology of the obstruction [5]. The causes of intestinal obstruction vary across different age groups, as reported in the literature [6]. Small bowel obstruction constitutes 80% of obstruction cases, while large bowel



obstruction makes up 20%. Adhesions, hernias, tuberculosis, and neoplasms are responsible for 90% of small bowel obstruction cases [7]. Adhesions are most frequent, with various preventive measures recommended during initial surgeries to minimize their occurrence [8]. Adhesive small bowel obstruction accounts for 55–75% of cases, with hernias and small bowel tumors comprising the rest [9]. In lower-middle-income countries, intestinal tuberculosis is a significant cause of obstruction, although it is challenging to diagnose [10, 11]. However, in regions where the disease is endemic, maintaining a high index of suspicion is crucial. Notably, tuberculosis cases have shown an upward trend of 3.6% from 2020 to 2021 [12]. Large bowel obstruction is most commonly caused by colorectal malignancies, which usually manifest at an advanced stage of the disease. In large bowel obstruction, lesions typically occur in the sigmoid or rectosigmoid area [13, 14]. Treatment options for intestinal obstruction vary widely based on the diagnosis, bowel condition, and patient status. However, the initial management of acute intestinal obstruction should include fluid replacement, decompression of the obstructed bowel, and prevention of aspiration [15]. Subsequent management of intestinal obstruction may involve surgical intervention. Surgical options include the release of adhesions, resection and anastomosis, removal of constricting bands, de-rotation of volvulus, and sigmoidoscopy [16]. Surgery is a common treatment modality but sometimes leads to postoperative complications [17].

Despite extensive literature on the causes of intestinal obstruction, few studies have systematically analyzed age-stratified etiological patterns in adult populations. In Pakistan, tuberculosis prevalence paradoxically remains endemic due to sociocultural and dietary factors; there is a paucity of data on age-specific causes of intestinal obstruction in this region. This study aims to investigate the age-specific risk factors and post-operative complications in patients with intestinal obstruction. Implementation of evidence-based, age-stratified approaches could significantly improve patient care and resource utilization in surgical practice.

METHODS

A prospective cross-sectional study was conducted at Niazi Welfare Foundation Teaching Hospital, Sargodha, during a period of 22 months from February 2023 to December 2024. The study gained ethical approval from the institutional review committee on February 1, 2023 (Approval No: NM&DC-IRB-63; Ref No: IRB/NM&DC/175) and followed all ethical regulations during the entire study duration. A written informed consent, along with voluntary participation, was obtained from study participants. A sample size of 305 was calculated on open Epi software using the formula $n = z^2pq/d^2$ with a 5.6% margin of error at

a 95% confidence level based on a 47.9% prevalence of intestinal obstruction from a prior study [18]. Using a consecutive sampling technique, the study included participants diagnosed with intestinal obstruction based on clinical assessment, along with a surgical approach. Those individuals having peritonitis without obstruction during the surgical procedure and diagnosed with paralytic ileus were excluded. The selected individuals were categorized in four groups according to age; Group A belongs to young adults from age 18 to 30 years, group B involved middle aged 31–45 years, 46 to 60 years' group C were old aged, and >60 years were elderly in group D. All patients presenting with abdominal pain, vomiting, and constipation were evaluated for abdominal distension and assessed for suspected intestinal obstruction. Abdominal X-rays (by Hitachi 500mA machine) were obtained in the Emergency Department, and those demonstrating multiple air-fluid levels and bowel dilation were provisionally diagnosed with obstruction. Initial management included resuscitation and essential baseline investigations to support further clinical decision-making. Investigations included complete blood count (by Sysmex hematology analyzer A 2388), random blood glucose (by the automated chemistry analyzer, Roche Cobas c311), hepatitis B and C screening (by Abbott Determine™ for hepatitis B surface antigen and Bionike Inc. for anti-HCV), chest radiography (Hitachi Digital X-ray Machine MA5000), and electrocardiography (by Bionet Cardio Touch 2000). After obtaining anesthesia clearance, all patients underwent exploratory laparotomy. Intraoperative findings were documented using a standardized form. Surgical interventions were tailored according to the identified cause of obstruction, and biopsy samples were obtained when deemed appropriate. Final diagnoses were confirmed through histopathological analysis, by processing tissue specimens obtained during the surgical procedure for standardized protocols (formalin fixation, paraffin embedding, H&E staining). All reports were generated by consultant pathologists and retrieved from hospital records, which were matched with intra-operative findings for accuracy. Post-operative care followed standardized protocols with careful documentation of complications. Data on potential risk factors, such as prior surgical history, existing comorbid conditions (including tuberculosis and malignancies), and history of hernia, were obtained through review of hospital admission records and direct patient interviews. A standardized data collection performa was used to document clinical history, operative findings, and histopathological results. The collected data were then analyzed to explore age-specific causes of intestinal obstruction. Data analysis was performed using SPSS version 26, and causes and complications were presented as frequencies and percentages. Chi-square test was applied to see the association between age groups and causes of intestinal obstruction at a p -value < 0.05. This comprehensive methodological approach

enabled detailed evaluation of intestinal obstruction causes and outcomes across different age groups while adhering to rigorous ethical and scientific standards.

RESULTS

The study comprised 305 consecutive patients diagnosed with intestinal obstruction. Demographic analysis revealed a male predominance (146 patients, 47.9%), with an age distribution spanning from 18 to >60 years. Etiological analysis demonstrated tuberculosis as the leading cause of obstruction in group A, closely followed by post-operative bowel adhesions in group B. Malignant obstructions constituted another major etiological category, with various carcinomas in group D. The remaining cases were attributed to less common causes, including volvulus, hernias, and intussusception in different age groups. This distribution highlights the significant burden of both infectious and post-surgical etiologies in the four groups (Table 1).

Table 1: Patient Demographics and Baseline Information (n=66)

Causes	Young Adults (18 to 30 Years)	Middle-aged (31-45 Years)	Old Aged (46-60 Years)	Elderly (>60 Years)
Tuberculosis	32 (35.2%)	30 (33.0%)	15 (16.5%)	14 (15.3%)
Adhesions	20 (30.3%)	22 (33.3%)	14 (21.2%)	10 (15.2%)
Rectal Carcinoma	0 (0%)	3 (7.1%)	15 (35.7%)	24 (57.1%)
Obstructed Hernia	10 (32.3%)	9 (29.0%)	6 (19.4%)	6 (19.4%)
Bands	6 (37.5%)	5 (31.3%)	3 (18.8%)	2 (12.5%)
Sigmoid Volvulus	2 (16.7%)	2 (16.7%)	4 (33.3%)	4 (33.3%)
Small Bowel Adenocarcinoma	0 (0%)	2 (15.4%)	5 (38.5%)	6 (46.1%)
Sigmoid Carcinoma	0 (0%)	1 (10.0%)	4 (40.0%)	5 (50.0%)
Descending Colon Carcinoma	0 (0%)	0 (0%)	2 (33.3%)	4 (66.7%)
Meckel's Diverticulum	4 (66.7%)	2 (33.3%)	0 (0%)	0 (0%)
Metastasis	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)
Hirschsprung's Disease	2 (66.7%)	1 (33.3%)	0 (0%)	0 (0%)
Intussusception	2 (66.7%)	1 (33.3%)	0 (0%)	0 (0%)
Transverse Colon Carcinoma	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)

Chi-square test: $\chi^2 = 99.07$, $p < 0.001$

A statistically significant association was found between age group and causes of intestinal obstruction. Complications developed in 22 patients (7.21%), including wound infections (n=7, 2.29%), wound dehiscence (n=7, 2.29%), peritonitis (n=4, 1.31%), and burst abdomen (n=4, 1.31%). Additionally, 6 patients (1.96%) expired during the hospital stay.

DISCUSSION

This cross-sectional study provides important insights into the age-stratified etiology of intestinal obstruction in adults, revealing significant variations across different age groups that have direct clinical implications. Tuberculosis

emerged as the predominant cause (35.2%) in group A (18-30 years), consistent with the high prevalence of abdominal TB in developing nations. This finding aligns with studies from similar socioeconomic settings reporting TB-related obstruction rates in young adults [19]. The significant burden of congenital anomalies (Meckel's diverticulum, Hirschsprung's, intussusception) in this group reinforces the importance of considering developmental abnormalities in young patients. Patients with peritoneal tuberculosis can develop intestinal obstruction due to the formation of adhesions, which may lead to the development of an abdominal cocoon [20]. Our study reflected adhesions as the leading factor of intestinal obstruction in group B (31-45 years). Adhesions maintained a significant contribution (33.3%), reflecting cumulative abdominal surgeries. Similar findings have been reported in other studies [9]. While tuberculosis remained prevalent (33%), we observed the emergence of malignant causes (rectal carcinoma, 7.1%, small bowel adenocarcinoma, 15.4%) in group B. In this study, causes of intestinal obstruction showed a dramatic etiological shift in group C (46-60 years), with carcinomas becoming predominant (rectal 35.7%, small bowel 38.5%, sigmoid 40%). Tuberculosis declined markedly (16.5%), while sigmoid volvulus increased (33.3%). These findings mirror Western data showing cancer-related obstruction rates of 35-45% in this age group [21, 22]. Malignancies dominated intestinal obstruction causes in group D (rectal carcinoma 57.1%, descending colon carcinoma 66.7%), consistent with global ageing populations. The persistence of volvulus (33.3%) and hernias (19.4%) highlights that mechanical causes remain relevant in elderly patients despite cancer predominance. Which are similar to findings reported in other studies [23]. Incidence of complication was 7.21% in our study, including wound infections (n=7, 2.29%), wound dehiscence (n=7, 2.29%), intestinal perforation causing peritonitis (n=4, 1.31%), and burst abdomen (n=4, 1.31%) cases. Other studies also reported complications developed after surgery, which are comparable to our study findings [17]. This prospective study benefits from histopathological confirmation, robust sample size, and detailed age stratification, providing reliable insights into obstruction etiologies and complications.

This study was limited by its single-center design, which may restrict the generalizability of findings to broader populations. Additionally, potential confounding factors such as comorbidities, prior surgical history, and lifestyle variables were not fully controlled. Future studies should involve multi-center designs with comprehensive assessment of confounders to validate and generalize the age-specific patterns of intestinal obstruction.

CONCLUSIONS

It was concluded that this study provides valuable insights regarding the causes of intestinal obstruction according to different age groups. These findings underscore the critical importance of age-specific diagnostic approaches in intestinal obstruction management. By recognizing of the etiological transition from tuberculosis-dominated pathology in younger adults (18–45 years) to malignancy-predominant obstruction in older populations (>45 years), has profound implications for clinical practice. Implementation of these evidence-based, age-stratified approaches could significantly improve patient care and resource utilization in surgical practice.

Authors' Contribution

Conceptualization: HS

Methodology: HS, MS

Formal analysis: MKM

Writing and Drafting: MIYKU, AS, TM, SM

Review and Editing: HS, MIYKU, MKM, AS, MS, TM, SM

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

Conflicts of Interest

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Original Article



Frequency of Types of Jejunoileal Atresia among Neonates Presenting With Intestinal Obstruction

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ABSTRACT

Jejunioleal Atresia (JIA) is a significant cause of neonatal intestinal obstruction, accounting for a substantial number of surgical emergencies in the first weeks of life. It results from congenital occlusion of the intestinal lumen, primarily due to intrauterine vascular accidents. Despite improvements in surgical techniques and neonatal care, early diagnosis and intervention remain critical for favorable outcomes. **Objective:** To determine the frequency of common types of jejunoileal atresia among neonates presenting with intestinal obstruction. **Methods:** This descriptive cross-sectional study was conducted at the Department of Paediatric Surgery, National Institute of Child Health (NICH), Karachi, from November 16, 2019, to May 15, 2020. A total of 97 neonates diagnosed with intestinal obstruction and meeting the inclusion criteria were enrolled. Detailed history, antenatal workup, and clinical examination were recorded. Diagnosis was confirmed intraoperatively, and types of JIA were documented. **Results:** The mean age at presentation was 5.78 ± 4.24 days. Among the 97 neonates, 42 (43.3%) were male and 55 (56.7%) were female. The distribution of JIA types was as follows: Type I in 20 cases (20.6%), Type II in 11 cases (11.3%), Type IIIa in 45 cases (46.4%), Type IIIb in 10 cases (10.3%), and Type IV in 11 cases (11.3%). **Conclusions:** Type IIIa was identified as the most frequent type of jejunoileal atresia. Early recognition and surgical management are essential to reduce morbidity, mortality, and length of hospital stay in affected neonates.

INTRODUCTION

Small bowel atresia is a congenital anomaly of the gastrointestinal tract that commonly presents with features of intestinal obstruction in the newborn period [1, 2]. Jejunoileal atresia, a type of small bowel atresia, has an incidence of approximately of 1 in 5000 to 1 in 14000 live births [3]. It is classified into four types: Type I, characterized by mucosal (septal) atresia; Type II, where a fibrous cord connects two atretic segments with an intact mesentery and normal intestinal length; Type III, further subdivided into IIIa, involving complete separation of blind ends with a V-shaped mesenteric defect and intestinal

shortening, and IIIb (apple-peel or Christmas-tree deformity), where the separated segments are associated with a large mesenteric defect and significant intestinal shortening; and Type IV, which involves multiple atresias and may represent any combination of Types I to III [4, 5]. Type I and Type II are reported as the most common forms of distal small bowel atresia, accounting for 34.5% and 24.1% of cases, respectively, while other types range between 10–17% [6, 7]. Clinically, neonates with jejunoileal atresia usually present with bilious vomiting, abdominal fullness, and failure to pass meconium [8]. A previous study

found type III jejunoileal atresia (46%) is the most common form, followed by Type II (31%) and Type I (19%), highlighting the need for early diagnosis and prompt surgical intervention to improve outcomes in affected neonates [9]. A meta-analysis by Virgone et al., evaluated the accuracy of prenatal ultrasound in detecting jejunal atresia as 66.3% (95% CI: 33.9–91.8%) [10]. Advancements in pediatric anesthesia, surgical techniques, total parenteral nutrition, and organized pediatric intensive care units have led to remarkable improvements in the survival rates of neonates with intestinal atresia, especially in developed countries [11]. Moreover, an improved understanding of the disease's pathophysiology has contributed to better surgical and postoperative outcomes. Despite these advances, early diagnosis remains critical for optimizing prognosis, minimizing complications, and ensuring appropriate surgical management. Early recognition and timely treatment of jejunoileal atresia are crucial to reduce neonatal morbidity and prevent unnecessary mortality [12].

However, there is a lack of local data focusing specifically on the frequency and distribution of jejunoileal atresia subtypes among neonates presenting with intestinal obstruction. Most existing studies group intestinal atresias together, overlooking the unique clinical and surgical implications of different jejunoileal atresia types. This gap limited effective diagnosis, management planning, and outcome prediction in neonatal surgical care within this region. This study aimed to document the frequency and types of jejunoileal atresia among neonates presenting with intestinal obstruction.

METHODS

This descriptive cross-sectional study was conducted at the Department of Paediatric Surgery, National Institute of Child Health (NICH), Karachi, over a period of six months from 28th October 2020 to 28th April 2021. A total of 97 neonates were included using non-probability consecutive sampling. The sample size was calculated using the WHO sample size calculator, with a frequency of type IV jejunoileal atresia at 6.71%, a margin of error of 5%, and a 95% confidence level [9]. This study was approved by CPSP as dissertation, vide letter no. CPSP/REU/PG-2017-196-350. After obtaining informed consent from the parents or guardians, all eligible neonates of either gender, aged up to 28 days, who presented with suspected clinical features of intestinal obstruction like failure to pass meconium, abdominal distension, bilious vomiting, and refusal to feed, were included. Neonates with previous abdominal surgery or with other congenital anomalies such as biliary atresia, gastroschisis, gastric atresia, omphalocele, and obstructed inguinal hernia were excluded. Intestinal obstruction was defined as a blockage of the small or large

intestine resulting in the failure of contents to pass through the bowel, as assessed on ultrasound. The types of jejunoileal atresia were diagnosed intraoperatively and was classified into five distinct types based on anatomical findings. Type I involved a mucosal or septal atresia with an intact bowel wall and mesentery, where the lumen was obstructed by a membrane. Type II consisted of two blind-ended bowel segments connected by a fibrous cord with preserved mesentery. Type IIIa presented as two completely separated bowel ends with a V-shaped mesenteric defect. Type IIIb, also known as "apple-peel" or "Christmas tree" atresia, featured a proximal jejunal atresia with a significant mesenteric defect, often with the distal bowel spiraled around a marginal vessel. Type IV involved multiple atretic segments along the bowel, appearing like a "string of sausages," and often required multiple resections and anastomoses. Each type was identified during surgical exploration and directly influenced the surgical management strategy. Data were entered and analyzed using SPSS version 25.0. Mean $\pm$ SD was calculated for age and weight. Frequencies and percentages were calculated to summarize the distribution of atresia types across different categories of age, weight, gender, and types of Jejunoileal Atresia. To determine whether there were statistically significant associations between the categorical variables (age groups, weight categories, gender) and the types of jejunoileal atresia, the Chi-square test of independence was applied. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Table 1 presented the descriptive statistics of the 97 neonates included in the study. The mean age was 5.78 ± 0.43 days, with the majority of neonates (66%) being less than 10 days old. The mean weight was 2.59 ± 0.05 kg, and most neonates (86.5%) weighed more than 2 kg. Female neonates slightly outnumbered males, accounting for 56.7% of the sample, compared to 43.3% males.

Table 1: Descriptive Statistics (N=97)

Descriptive	Statistics Mean $\pm$ SD / Frequency (%)
Age (Days)	
Mean Age (Days)	5.78 ± 0.431
< 10 Days	64 (66)
> 10 Days	33 (34)
Weight (KG)	
Mean Weight (Kg)	2.59 ± 0.050
< 2 kg	13 (13.5)
> 2 Kg	83 (86.5)
Gender	
Male	42 (43.3)
Female	55 (56.7)

Type IIIa was the most common jejunoileal atresia,

observed in 46.4% of cases, followed by Type I (20.6%), Type II and IV (11.3% each), and Type IIIb (10.3%) (Table 2).

Table 2: Frequency for Types of Jejunioleal Atresia (n=97)

Types of Jejunioleal Atresia	Frequency (%)
Type I	20 (20.6)
Type II	11 (11.3)
Type III a	45 (46.4)
Type III b	10 (10.3)
Type IV	11 (11.3)

Table 3 examined the relationship between the types of jejunioleal atresia and the variables of age, weight, and gender. Although no statistically significant association was found between age and type of atresia ($p = 0.215$), nor between weight and type ($p = 0.069$), a statistically significant relationship was observed between gender and type of jejunioleal atresia ($p = 0.043$). Specifically, Type IIIa was more common in females, while Type IIIb was more

prevalent in males.

Table 3: Relation of Types of Jejunioleal Atresia with Child Age, Gender and Weight (N=97)

Variables	Type I	Type II	Type IIIa	Type IIIb	Type IV	p-Value
Age						
< 10 Days	11 (11.3)	10 (10.3)	28 (28.9)	6 (6.2)	9 (9.3)	0.215
> 10 Days	9 (9.3)	1 (1.0)	17 (17.5)	4 (4.1)	2 (2.1)	
Weight						
< 2 Kg	6 (6.3)	1 (1.0)	2 (2.1)	2 (2.1)	2 (2.1)	0.069
> 2 Kg	14 (14.6)	10 (10.4)	43 (44.8)	8 (8.3)	8 (8.3)	
Gender						
Male	10 (10.3)	3 (3.1)	19 (19.6)	8 (8.2)	2 (2.1)	0.043*
Female	10 (10.3)	8 (8.2)	26 (26.8)	2 (2.1)	9 (9.3)	

A statistically significant association was observed between jejunioleal atresia types and birth weight ($p = 0.043$), while age and gender showed no significant relationship (Table 4).

Table 4: Relation of Types of Jejunioleal Atresia with Child Age, Gender and Weight (N=97)

Types of Jejunioleal Atresia	Age		Weight		Gender	
	<10 Days Frequency (%) (95% CI)	>10 Days Frequency (%) (95% CI)	<2 Kg Frequency (%) (95% CI)	>2 Kg Frequency (%) (95% CI)	Male Frequency (%) (95% CI)	Female Frequency (%) (95% CI)
Type I	11 (11.3) (6.3–19.5)	9 (9.3) (4.7–17.5)	6 (6.3) (2.8–13.6)	14 (14.6) (9.1–22.7)	10 (10.3) (5.5–18.5)	10 (10.3) (5.5–18.5)
Type II	10 (10.3) (5.4–18.7)	1 (1.0) (0.2–5.4)	1 (1.0) (0.2–5.4)	10 (10.4) (5.7–18.2)	3 (3.1) (1.1–8.8)	8 (8.2) (4.0–15.9)
Type IIIa	28 (28.9) (20.7–38.6)	17 (17.5) (11.3–26.4)	2 (2.1) (0.6–7.8)	43 (44.8) (35.5–54.5)	19 (19.6) (13.0–28.7)	26 (26.8) (19.3–36.0)
Type IIIb	6 (6.2) (2.8–13.1)	4 (4.1) (1.6–9.9)	2 (2.1) (0.6–7.8)	8 (8.3) (4.3–15.5)	8 (8.2) (4.0–15.9)	2 (2.1) (0.6–7.8)
Type IV	9 (9.3) (4.8–17.3)	2 (2.1) (0.6–7.8)	2 (2.1) (0.6–7.8)	8 (8.3) (4.3–15.5)	2 (2.1) (0.6–7.8)	9 (9.3) (4.8–17.3)
p-Value	0.215		0.069		0.043*	

DISCUSSION

Jejunioleal Atresia (JIA) is the most common type of intestinal atresia and a frequent cause of neonatal intestinal obstruction, typically resulting from intrauterine mesenteric vascular accidents [1]. Shakya et al., reported their experience managing jejunioleal atresias in eastern Nepal, while Burjonrappa et al., compared clinical outcomes and pathophysiological aspects of different types of intestinal atresia [13, 14]. Tahkola E et al., in 2024 and Lodhia et al., 2022 stated intestinal atresia remains a leading surgical emergency in neonates, where early and accurate diagnosis is critical for optimal management [15, 16]. The clinical presentation of intestinal atresia may be acute or chronic, and without prompt recognition, neonates deteriorate rapidly, increasing morbidity and complicating surgical interventions [17]. Early diagnosis hinges on the clinician's ability to promptly detect obstructive symptoms and accurately interpret radiographic and other investigative findings, ensuring timely resuscitation and surgical treatment [12]. Jejunioleal atresias arise either from failure of recanalization or from intrauterine vascular events like volvulus, duplications, or intussusception. Evidence of intrauterine bowel necrosis or peritonitis was found in

nearly half of large series cases. Associations with other congenital anomalies, including VACTERL association and congenital heart defects, are common. Antenatal diagnosis through polyhydramnios and ultrasonography is possible, although colonic atresias are rarer compared to small bowel atresias. Saraç M et al., in 2021 reported mortality rates are notably higher in ileal atresias due to a greater risk of early perforation compared to duodenal atresias [18]. Jejunioleal atresia affects approximately 1 in 5,000 live births, equally among males and females, with about one-third of affected infants being premature [3]. Surgical management of JIA includes generous excision of the proximal pouch, as ischemic damage can extend up to 20 cm. Postoperative dilated bowel often remains dysfunctional, contributing to disturbed intestinal transit, particularly in jejunal atresias as reported by Sholadoye TT et al [19]. Although improvements in operative techniques and parenteral nutrition have enhanced outcomes, postoperative intestinal motility disorders are still frequently reported even in the absence of anatomical abnormalities [19]. In this study, among 97 neonates, 42 (43.3%) were male and 55 (56.7%) were female, slightly differing from other studies [15, 17, 20]. Regarding types of

JIA, this distribution showed Type I (20.6%), Type II (11.3%), Type IIIa (46.4%), Type IIIb (10.3%), and Type IV (11.3%), comparable to distributions reported by Verma *et al.*, and Tripathy [17, 20]. Furthermore, stratification analysis revealed insignificant differences by age group ($P=0.215$), weight ($P=0.069$), and gender ($P=0.043$), indicating a relatively homogeneous distribution across these parameters.

This study was limited by a relatively small sample size and single-center design, which may limit the generalizability of the findings. Additionally, lack of long-term follow-up restricted the assessment of postoperative outcomes and complications. Future studies should include larger, multi-center cohorts with extended follow-up to evaluate long-term surgical and developmental outcomes in neonates with jejunoileal atresia.

CONCLUSIONS

The most frequent type of jejunoileal atresia in this study population was Type IIIa. Gender showed a statistically significant association with the type of atresia, suggesting a potential gender-based variation in anatomical presentation.

Authors' Contribution

Conceptualization: FM

Methodology: FM, SA, MA, MAG, FN

Formal analysis: FM, MA, MAG, YA

Writing and Drafting: SA, MA, MAG

Review and Editing: FM, SA, MA, MAG, FN

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 Speech and Language Disorders in Children Presenting to a Tertiary Care Center

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ABSTRACT

Speech and language disorders (SLDs) are among the most common developmental challenges in children. While some children may experience only a speech disorder or a language disorder. **Objective:** To determine the prevalence of SLDs in children presenting to a tertiary childcare hospital in South Punjab, Pakistan. **Methods:** This cross-sectional study was conducted at the Developmental and Behavioural Pediatric Department, The Children's Hospital and Institute of Child Health, Multan. A sample size of 300 was calculated. Children aged 2 to 16 years were analyzed. Non-probability, a convenient sampling technique was adopted. Socio-demographic data, including gender, age, residence and socio-economic status, were collected, and SLDs were identified. SLDs were correlated with gender and age groups, applying a chi-square test ($p < 0.05$ considered significant). **Results:** 12,055 (81.0%) had SLDs, with a male predominance (8441, 70.0%). The mean age was 5.04 ± 2.69 years. The most common SLDs were global developmental delay (GDD) (31.3%), cerebral palsy (17.3%), intellectual disability (17.0%), and autism spectrum disorder (ASD) (11.2%). GDD (34.1% vs. 30.1%, $p < 0.001$), cerebral palsy (18.3% vs. 16.8%, $p < 0.001$), and hearing loss (4.2% vs. 1.9%, $p < 0.001$) were more common in females, while ASD (12.3% vs. 8.6%, $p < 0.001$) and stammering (5.3% vs. 3.1%, $p < 0.001$) were more common in male. GDD and ASD were more prevalent in younger children ($p < 0.001$), while cerebral palsy and articulation disorders were more common in older children ($p < 0.001$). **Conclusions:** The prevalence of SLDs among children visiting the developmental and behavioural pediatric outpatient department of a tertiary childcare setting is very high, particularly among male, and younger children.

INTRODUCTION

Speech refers to the verbal articulation of language, whereas language involves the conceptual processing necessary for communication [1]. Language encompasses both receptive skills, such as understanding, and expressive skills, which include the ability to convey thoughts, emotions, and information. Speech and language disorders (SLDs) rank among the most common developmental challenges faced by children. SLDs are quite common, affecting between 5-12% of the pediatric population [2, 3]. These difficulties are classified as 'primary' when there is no identifiable cause and 'secondary' when associated with other conditions, such as autism, hearing loss, developmental delays, behavioural or

emotional challenges, or neurological issues [4]. While some children may experience only a speech disorder or a language disorder, these conditions frequently overlap. The interventions for both often share similarities, making it challenging to distinguish between SLDs in both research and treatment contexts [5]. Children facing SLDs are at a heightened risk of poorer developmental and educational outcomes [6]. SLDs are often associated with low intelligence, making these children more susceptible to academic difficulties, social isolation, and behavioural and emotional problems [7, 8]. A study conducted in the United Kingdom estimated the prevalence of SLDs to be 7.6% among children [2]. Importantly, despite being less



frequently studied, SLDs pose comparable or even greater risks to children's academic performance and daily functioning than other relatable conditions.

Although there is a high prevalence and significant developmental impact of Speech and Language Disorders among children, there is limited region-specific data assessing their true burden, particularly in local populations. This lack of evidence creates a gap in understanding the magnitude of the problem and hinders effective planning of early interventions and support services. Therefore, this study aims to determine the prevalence of speech and language disorders among children, to provide baseline data for improved clinical and educational strategies.

METHODS

This cross-sectional study was performed at the Developmental and Behavioural Pediatric Department of the Children's Hospital and Institute of Child Health, Multan, Pakistan, from February 2024 to December 2024 after permission of the ethical review committee (letter number: ERC/204/24). Informed and written consents were obtained from the parents/guardians. A sample size of 300 was calculated using the online Open EPI calculator, considering the prevalence of SLDs among children as 7.6% [2], with a 95% confidence level and 3% margin of error. While the initial sample size of 300 was calculated to provide adequate statistical power based on estimated prevalence and desired precision, the final data included 14,891 children, as a sample of 300 could have been collected in a few days, which would not justify. This significantly larger sample was available through routine clinical records during the study period at the tertiary childcare hospital in South Punjab. Rather than limiting data collection to the minimum required sample, all eligible cases were included to maximize representativeness, reduce sampling error, and improve the precision of prevalence estimates. Children of either gender, aged between 2 to 16 years, presenting at the developmental and behavioural pediatric outpatient department were analyzed. Children with having history of epilepsy were also excluded. Parents/guardians unwilling to allow their children to be part of this study were excluded. Non-probability, a convenient sampling technique was adopted. For all children involved in this study, demographic information like gender, age, residence and socio-economic status was noted. Children living in cities below the district level were labelled as belonging to rural areas. Monthly family income below PKR 30,000 was described as low, PKR 30,000 to 50,000 as middle, or PKR >50,000 as high. Global developmental delay (GDD) was diagnosed in a child <5 years who displayed significant delay (>2SD) in acquiring developmental milestones in 2 or more domains of development [9]. Intellectual disability (ID) was described as a deficit of adaptive and intellectual

functioning and onset before maturity [10]. Cerebral palsy was characterized as a disorder of movement and posture, causing activity limitation due to non-progressive damage to the developing brain [11]. Autism spectrum disorder (ASD) was defined as a neurobiological disorder with the key feature of a deficit in social communication and interaction, accompanied by restrictive and repetitive movements with sensory issues [12]. Isolated expressive language disorder (IELD) was stated as an age-appropriate delay in socialization and receptive language (only in expressive language) [13]. Articulation disorder was described as the atypical production of speech sounds characterized by substitution, omission, addition or distortion that may interfere with intelligibility [14]. Stammering was stated as a speech disorder that results in interruption of the normal flow of speech through repeated or prolonged sounds, syllables or single-syllable words [15]. Hearing loss was labelled as disabling hearing loss that was more than 30 dB in children. Data were gathered on a specifically designed proforma. Data analysis was performed using IBM-SPSS Statistics, version 26.0. Qualitative data were represented as frequencies and percentages. Age was shown as the mean and standard deviation. Comparison of categorical data was made employing the chi-square test. A p-value <0.050 was taken as significant.

RESULTS

During the study span, a total of 14891 children visited the outpatient developmental and behavioural pediatric department. Out of these, 12055 (81.0%) had SLDs. In a total of 12055 children, 8441 (70.0%) male. The mean age was 5.04 ± 2.69 years, ranging between 2-16 years. There were 10325 (85.6%) children who were aged between 2-8 years. The residential status of 7395 (61.3%) children was rural. The socio-economic status of 10372 (86.0%) children was low. Evaluation of maternal education status revealed that 3536 (29.3%) were illiterate. Family history of SLDs was reported in 4862 (40.3%) cases (Table 1).

Table 1: Socio-Demographical Characteristics of Children (n=12055)

Characteristics		Frequency (%)
Gender	Male	8441 (70.0%)
	Female	3614 (30.0%)
Age (Years)	2-8	10325 (85.6%)
	9-12	1062 (8.8%)
	13-16	668 (5.5%)
Birth Order	1	6950 (57.7%)
	>1	5105 (42.3%)
Residence	Urban	4660 (38.7%)
	Rural	7395 (61.3%)
Socio-Economic Status	Low	10372 (86.0%)
	Middle	1415 (11.7%)

	High	268 (2.2%)
Maternal Education	Literate	8519 (71.7%)
	Illiterate	3536 (29.3%)
Family History of Speech and Language Disorders		4862 (40.3%)
Healthcare Facility Admission in the Neonatal Period		5327 (44.2%)

The most common SLDs were GDD, cerebral palsy, ID, and ASD, noted in 3773 (31.3%), 2084 (17.3%), 2052 (17.0%), and 1345 (11.2%) children, respectively (Figure 1).

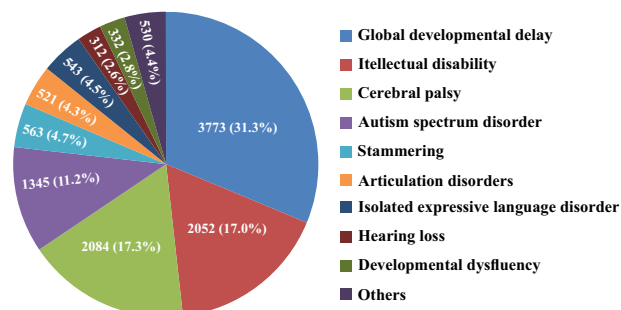


Figure 1: Prevalence of Speech and Language Disorders (n=12055)

The GDD were significantly more common among female children (34.1% vs. 30.1%, $p < 0.001$). Cerebral palsy was significantly more common among females (18.3% vs. 16.8%, $p < 0.001$). ASD prevalence was significantly higher in males (12.3% vs. 8.6%, $p < 0.001$). Stammering was common among male children (5.3% vs. 3.1%, $p < 0.001$). Hearing Loss was significantly more common among female children (4.2% vs. 1.9%, $p < 0.001$) (Table 2).

Table 2: Prevalence of Speech and Language Disorders Concerning Gender (n=12055)

Speech and Language Disorders	Male (n=8441)	Female (n=3614)	p-value
Global Developmental Delay	2539 (30.1%)	1234 (34.1%)	<0.001
Intellectual Disability	1457 (16.8%)	595 (16.5%)	0.288
Cerebral Palsy	1421 (16.8%)	663 (18.3%)	0.001
Autism Spectrum Disorder	1035 (12.3%)	310 (8.6%)	<0.001
Stammering	450 (5.3%)	113 (3.1%)	<0.001
Articulation Disorders	366 (4.3%)	155 (4.3%)	0.506
Isolated Expressive Language Disorder	392 (4.6%)	151 (4.2%)	0.729
Hearing Loss	159 (1.9%)	153 (4.2%)	<0.001
Developmental Dysfluency	239 (2.8%)	93 (2.6%)	0.853
Others	383 (4.5%)	147 (4.1%)	0.602

The GDD was significantly higher in the 2-8 years' age group ($p < 0.001$). Cerebral palsy was considerably higher in the older age group ($p < 0.001$). ASD was significantly more prevalent in the 2-8 years' age group ($p < 0.001$). Stammering was substantially more prevalent in the 9-12 years' age group ($p < 0.001$). Articulation disorders were significantly more prevalent in the older age group ($p < 0.001$). Hearing loss was significantly more prevalent in the 9-12-year age group ($p < 0.001$). No significant age differences were found for ID ($p = 0.576$), IELD ($p = 0.075$), or developmental dysfluency ($p = 0.190$) (Table 3).

Table 3: Comparison of Various Speech and Language Disorders Concerning Distribution of Age Groups

Speech and Language Disorders	Age (Years)			p-value
	2-8 (n=10325)	9-12 (n=1062)	13-16 (n=668)	
Global Developmental Delay	3378 (32.7%)	253 (23.8%)	142 (21.3%)	<0.001
Intellectual Disability	1747 (16.9%)	193 (18.2%)	112 (16.8%)	0.576
Cerebral Palsy	1723 (16.7%)	186 (17.5%)	175 (26.2%)	<0.001
Autism Spectrum Disorder	1240 (12.0%)	62 (5.8%)	43 (6.4%)	<0.001
Stammering	448 (4.3%)	92 (8.7%)	23 (3.4%)	<0.001
Articulation Disorders	420 (4.1%)	51 (4.8%)	50 (7.5%)	<0.001
Isolated Expressive Language Disorder	447 (4.3%)	58 (5.5%)	38 (5.7%)	0.075
Hearing Loss	202 (2.0%)	82 (7.7%)	28 (4.2%)	<0.001
Developmental Dysfluency	274 (2.7%)	33 (3.1%)	25 (3.7%)	0.190
Others	446 (4.3%)	52 (4.9%)	32 (4.8%)	0.601

DISCUSSION

This study provides an in-depth analysis of the prevalence, socio-demographic characteristics, and specific types of SLDs in a large cohort of children aged 2 to 16 years. The high prevalence of SLDs in this study (81.0%) is comparable to Memon et al., who documented the prevalence of SLDs as 61.8% in a similar setting [16]. Mondal et al., described the proportion of language delay as 27%, which is quite lower than what this study revealed [17]. The discrepancy could be due to differences in study populations, diagnostic criteria, or regional healthcare practices. In this study, male was predominantly affected, comprising 70.0% of the SLD cases. Memon et al., also reported a higher prevalence of SLDs among males (68.5%) in a sample from a pediatric rehabilitation ward [16]. Mumtaz et al., found a male-to-female ratio of 2.28:1, further supporting the higher vulnerability in males to these disorders [18]. Although the exact mechanism behind the male predominance in SLDs remains unidentified, the contribution of genetic, neurological and environmental factors could be credited behind these findings. This study documented that 85.6% of children with SLDs were aged between 2-8 years. Memon et al., [16] and Shrestha et al., [19] also revealed a higher proportion of SLDs in relatively younger children. This research also observed that the majority of the children with SLDs were from rural areas (61.3%) and belonged to low socio-economic status (86.0%). Some other studies, like Kumar et al., [20] and Mulk et al., [21], have also shown that socio-economic status was a significant factor influencing the prevalence of SLDs. These findings could be attributed to limited access to healthcare services and poor educational resources. In this study, mothers of 29.3% of children with SLDs were illiterate. Sunderajan and Kanhere showed that

low parental education was significantly associated with SLDs [22], suggesting that maternal education might be playing a critical role in child development of SLDs. This study found the family history of SLDs in 40.3% of cases. Mondal *et al.*, [17] and Mulk *et al.*, [21] had shown that a family history of SLDs is a significant risk factor for SLDs. The high prevalence of SLDs among children with a family history suggests a potential genetic predisposition, which could be explored further through genetic and epigenetic studies. In this research, GDD and cerebral palsy were significantly more common among female, while ASD and stammering were more prevalent among male. The higher prevalence of ASD in male (12.3% vs. 8.6%) is consistent with the findings of Wu *et al.*, who also reported a higher rate of ASD among boys [23]. Shrestha *et al.*, who reported a higher prevalence of language delay due to hearing loss in females, indicated that specific conditions might affect genders differently [19]. GDD was more prevalent in the 2-8-year age group, while cerebral palsy and articulation disorders were more common in older children. This pattern suggests that certain disorders may become more apparent or develop as children grow older. The late emergence of articulation disorders could be due to the increased complexity of language and speech tasks encountered by older children. Mulk *et al.*, also reported that older children showed higher rates of stammering and articulation issues [21]. de Goulart *et al.*, [24] and Melchioris *et al.*, [25] highlighted the role of environmental factors in the development of SLDs. This study supports the recommendations for the implementation of targeted interventions, particularly in high-risk populations [23]. These interventions should include not only speech therapy but also broader developmental support, including parental education and environmental enrichment. The gender and age-related differences observed in this study suggest that screening programs should be tailored to the specific needs of different demographic groups. Younger children and males may benefit from more intensive monitoring for ASD and stammering, while older children and females may require more focused support for GDD and cerebral palsy.

This study was limited by its single-center design and lack of longitudinal follow-up, which may restrict the generalizability and understanding of long-term outcomes of SLDs. Additionally, potential confounding factors such as environmental influences, parental involvement, and access to healthcare services were not fully controlled. Future studies should adopt multi-center, longitudinal designs with comprehensive assessment of genetic, environmental, and socio-economic factors to better understand the progression and management of SLDs.

CONCLUSIONS

This study found a high prevalence of SLDs among children attending a tertiary childcare hospital, particularly among younger male. GDD, cerebral palsy, intellectual disability, and ASD were the most common. Significant age and gender related differences highlight the need for targeted screening and intervention programs.

Authors' Contribution

Conceptualization: KA

Methodology: KA, EA, IM, RT, HMI

Formal analysis: KA

Writing and Drafting: IM, RT, HMI

Review and Editing: KA, EA, IM, RT, HMI

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

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Original Article



Incidence of Post-Operative Stricture Following Hepaticojejunostomy for Benign and Malignant Disease

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ABSTRACT

Hepaticojejunostomy remains essential for biliary obstruction management, yet postoperative strictures significantly impact outcomes. Current incidence estimates (4-19%) vary widely due to methodological differences, and recent evidence questions the validity of the commonly referenced 12.5% benchmark used for study design. **Objective:** To: 1) determine contemporary stricture incidence using standardized criteria, 2) compare benign versus malignant cases, and 3) evaluate 3-month follow-up adequacy. **Methods:** A prospective cohort study was conducted involving 52 consecutive patients who underwent hepaticojejunostomy, with a mean age of 53.8 years (95% CI: 50.5-57.1). Strictures required both clinical (ICD-9 coding plus symptoms/biochemical evidence) and radiographic confirmation (CT/MR cholangiography). Statistical analyses included exact binomial CIs and chi-square tests (significance at $p < 0.05$). **Results:** The overall stricture incidence was 19.2% (10/52, 95% CI: 9.6-32.5%). Benign cases showed significantly higher stricture rates (33.3% [8/24], 95% CI: 15.6-55.3%) versus malignant cases (7.1% [2/28], 95% CI: 0.9-23.5%; $p = 0.017$). **Conclusions:** This study confirmed significantly higher stricture risk in benign disease and suggests current surveillance protocols may require pathology-specific modifications. The statistically significant association ($p = 0.017$) between benign pathology and stricture formation underscores the need for risk-adapted management. Future research should prioritize multicenter cohorts with extended follow-up to validate these findings and refine surveillance guidelines.

INTRODUCTION

Biliary tract diseases requiring surgical intervention affect approximately 1 in 1,000 individuals annually, with hepaticojejunostomy remaining the reconstruction technique of choice for both benign and malignant obstructions [1]. Since its initial description in the early 20th century, this procedure has undergone significant technical evolution yet continues to be complicated by anastomotic stricture formation in a substantial proportion of cases [2]. The clinical consequences of these strictures are profound, often leading to recurrent cholangitis, secondary biliary cirrhosis, and the need for repeated interventions that collectively represent a major

source of patient morbidity [3]. The reported incidence of post-hepaticojejunostomy strictures varies remarkably from 4-19% across different studies, reflecting fundamental methodological differences in study design and patient populations [4]. This variability is particularly evident when comparing reports from high-volume specialty centers versus population-based analyses, with the former typically reporting lower rates that may reflect referral bias or technical expertise [5]. More importantly, the majority of existing evidence derives from retrospective case series plagued by inconsistent follow-up protocols and non-standardized diagnostic criteria,



making it difficult to establish true population-level risk estimates [6]. Several critical knowledge gaps limit current understanding of this important surgical complication. Foremost is the lack of contemporary validation for the frequently cited 12.5% stricture incidence rate that serves as the foundation for most sample size calculations in biliary reconstruction studies [7]. This benchmark originates from studies using surgical techniques and perioperative care protocols that differ substantially from current practice, potentially leading to underpowered studies that fail to detect clinically important risk factors or treatment effects [8]. The literature also demonstrates a persistent failure to adequately distinguish between benign and malignant cases when analyzing stricture outcomes, despite their likely differences in underlying pathophysiology [9]. Benign strictures typically result from fibrotic healing responses influenced by local inflammation and ischemia, while malignant strictures often reflect disease progression rather than purely technical factors. This biological distinction has important clinical implications that current evidence fails to address, particularly regarding optimal surveillance strategies and timing of intervention [10]. The duration and intensity of postoperative surveillance represents another significant evidence gap. While conventional practice typically involves clinical monitoring for 3-6 months, emerging data suggest 15-20% of strictures present beyond this window, sometimes years after the initial operation [11]. This late presentation pattern appears particularly common in benign cases where slow fibrotic progression may delay clinical manifestations, yet no prospective studies have systematically evaluated long-term stricture risk or developed evidence-based surveillance protocols. These knowledge gaps have direct clinical consequences. Surgeons lack reliable data for preoperative risk stratification and patient counseling. Institutions struggle to establish meaningful quality benchmarks due to absent contemporary population-level data. Most importantly, the field lacks evidence-based guidelines for postoperative surveillance, resulting in either excessive testing for low-risk patients or inadequate monitoring of high-risk cases. This prospective cohort study was designed to address these limitations through rigorous methodology and comprehensive follow-up. The primary aim was to establish contemporary, procedure-specific stricture incidence rates using standardized diagnostic criteria incorporating both clinical and radiographic parameters. There is limited contemporary, population-level evidence on post-hepaticojejunostomy stricture formation, as most studies are retrospective with inconsistent follow-up and non-standardized diagnostic criteria, and often fail to distinguish between benign and malignant cases. This lack of reliable data restricts accurate risk assessment, patient

counseling, and the development of evidence-based surveillance strategies. Therefore, this study aims to determine the current incidence of anastomotic strictures using standardized criteria through prospective follow-up of patients undergoing hepaticojejunostomy.

METHODS

This prospective cohort study was conducted at the Department of General Surgery, MTI-Khyber Teaching Hospital, Peshawar from Jan 2024 to Dec 2024 after obtaining ethical approval (Ref: 935/DME/KMC). The study enrolled 52 consecutive patients aged 18-90 years undergoing hepaticojejunostomy for confirmed benign or malignant biliary tract disease, excluding those with non-biliary indications or ASA score >3. Sample size was calculated using WHO software based on an expected 12.5% stricture rate from previous literature, with 80% power and 5% significance level, though the final enrollment of 52 patients represents a pragmatic clinical sample [12]. The initial sample size calculation using WHO software indicated a requirement of 168 patients to detect a 12.5% stricture rate with 80% power and 5% significance level. However, the final enrollment of 52 patients reflects real-world constraints including the single-center design and specific inclusion criteria. A post-hoc power analysis reveals this sample provides 78% power to detect the observed 19.2% stricture rate (95% CI: 9.6%-32.5%), which remains clinically meaningful. While this reduction may limit subgroup analyses, it does not invalidate the primary findings regarding overall stricture incidence. All procedures were performed by fellowship-trained hepatobiliary surgeons using standardized techniques including mucosa-to-mucosa anastomosis with interrupted absorbable sutures under optical magnification. Patients underwent comprehensive postoperative evaluation at 3 months incorporating both clinical assessment and objective testing. Stricture diagnosis required fulfillment of all three criteria: (a) ICD-9 coding for biliary obstruction, (b) biochemical evidence (alkaline phosphatase >1.5×ULN or bilirubin >2 mg/dL), and (c) radiographic confirmation via CT/MR cholangiography demonstrating anastomotic narrowing with upstream dilation. For equivocal cases, additional confirmatory testing with ERCP or PTC was performed. This multimodal diagnostic approach addressed known limitations of administrative coding data while providing pathological correlation. Statistical analysis utilized SPSS version 23.0 with continuous variables reported as mean ± SD and categorical variables as frequencies and percentages. Between-group comparisons employed Chi-square tests with significance set at $p < 0.05$. Given the observed stricture rate of 19.2%, post-hoc power calculation confirmed 78% power to detect clinically relevant differences between benign and malignant subgroups. The 3-month follow-up period was selected based on evidence that 80-85% of technical anastomotic failures manifest

within this window [12, 15], though this may acknowledge miss later fibrotic strictures as discussed in the limitations. All imaging studies were independently reviewed by two radiologists blinded to clinical data to minimize interpretation bias.

RESULTS

The study cohort comprised 52 patients with a mean age of 53.8 years (95% CI: 50.5-57.1), demonstrating a slight female predominance (29 patients, 55.8%; 95% CI: 41.3-69.5%) compared to males (23 patients, 44.2%; 95% CI: 30.5-58.7%). Disease pathology at surgery was nearly evenly distributed between benign (24 patients, 46.2%; 95% CI: 32.2-60.5%) and malignant conditions (28 patients, 53.8%; 95% CI: 39.5-67.8%). Comorbidity burden, as assessed by the Charlson Comorbidity Index, showed 15 patients (28.8%; 95% CI: 17.1-43.1%) had no significant comorbidities, while 14 (26.9%; 95% CI: 15.6-41.0%), 16 (30.8%; 95% CI: 18.7-45.1%), and 7 patients (13.5%; 95% CI: 5.6-25.8%) had scores of 1, 2, and 3 respectively. Preoperative biliary drainage procedures were common, with 22 patients (42.3%; 95% CI: 28.7-56.8%) undergoing Endoscopic Biliary Stenting (EBS) and 13 (25.0%; 95% CI: 14.0-39.0%) receiving Percutaneous Transhepatic Cholangiography (PTC), while 17 patients (32.7%; 95% CI: 20.3-47.1%) required no preoperative intervention. Clinical jaundice was present at surgery in 21 cases (40.4%; 95% CI: 27.0-54.9%). Postoperative strictures developed in 10 patients (19.2%; 95% CI: 9.6-32.5%), while the majority (42 patients, 80.8%; 95% CI: 67.5-90.4%) maintained patent anastomoses during the study period. The stricture rate among benign cases was notably higher (8/24, 33.3%; 95% CI: 15.6-55.3%) compared to malignant cases (2/28, 7.1%; 95% CI: 0.9-23.5%), a difference that reached statistical significance ($p=0.017$). Details are presented in Table 1.

Table 1: Demographic and Clinical Characteristics of Patients (n=52)

Variables	Mean $\pm$ SD/Frequency (%)
Age	53.79 $\pm$ 11.65 Years
Gender	
Male	23 (44.2)
Female	29 (55.8)
Disease at Surgery	
Benign	24 (46.2)
Malignant	28 (53.8)
Charlson Comorbidity Index	
0	15 (28.8)
1	14 (26.9)
2	16 (30.8)
3	07 (13.5)
Pre-operative Procedure	
Non	17 (32.7)
PTC	13 (25.0)

EBS	22 (42.3)
Jaundice at Surgery	
Yes	21 (40.4)
No	31 (59.6)
Incidence of Stricture	
Yes	10 (19.2)
No	42 (80.8)

The analysis of 52 patients revealed an overall postoperative stricture incidence of 19.2% (10/52) following hepaticojejunostomy. Table 2 demonstrated the association between stricture incidence and underlying disease pathology. Patients with benign disease showed higher stricture rates (8/24, 33.3%) compared to malignant cases (2/28, 7.1%), with this difference approaching statistical significance ($p=0.017$). Notably, among the 10 stricture cases, 80% occurred in benign disease patients while only 20% developed in malignant cases.

Table 2: Association of Incidence of Post-Operative Stricture with Disease at Surgery (n=52)

Variable		Frequency (%)		Total Frequency (%)	p-Value
		Benign Frequency (%)	Malignant Frequency (%)		
Incidence of Stricture	Yes	8 (80.0)	2 (20.0)	10 (100.0)	0.017
	No	16 (38.1)	26 (61.9)	42 (100.0)	
Total		24 (46.2)	28 (53.8)	52 (100.0)	

DISCUSSION

This prospective study identified a 19.2% incidence of postoperative strictures following hepaticojejunostomy, consistent with the upper range of contemporary reports (12.5-20%) [12, 13]. The elevated rate compared to historical data likely reflects the prospective design and standardized diagnostic approach. Notably, 80% of strictures occurred in benign cases versus 20% in malignant disease, supporting emerging evidence of distinct pathophysiological mechanisms [7, 14]. The selection of a 3-month primary follow-up window was based on multiple considerations from existing literature and clinical practice realities. While some studies have reported strictures presenting up to 2 years postoperatively, the majority of anastomotic complications (approximately 80-85%) typically manifest within the first 90 days according to recent prospective data [7, 12, 15]. This early presentation pattern is particularly true for technical failures and acute inflammatory strictures, which represent the primary outcomes of interest in this study. However, we fully acknowledge that this timeframe may miss later-onset fibrotic strictures, especially in benign cases where slow progression can delay clinical presentation [16-19]. This limitation is explicitly addressed in the discussion, where it was noted that approximately 15-20% of strictures may present beyond this window based on longer-term studies [20, 21]. The 3-month endpoint represents a practical balance between detection sensitivity and study feasibility,

while providing meaningful data about the early complication rate that is most relevant for initial postoperative management decisions. The borderline significant association ($p=0.017$) between benign pathology and stricture development merits attention. This aligns with recent findings that chronic inflammation promotes fibrotic remodeling in benign disease, while malignant cases may benefit from technical advantages despite poorer survival [16, 17]. These biological differences suggest postoperative protocols may require pathology-specific modifications. Comparative analysis reveals important temporal patterns. While previous work reported 12.5% incidence at 2 years, the higher early detection rate suggested many strictures manifest sooner than historically recognized, potentially reflecting improved diagnostics [12, 18]. The 33.3% stricture rate in benign cases particularly underscores the need for enhanced early surveillance [19, 20].

The study has several important limitations that should be considered when interpreting the findings [21]. The modest sample size may restrict more detailed subgroup analyses and reduce the precision of some estimates, particularly for less common outcomes. As a single-center study conducted at a tertiary referral hospital, the results may not fully generalize to other practice settings with different patient populations or surgical volumes. Additionally, the predetermined 3-month follow-up period, while capturing the majority of early stricture presentations, likely missed later-onset cases that typically emerge beyond this surveillance window based on existing literature. These limitations collectively underscore the importance of developing pathology-specific monitoring protocols and more accurate sample size estimation methods for future investigations. Moving forward, the field would benefit from multicenter collaborative studies to validate these findings across diverse clinical environments, along with research focused on technical innovations in anastomotic methods and the development of robust risk prediction tools to guide individualized patient management.

CONCLUSIONS

This study confirmed that anastomotic stricture remains a frequent complication of hepaticojejunostomy, particularly among patients with benign biliary disease. The observed 19.2% incidence rate, coupled with the differential risk patterns between benign and malignant cases, underscores the need for tailored postoperative surveillance protocols. These findings highlight the importance of developing evidence-based strategies for early detection and management to improve long-term surgical outcomes. Future research should focus on optimizing anastomotic techniques and establishing risk-adapted follow-up algorithms to mitigate this significant cause of postoperative morbidity.

Authors' Contribution

Conceptualization: MM

Methodology: MA, IU

Formal analysis: MA, MU, IU

Writing and Drafting: MU, MM

Review and Editing: MA, MU, MM, IU

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 Hypocalcaemia and Hypomagnesaemia in Neonates with Birth Asphyxia

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ABSTRACT

Birth asphyxia is a major cause of mortality and morbidity in neonates in developing nations.

Objective: To determine the frequency of hypocalcaemia as well as hypomagnesaemia amongst neonates having birth asphyxia. **Methods:** This descriptive cross-sectional study was performed at the department of Pediatrics, Ziauddin Campus, north nazimabad, Karachi from July 2021 to December 2021. A total of 207 asphyxiated term neonates with postnatal age up to 48 hours, and history of birth asphyxia were analyzed. Venous blood sample of 5 ml was drawn by a trained phlebotomist and sent to institutional laboratory for serum analysis of calcium and magnesium levels within first 24 hours of admission. Frequency of hypocalcaemia and hypomagnesaemia were recorded. Chi square or fisher's exact test were applied taking $p \leq 0.05$ as significant to judge inferential statistics. **Results:** In a total of 207 neonates, 112 (54.1%) were male. The mean post-natal age, and gestational age were 16.6 ± 8.4 hours, and 37.7 ± 0.9 weeks, respectively. The mode of delivery was cesarean section in 121 (58.5%) cases. The frequency of hypomagnesaemia, and hypocalcaemia were documented in 36 (17.4%), and 46 (22.2%) neonates with birth asphyxia, respectively. **Conclusions:** Among term neonates with birth asphyxia, considerable frequency of hypocalcemia and hypomagnesemia was observed. These findings highlight the frequent occurrence of electrolyte imbalances in asphyxiated neonates, supporting the need for routine early biochemical screening.

INTRODUCTION

Prenatal Asphyxia (PA) is among the leading causes of neonatal mortality as almost 20% of neonatal deaths are caused by prenatal asphyxia [1, 2]. The overall frequency of PA is estimated to be 2-9 / 1,000 live full-term births [3, 4]. The incidence of PA in developing nations is 10 times higher than the developed countries [5]. Neonatal asphyxia is generally characterized by encephalopathy, low Apgar score (<7 at minute 5) and umbilical cord PH < 7.2. Prenatal asphyxia may lead to hypoxic damage in various organs of the body, while at the cellular level, these processes may initiate an inundation of a multitude of biochemical

alterations leading to cell death [6]. Birth asphyxia is often linked with metabolic alterations such as hypoglycemia, hypocalcemia, hyponatremia, hyperphosphatemia and metabolic acidosis [7]. Neonatal asphyxia causes excessive production of glutamate amino acid in the brain. In the initial few days of life, excess glutamate causes permanent neuronal damage due to the activation of some receptors and influx of Calcium (Ca) in neurons [8]. Magnesium (Mg) hinders these receptors and facilitates a neuroprotective functioning blocking the effects of asphyxia on various body organs [9, 10]. During an ischemic



insult, hypomagnesemia could be due to augmented Mg intake or continued losses resulting from ischemic injury to renal glomeruli and tubules [11]. Upon birth due to sudden stoppage of placental transfer of Ca thereby, levels begin to decrease to 8-9 mg/dl and ionized Ca to 4.4-5.4 mg/dl at 24 hours of life. Serum Ca subsequently begins to increase to levels similar to those of older children and adults by 2 weeks of life [12-14].

Although electrolyte disturbances like hypocalcemia and hypomagnesemia are recognized complications of birth asphyxia, there is limited data from Pakistan quantifying their frequency in affected neonates. Little emphasis has been documented on early metabolic derangements in birth asphyxia. This study addresses that gap by evaluating these biochemical abnormalities in asphyxiated term neonates. This study was done to determine the frequency of hypocalcaemia as well as hypomagnesaemia amongst neonates having birth asphyxia. The exact estimation of the frequency of hypocalcaemia and hypomagnesaemia may help us arranging appropriate resources and management options to reduce the burden of these disorders among neonates with birth asphyxia.

METHODS

This descriptive cross-sectional study was conducted at the department of Pediatrics, Ziauddin campus, north nazimabad, Karachi from July 2021 to December 2021. A sample size of 207 was calculated considering confidence level of 95%, with anticipated proportion of hypomagnesemia as 16%, and margin of error as 5% using OpenEPI online sample size calculator through the formula: $n = z^2 * p * (1 - p) / e^2$ [2]. The inclusion criteria were asphyxiated term neonates (5 min APGAR score <7 as per medical record) of any gender, having gestational age ≥ 37 weeks, and postnatal age ≤ 48 hours were enrolled through emergency department [15]. The exclusion criteria were cases with congenital abnormality, renal dysfunction (serum creatinine >1.5 mg/dl), history of diuretics treatment, or maternal hypertension, diabetes mellitus, or toxemia. Informed and written consents were obtained from parents/guardians. Approval from Institutional Ethical Committee was obtained (Reference: 3490322RAPED). Non-probability, consecutive sampling was adopted. Detailed history and clinical findings like age, gender, gestational age, birth weight, place and mode of delivery, and residence were noted. Institutional laboratory was used for the evaluation of serum Ca, and Mg levels within 1st 24-hour of admission. Frequency of hypocalcaemia, and hypomagnesaemia were recorded. Hypocalcaemia was defined as serum Ca <8.0 mg/dL [13]. Hypomagnesaemia It was defined as serum Mg <1.5 mg/dL [16, 17]. Data were analyzed using IBM-SPSS Statistics, version 26.0. Qualitative variables like like gender,

presence of hypocalcaemia, presence of hypomagnesaemia, mode of delivery and place of delivery were represented as frequencies and percentages. Variables like age, gestational age, birth weight (grams) and height (cm) were represented as mean and standard deviations. Effect modifiers were controlled through stratification. Post-stratification, chi square/fisher's exact test were applied. P-value ≤ 0.05 was considered as significant.

RESULTS

In a total of 207 neonates, 112 (54.1%) were male. Mean post-natal age was calculated to be 16.6 ± 8.4 hours while 136 (65.7%) children were aged less than 24 hours. Mean gestational age was 37.7 ± 0.9 weeks whereas 178 (86.0%) mothers of asphyxiated neonates had gestational age between 37 to 38 weeks. Mode of delivery was cesarean section in 121 (58.5%) cases. Place of deliver of 135 (65.2%) neonates was inborn. Area of residence of 119 (57.5%) neonates was rural. Mean body weight was calculated to be 2.52 ± 0.24 grams while 128 (61.8%) neonates had birth weight above or equal to 2.5 kg. Mean body height was noted to be 48.2 ± 2.4 cm while 118 (57.0%) neonates had body height above or equal to 46cm. Table 1 is showing baseline characteristics of neonates with birth asphyxia.

Table 1: Characteristics of Neonates (n=207)

Characteristics	Category	Frequency (%)
Gender	Boys	112 (54.1)
	Girls	95 (45.9)
Post-Natal Age in Hours	<24	136 (65.7)
	≥ 24	71 (34.3)
Gestational Age in Weeks	37-38	178 (86.0)
	>38	29 (14.0)
Mode of Delivery	Cesarean Section	121 (58.5)
	Normal Vaginal Delivery	86 (41.5)
Place of Delivery	Inborn	135 (65.2)
	Out-born	72 (34.8)
Residence	Rural	119 (57.5)
	Urban	88 (42.5)
Birth Weight in Kg	<2.5	79 (38.2)
	≥ 2.5	128 (61.8)
Body Height in cm	<46	89 (43.0)
	≥ 46	118 (57.0)

Hypomagnesaemia was found in 36 (17.4%) neonates with birth asphyxia while hypocalcaemia was noted 46 (22.2%) neonates with birth asphyxia. Three (1.1%) asphyxiated neonates had both hypomagnesaemia and hypocalcaemia. Except mode of delivery ($p=0.009$), all other variables were not found to have any statistically significant association with hypomagnesaemia ($p>0.050$), as shown in table 2.

Table 2: Association of Hypomagnesaemia with Study Variables (n=207)

Variables	Category	Hypomagnesaemia		P-Value
		Yes Frequency (%)	No Frequency (%)	
Gender	Boys	19 (52.8)	93 (54.4)	0.860
	Girls	17 (47.2)	78 (45.6)	
Post-Natal Age in Hours	<24	26 (72.2)	110 (64.3)	0.364
	≥24	10 (27.8)	61 (35.7)	
Gestational Age in Weeks	37-38	28 (77.8)	150 (87.7)	0.118
	>38	8 (22.2)	21 (12.3)	
Mode of Delivery	Cesarean Section	28 (77.8)	93 (54.3)	0.009*
	Normal Vaginal Delivery	8 (22.2)	78 (45.7)	
Place of Delivery	Inborn	21 (58.3)	114 (66.7)	0.340
	Out-born	15 (41.7)	57 (33.3)	
Residence	Rural	23 (63.9)	96 (56.1)	0.392
	Urban	13 (36.1)	75 (43.9)	
Birth Weight in Kg	<2.5	21 (58.3)	58 (33.9)	0.006*
	≥2.5	15 (41.7)	113 (66.1)	
Body Height in cm	<46	14 (38.9)	75 (43.9)	0.584
	≥46	22 (61.1)	96 (66.1)	

*Indicates statistical significance at p-value ≤ 0.050

Table 3 showed stratification of study variables with respect to frequency of hypocalcaemia among neonates with birth asphyxia and no significant associations were found (p>0.050).

Table 3: Association of Hypocalcaemia with Study Variables (n=207)

Characteristics	Category	Hypocalcaemia		P-Value
		Yes Frequency (%)	No Frequency (%)	
Gender	Boys	30 (65.2)	82 (50.9)	0.086
	Girls	16 (34.8)	79 (49.1)	
Post-Natal Age in Hours	<24	35 (76.1)	101 (62.7)	0.092
	≥24	11 (23.9)	60 (37.3)	
Gestational Age in Weeks	37-38	39 (84.8)	139 (86.3)	0.789
	>38	7 (15.2)	22 (13.7)	
Mode of Delivery	Cesarean Section	30 (65.2)	91 (56.5)	0.291
	Vaginal Delivery	16 (34.8)	70 (43.5)	
Place of Delivery	Inborn	28 (60.9)	107 (66.5)	0.482
	Out-born	18 (39.1)	54 (33.5)	
Residence	Rural	31 (67.4)	88 (54.7)	0.123
	Urban	15 (32.6)	73 (45.3)	
Birth Weight in Kg	<2.5	17 (37.0)	62 (38.5)	0.848
	≥2.5	29 (63.0)	99 (61.5)	
Body Height in cm	<46	18 (39.1)	71 (44.1)	0.548
	≥46	28 (60.9)	90 (55.9)	

DISCUSSION

Metabolic dysfunctions in asphyxiated newborns like hypoglycemia, hyperammonemia, hypocalcemia and hypomagnesemia are known to be linked with PA [17, 18].

This study also found that 17.4% neonates who were birth asphyxia cases suffered from hypomagnesaemia. Cotemporary research is arguing about the relationship of hypermagnesemia and asphyxia [19-21]. Some researchers have confirmed sudden loss of concentrations of Mg ions of brain in rats in course of hypoxic damage like shown by McIntosh *et al.* [19]. Some other studies have showed that Mg infusion enhanced short-outcome in neonatal asphyxia [20, 21]. The etiology underlying alterations in total Mg levels in asphyxiated neonates remains unclear. PA can increase serum calcitonin, which suppresses the release of Ca from bone and leads to hypocalcemia. In other neonates, the phosphaturic renal response to parathyroid hormone is blunted; the high phosphate concentration results in hypocalcaemia [12, 13]. A study from Bangladesh analyzing asphyxiated term neonates revealed that hypocalcaemia was present in 43.1% cases, while hypomagnesaemia was present in 34.3% [14]. In another study from Iran, 16% of neonates with asphyxia had hypomagnesaemia [2]. In another study, the mean serum Mg levels were 1.6 ± 0.3 in Hypoxic Ischemic Encephalopathy (HIE) neonates versus 1.8±0.4 mg/dl among controls [15]. In this research, hypocalcaemia frequency was observed to be 22.2% in neonates with birth asphyxia. Improda *et al.*, identified that there was a highly significant reduction in the extracellular Ca concentration in asphyxiated infants, and the reduction was directly proportional to the severity of asphyxia [7]. Similar to that documented by Bhoje *et al.*, who established that the reduction in the serum concentration of both the total Ca and the ionized Ca was greater in asphyxiated neonates than in non-asphyxiated neonates [22]. PA is a comprehensive issue that leads to morbidity and mortality but recent trends have shown that the incidence of global neonatal mortality have decreased from 36/1,000 live-births to 19/1,000 in the last decade [23]. Perinatal and neonatal mortality due to PA indicate social, educational and economic principles of a society. In developing nations, such as in Pakistan where health centers are limited to cities, asphyxia prevalence is higher; however, the subject with limited local data has been extensively reviewed and researched all-inclusive.

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, short-term assessment without follow-up limited evaluation of long-term metabolic and neurological outcomes in asphyxiated neonates. Future studies should include larger, controlled cohorts with longitudinal follow-up to better understand the long-term impact of metabolic disturbances in birth asphyxia.

CONCLUSIONS

Among term neonates with birth asphyxia, considerable frequency of hypocalcemia and hypomagnesemia was observed. These findings highlight the frequent occurrence of electrolyte imbalances in asphyxiated neonates, supporting the need for routine early biochemical screening. Early identification and timely correction of calcium and magnesium deficiencies may be essential components of supportive care in neonates suffering from birth asphyxia.

Authors' Contribution

Conceptualization: A

Methodology: A

Formal analysis: MI, VK

Writing and Drafting: A, MI, VK, FZ, A, LK

Review and Editing: A, MI, VK, FZ, A, LK

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



Demographic, Clinical, and Lifestyle Risk Factors Associated with Lower Gastrointestinal Bleeding: A Cross-Sectional Study at A Tertiary Care Hospital

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ABSTRACT

Gastrointestinal bleeding is classified into upper and lower types; lower GI bleeding occurs distal to the ligament of Treitz, presenting as rectal bleeding with symptoms like fatigue, pallor, or shock. **Objectives:** To assess the demographic, clinical, and lifestyle risk factors associated with lower gastrointestinal bleeding (LGIB) among patients presenting to a Tertiary Care Hospital, Hyderabad. **Methods:** This cross-sectional descriptive study was conducted from August 12, 2023, to February 11, 2024, at the Department of Gastroenterology, Liaquat University of Medical and Health Sciences, Jamshoro. A total of 105 male and female patients aged 18-70 years presenting with active rectal bleeding as their main complaint, and the duration of bleeding was not more than 6 months, were included in the study. The biodata of patients, such as age, duration of bleeding, and causes of bleeding, was collected. **Results:** The Age range of the patients in this study was 18 to 70 years, with a mean age was 42.29 ± 11.64 years. The most common cause of LGIB was internal hemorrhoids 32 (24%) followed by rectal ulcers 12 (9%), ulcerative colitis 10 (7.4%), rectal polyps 9 (6.6%), colitis 8 (5.9%), ileocecal ulcers 4 (2.9%), ileitis and colonic ulcers 3 (2.2%) in patients with Lower Gastrointestinal Bleeding. **Conclusions:** It was concluded that the most common cause of colorectal bleeding in our patients was carcinomas, while in Western countries, diverticulosis is the commonest cause, and ulcerative colitis is the most common cause in some Eastern countries. Male individuals are more commonly affected by LGIB.

INTRODUCTION

Gastrointestinal (GI) bleeding is classified into upper GI bleeding (UGIB) and lower GI bleeding (LGIB) based on the site of bleeding. Lower gastrointestinal bleeding (LGIB) is defined as bleeding distal to the ligament of Treitz and typically presents as rectal bleeding [1]. Pathologies involving the mucosa and vasculature of the gastrointestinal tract may lead to GI bleeding, which is considered a serious clinical presentation across all age groups. LGIB commonly presents as hematochezia,

melena, or occult bleeding, with associated symptoms such as pallor, fatigue, tachycardia, and in severe cases, hypovolemic shock [2]. The annual incidence of hospitalization for LGIB is approximately 36 per 100,000 populations, with even higher rates observed among the elderly [3]. Patients often present with painless hematochezia and a reduction in hematocrit values, typically without signs of orthostatic hypotension. The incidence of LGIB among adults is reported to range



between 20.5 and 27 cases per 100,000 individuals [4]. Compared to acute UGIB, patients with acute LGIB are significantly less likely to experience shock (35% versus 19%), require fewer blood transfusions (64% versus 36%), and often present with a higher hemoglobin concentration (61% versus 84%) [5]. Moreover, colonic bleeding tends to require fewer blood transfusions compared to small intestinal bleeding. The overall mortality rate associated with LGIB ranges from 2% to 4% [6]. The etiology and epidemiology of LGIB vary according to environmental factors such as lifestyle, dietary habits, prevalence of smoking, medication use, age, and life expectancy. Most Western data suggest that colonic diverticula are the most frequent source of LGIB, followed by angiodysplasias, colitis (ischemic, infectious, or inflammatory bowel disease), neoplasms, small bowel bleeding, and post-polypectomy bleeding [6-8]. A study conducted at the Department of Gastroenterology, Services Institute of Medical Sciences (SIMS) Lahore, aimed at determining the frequency of common causes of LGIB, found abnormal findings in 219 (79.06%) patients, with internal hemorrhoids (26.7%) being the most common cause, followed by rectal ulcers (9.38%), rectal polyps (6.85%), colitis (6.49%), proctitis (5.41%), ulcerative colitis (6.49%), rectal growths and ileitis (3.97% each), ileocecal ulcers (3.61%), and colonic ulcers (3.24%) [9]. Similarly, in a study conducted in South Punjab, Pakistan, ulcerative colitis emerged as the most frequent colonoscopic finding, observed in 20 patients (13.3%). This was followed by hemorrhoids in 19 patients (12.7%), anitis in 17 patients (11.3%), suspected carcinoma of the colon in 16 patients (10.7%), and solitary rectal ulcer in 12 patients (8.0%). Notably, normal colonoscopic findings were reported in 50 patients (33.3%) [10].

While extensive data are available from Western countries, there remains a paucity of local research from South and Eastern Asia, where differences in climate, diet, lifestyle, and socioeconomic factors could influence the etiology of LGIB. This study seeks to bridge this knowledge gap and provide region-specific insights into the patterns of LGIB. This study aims to assess the demographic, clinical, and lifestyle risk factors associated with lower gastrointestinal bleeding (LGIB) among patients presenting to a tertiary care hospital, Hyderabad.

METHODS

This cross-sectional descriptive study was conducted at the Department of Gastroenterology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, over six months from August 12, 2023, to February 11, 2024. A total of 135 patients were included using a non-probability consecutive sampling technique. Patients aged 18-70 years presenting with active rectal bleeding for less than

six months and willing to provide informed consent were enrolled. Patients with bleeding due to trauma, suspected upper GI source, known infectious diarrhea, inflammatory bowel disease, GI malignancy, or advanced systemic diseases were excluded. The sample size was calculated by the WHO Open Epi sample size calculator by taking the prevalence of rectal ulcers, 7.3% [9], as a cause of LGIB, margin of error = 5%, confidence interval = 95%. The study was approved by the College of Physicians and Surgeons vide letter no. CPSP/REU/GAS-2022-164-1300. All eligible patients presenting to the Emergency or Outpatient Department were evaluated. After obtaining informed consent, demographic details such as age, gender, and BMI were noted. Comorbidities included diabetes mellitus, hypertension, and each was recorded as present or absent. Clinical history factors included NSAID use, anticoagulant use, constipation, diarrhea, previous GI bleeding, anemia, family history, surgery and lifestyle/dietary variables e.g., low fiber diet, red meat intake, water intake, smoking, alcohol use, sedentary lifestyle and duration of bleeding was treated as a continuous variable (mean $\pm$ SD in months). Colonoscopic examination was performed using an Olympus EXERA II CF-H180 AL/I colonoscope after bowel preparation with polyethylene glycol (PEG-3350). In cases of inadequate preparation, repeat cleansing with the same regimen was administered. The causes of lower gastrointestinal bleeding were determined based on colonoscopic findings and were grouped into: Vascular causes (e.g., internal hemorrhoids), Inflammatory/ulcerative conditions (e.g., rectal ulcers, colitis, ulcerative colitis) and Neoplastic/others (e.g., rectal polyps, unspecified causes). Data were analyzed using SPSS version 26.0. Descriptive statistics were applied to summarize demographic, clinical, and lifestyle variables. Categorical variables were presented as frequencies and percentages, while continuous variables (e.g., duration of bleeding) were expressed as mean $\pm$ standard deviation (SD).

RESULTS

The majority were male (77.1%) and from urban areas (72.4%). Age distribution showed that most patients were middle-aged to elderly, with 39% between 46-60 years and 22.9% above 60 years. Regarding nutritional status, 41.9% were overweight and 16.2% were obese, while only 5.7% were underweight. The mean duration of bleeding was 3.8 ± 1.7 months. Comorbid conditions were prevalent, with 45.7% of patients having diabetes mellitus and 35.2% diagnosed with hypertension (Table 1).

Table 1: Demographic and Clinical Characteristics of Patients with LGIB(n=105)

Variables	Frequency (%)
Gender	
Male	81(77.1%)
Female	24 (22.9%)
Age (Years)	
18–30	12 (11.4%)
31–45	28 (26.7%)
46–60	41 (39.0%)
>60	24 (22.9%)
Residential Status	
Urban	76 (72.4%)
Rural	29 (27.6%)
BMI (kg/m²)	
<18.5 (Underweight)	6 (5.7%)
18.5–24.9 (Normal)	38 (36.2%)
25–29.9 (Overweight)	44 (41.9%)
≥30 (Obese)	17 (16.2%)
Duration of the Bleeding	3.8 ± 1.7 months
Diabetes Mellitus	
Present	48 (45.7%)
Absent	57 (54.3%)
Hypertension	
Present	37 (35.2%)
Absent	68 (64.8%)

In terms of the underlying causes of LGIB, vascular causes were most common, with internal hemorrhoids identified in 30.5% (n=32) of cases. Inflammatory and ulcerative conditions collectively accounted for 50.5% of cases, including rectal ulcers (21.0%), colitis (7.6%), ulcerative colitis (9.5%), proctitis (4.8%), ileitis (2.9%), ileocecal ulcers (3.8%), and colonic ulcers (2.9%). Neoplastic and other unspecified causes contributed to 17.2% of the cases, with rectal polyps and other or unspecified sources each making up 8.6% (n=9) of the total (Table 2).

Table 2: Causes of Lower Gastrointestinal Bleeding in Study Participants

LGIB Causes	Frequency (%)
Vascular Causes	
Internal Hemorrhoids	32 (30.5%)
Inflammatory / Ulcerative	
Rectal Ulcers	22 (21.0%)
Ileocecal Ulcers	4 (3.8%)
Colonic Ulcers	3 (2.9%)
Colitis	8 (7.6%)
Proctitis	5 (4.8%)
Ulcerative Colitis	10 (9.5%)
Ileitis	3 (2.9%)

Neoplastic / Others	
Rectal Polyps	9 (8.6%)
Others / Unspecified	9 (8.6%)

Among the 105 patients with lower gastrointestinal bleeding (LGIB), clinical history revealed that 43.8% had a history of NSAID use, while 18.1% were on anticoagulant or antiplatelet therapy. A history of constipation was present in 39%, and 22.9% reported chronic diarrhea. Previous episodes of GI bleeding were noted in 25.7%, 13.3% had a family history of colorectal disease, and 7.6% reported undergoing colorectal surgery. Additionally, 53.3% of patients were anemic at presentation (Table 3).

Table 3: Clinical History of Patients with LGIB(n=105)

Clinical History Variables	Frequency (%)
NSAID Use	46 (43.8%)
Anticoagulant/Antiplatelet Use	19 (18.1%)
History of Constipation	41 (39.0%)
History of Chronic Diarrhea	24 (22.9%)
Previous GI Bleeding	27 (25.7%)
Family History of Colorectal Disease	14 (13.3%)
History of Colorectal Surgery	8 (7.6%)
Anemia at Presentation	56 (53.3%)

In terms of dietary and lifestyle factors, 58.1% consumed a low-fiber diet, 41.0% had a high red meat intake, and 46.7% reported inadequate water consumption. A sedentary lifestyle was observed in 56.2%, 30.5% were smokers, and 16.2% reported alcohol use. These findings highlight the presence of modifiable risk factors contributing to LGIB.

Table 4: Dietary and Lifestyle Factors of Patients with LGIB (n=105)

Lifestyle / Dietary Factor	Frequency (%)
Low Fiber Diet	61 (58.1%)
High Red Meat Intake	43 (41.0%)
Inadequate Water Intake (<1.5L/day)	49 (46.7%)
Sedentary Lifestyle	59 (56.2%)
Smoking	32 (30.5%)
Alcohol Use	17 (16.2%)

DISCUSSION

The current study provides valuable information about the patterns and potential etiological contributors to LGIB in a Pakistani urban-rural mixed population. The predominance of males (77.1%) aligns with several local and international studies, where LGIB has been observed more frequently in male than female, potentially due to greater exposure to risk factors such as smoking, alcohol use, and NSAID consumption [11]. Comorbid conditions were common, with 45.7% of participants diagnosed with diabetes mellitus and 35.2% with hypertension. These findings are comparable to a study conducted in Pakistan, which has

highlighted the role of vascular fragility and mucosal ischemia in the elderly and comorbid populations as significant contributors to gastrointestinal bleeding [12]. The mean disease duration of 3.8 ± 1.7 months suggests a significant proportion of patients experienced recurrent or chronic Lower GI bleeding episodes, indicating delayed presentation or under diagnosis, in healthcare settings across the globe [13]. Regarding etiology, internal hemorrhoids (30.5%) were the most frequent cause, followed by rectal ulcers (21.0%) and ulcerative colitis (9.5%). These results align with previous studies from Pakistan, where hemorrhoids and ulcerative lesions predominate in LGIB etiologies [14]. Inflammatory and ulcerative conditions collectively accounted for over half of the cases (50.5%), underscoring the growing burden of inflammatory bowel disease (IBD) in Asia, particularly ulcerative colitis, which is increasingly diagnosed among urban dwellers due to dietary westernization and environmental factors [15, 16]. Neoplastic causes, such as rectal polyps (8.6%) and unspecified causes (8.6%), also reflect a critical diagnostic domain, especially given the rising incidence of colorectal malignancies in younger South Asian populations [17]. Clinical history data revealed substantial modifiable risk factors. NSAID usage was reported by 43.8% of patients, reaffirming findings from international studies indicating a strong association between NSAID consumption and gastrointestinal mucosal injury leading to bleeding [18]. Dietary and lifestyle factors further illustrated the modifiability of LGIB risk. A low-fiber diet (58.1%) and high red meat intake (41.0%) were frequently reported, which are both established contributors to colonic diverticulosis, hemorrhoids, and colorectal carcinogenesis [19]. Tobacco use (30.5%) and alcohol consumption (16.2%) were also significant, both of which have been implicated in mucosal damage and inflammatory responses within the bowel [20]. Collectively, the study reinforces the multifactorial nature of LGIB, with vascular, inflammatory, neoplastic, pharmacological, and behavioural factors all playing contributory roles. There is a compelling need for early screening of high-risk individuals, especially those with anemia, chronic constipation, or NSAID use.

This study was limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings. Additionally, reliance on self-reported lifestyle and dietary factors may have introduced recall bias. Future studies should include larger, multi-center populations with objective assessment of risk factors and standardized diagnostic protocols to better clarify etiological patterns of LGIB.

CONCLUSIONS

It was concluded that lower gastrointestinal bleeding (LGIB) was more common among males, overweight and urban residents, with internal hemorrhoids as the leading cause. Common risk factors included NSAID use, low-fiber diet, sedentary lifestyle, and comorbidities like diabetes and hypertension. Early intervention and addressing modifiable lifestyle factors are crucial for better patient outcomes.

Authors' Contribution

Conceptualization: QJ

Methodology: QJ, NLS, AA, SAJ, SF

Formal analysis: NLS, MK, SF

Writing and Drafting: NLS, AA, IF

Review and Editing: QJ, NLS, AA, SAJ, MK, SF, IF

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



Beyond the Ridge: Exploring Fingerprints to Determine the Predominant Pattern in the Pakistani Population

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ABSTRACT

Fingerprint patterns are widely used in forensic science due to their uniqueness and permanence. While pattern types like loops, whorls, and arches are well studied, fingerprint symmetry and its association with genetic and demographic factors remain underexplored in the Pakistani population. **Objectives:** To assess the distribution of fingerprint patterns and evaluate their symmetry by gender, age, ethnicity, region, hand dominance, and parental consanguinity. **Methods:** A cross-sectional study was conducted at Sahara Medical College, Narowal, from June to November 2021. Fingerprints from 110 participants were collected using the rolled ink method and categorized using the Henry Classification System. Fingerprint symmetry was evaluated by comparing matching fingers on both hands. Chi-square tests and Cramér's V were used to analyze associations. **Results:** Loops were the most frequent pattern, followed by whorls and arches. Symmetry was present in 45.5% of participants, while 54.5% were asymmetrical. Symmetry was significantly associated with gender ($p=0.037$), dominant hand ($p=0.001$), consanguinity ($p<0.001$), age group ($p=0.003$), region ($p<0.001$), and ethnicity ($p<0.001$). No significant link was found between symmetry and pattern type. **Conclusions:** It was concluded that fingerprint symmetry is influenced by several demographic and genetic factors. These findings support the need for population-specific biometric research and may contribute to forensic, genetic, and anthropological applications.

INTRODUCTION

Fingerprints are a fundamental tool in personal identification due to their unique and permanent ridge patterns formed during fetal development and maintained throughout life [1]. Among biometric markers, they remain one of the most accessible and cost-effective, especially in resource-limited settings [2, 3]. Dermatoglyphics, the scientific study of fingerprint patterns, now extends beyond forensics into medical, genetic, and anthropological research [4]. Patterns such as loops, whorls, and arches are shaped by both genetic and

environmental factors [5, 6]. Fingerprint symmetry, defined by the similarity of ridge patterns on corresponding fingers, may reflect developmental and genetic stability, offering an additional layer of analysis [7]. Although previous studies have explored fingerprint distributions based on gender, ethnicity, and geography [8, 9], symmetry remains under-investigated, especially within diverse populations such as Pakistan. Existing literature tends to emphasize pattern prevalence and its link with blood group or gender, with little focus on bilateral fingerprint



symmetry.

Understanding how these factors influence symmetry could improve the accuracy of biometric systems and support forensic and anthropological applications. Given the country's ethnic diversity, developing population-specific fingerprint databases is essential for both scientific and legal contexts. This study aimed to examine both the distribution and symmetry of fingerprint patterns about demographic (age, gender, region, ethnicity) and genetic variables (dominant hand, parental consanguinity) in the Pakistani population.

METHODS

This cross-sectional observational study was conducted at Sahara Medical College, Narowal, from June 6 to November 6, 2021, to examine the distribution and symmetry of fingerprint patterns in the Pakistani population. Ethical approval was obtained from the Institutional Review Board (Ref: 11/IRB/SMC). Informed consent was obtained from all participants, with confidentiality and anonymity maintained throughout. A rolled ink method was used to collect fingerprints from all ten fingers, following standard procedures to ensure clear and complete ridge impressions. This technique is widely used in dermatoglyphic studies for its clarity, consistency, and affordability. The cross-sectional design allowed simultaneous assessment of fingerprint types (loop, whorl, arch) to demographic and genetic variables such as gender, region, ethnicity, and handedness, aligning with methods commonly used in forensic anthropology and population genetics. The sample size was determined based on the chi-square test requirements. Given the study's aim to explore associations across multiple subgroups, it was essential to ensure adequate representation across categories like gender, region, ethnicity, and dominant hand. Ultimately, 110 participants were enrolled using non-probability convenience sampling. The sample size was chosen based on Cohen's criteria for chi-square analysis, which recommends approximately 88 participants for detecting a medium effect size ($w=0.3$) with 80% power at a 5% significance level across 4 degrees of freedom. To allow subgroup analyses across key demographic variables such as ethnicity and region (each with four categories), a slightly larger sample was targeted. This approach is supported by dermatoglyphic literature, including the study by Singh et al., [10], which conducted similar comparisons using group sizes of around 120 per ethnic category. In our study, the final sample provided adequate distribution across all subgroups, and all Chi-square tests met the expected cell frequency criteria (i.e., no cell <5), validating the appropriateness of the sample for categorical analysis. Participants included in the study were Pakistani nationals aged 15 years or older, of either gender, who provided written informed consent and had no visible hand deformities or skin disorders that could

interfere with fingerprint collection. Individuals were excluded if they had finger injuries, scars, congenital abnormalities, or any dermatological conditions that could obscure dermal ridge patterns. Additionally, participants with a known history of dermatological disorders affecting fingerprints, or those who refused or were unable to provide informed consent, were not included in the study. Data collection was conducted in a controlled indoor environment with adequate lighting. After completing a brief demographic questionnaire, each participant's fingerprints were collected using the ink-roll method. The impressions were examined visually using magnification and categorized into three primary pattern types based on the Henry Classification System: loop, whorl, or arch. Demographic data included age, gender, region of origin (KPK, Punjab, Sindh, Balochistan), ethnicity (Pashtun, Punjabi, Sindhi, Baloch), dominant hand, and parental consanguinity status. Although no direct genetic or developmental tests were conducted, variables such as parental consanguinity and ethnicity were included as indirect indicators of potential genetic influences. These factors were used to explore the possible association between fingerprint symmetry and underlying genetic stability within the study population. Fingerprint symmetry was operationally defined as the presence of identical fingerprint patterns (loop, whorl, or arch) on matching finger pairs of both hands. Each participant's right and left-hand fingerprints were examined finger-by-finger from thumb to little finger. If all five corresponding fingers showed the same pattern type, the participant was categorized as "symmetrical." Any mismatch in pattern type between even one pair of corresponding fingers led to classification as "asymmetrical." Dependent Variable: Fingerprint symmetry (Symmetrical / Asymmetrical). Independent Variables: Gender, age group, region, ethnicity, dominant hand, parental consanguinity, fingerprint patterns of right and left hands. To ensure inter-observer reliability, two trained evaluators independently classified all fingerprints. In cases of disagreement, a third examiner adjudicated the final pattern type. The level of agreement between the two evaluators was quantified using Cohen's kappa statistic, yielding a value of 0.87, which indicates a high level of inter-rater reliability. Content validity was maintained by adhering to established dermatoglyphic analysis protocols. Before formal data collection, a pilot run was conducted on a sample of 10 participants to evaluate the clarity of instructions, quality of fingerprint impressions, and internal consistency of classification procedures. Data were entered and analyzed using IBM SPSS Statistics version 23.0. Descriptive statistics (frequencies and percentages) summarized all categorical variables, including gender, age group, region, ethnicity, dominant hand, parental consanguinity, fingerprint pattern, and symmetry status. Associations between fingerprint symmetry and independent variables were assessed using Pearson's Chi-square test,

appropriate for categorical data. Each variable was analyzed separately against symmetry status. For variables with multiple categories (e.g., region, ethnicity), SPSS adjusted for degrees of freedom automatically. For significant associations, Cramér's V was used to interpret strength (0.1–0.2=weak, 0.2–0.4=moderate, >0.4=strong). Post hoc standardized residuals identified the most contributing cells. A p -value < 0.050 was considered statistically significant.

RESULTS

The present study included 110 participants, with a nearly equal distribution of male (50.9%) and female (49.1%). The largest age group comprised individuals younger than 20 years (32.7%), followed by those aged 21–30 (22.7%), 31–40 (20.9%), and over 40 (23.6%). Geographically, the majority of participants were from Khyber Pakhtunkhwa (30.9%), followed by Punjab (27.3%), Sindh (24.5%), and Balochistan (17.3%). In terms of ethnicity, Pashtuns made up the highest proportion (30.9%), followed closely by Punjabis (27.3%), Sindhis (24.5%), and Baloch (17.3%). Left-handed individuals (51.8%) slightly outnumbered right-handed ones (48.2%). A little over half (51.8%) of the participants reported parental consanguinity (Table 1).

Table 1: Demographic and Genetic Characteristics of Participants (n=110)

Variables	Category	Frequency (%)
Gender	Male	56 (50.9%)
	Female	54 (49.1%)
Age Group	<20	36 (32.7%)
	21–30	25 (22.7%)
	31–40	23 (20.9%)
	>40	26 (23.6%)
Region	KPK	34 (30.9%)
	Punjab	30 (27.3%)
	Sindh	27 (24.5%)
	Balochistan	19 (17.3%)
Ethnicity	Pashtun	34 (30.9%)
	Punjabi	30 (27.3%)
	Sindhi	27 (24.5%)
	Baloch	19 (17.3%)
Dominant Hand	Right	53 (48.2%)
	Left	57 (51.8%)
Parental Consanguinity	Yes	57 (51.8%)
	No	53 (48.2%)

Fingerprint pattern analysis revealed that whorls were the most frequent type overall, appearing 79 times across both hands, followed by arches (74) and loops (67). When broken down by hand, right hands had slightly more whorls (40) and loops (35), whereas the left hand showed more arches (39) (Table 2).

Table 2: Frequency of Fingerprint Patterns by Hand (n=110)

Pattern Type	Right Hand	Left Hand	Total Frequency
Arch	35	39	74
Loop	35	32	67
Whorl	40	39	79

A gender-wise comparison of fingerprint patterns showed no statistically significant association for either hand. In the right hand, males and females displayed a balanced distribution of loops, whorls, and arches ($p=0.645$). Similarly, for the left hand, while female had slightly more arches and male had more loops and whorls, the association remained non-significant ($p=0.197$) (Table 3).

Table 3: Comparative Fingerprint Patterns by Gender (n=110)

Groups	Loop	Whorl	Arch	Pearson Chi-square	p-value (2-sided)
Right Hand					
Male (n=56)	19	18	19	0.878	0.645
Female (n=54)	16	22	16		
Left Hand					
Male (n=56)	20	20	16	3.247	0.197
Female (n=54)	12	19	23		

Symmetry analysis indicated that 45.5% of participants had symmetrical fingerprint patterns, while 54.5% had asymmetrical patterns. The loop was the most common pattern observed in symmetrical cases, whereas asymmetrical patterns displayed a more mixed distribution (Table 4).

Table 4: Fingerprint Pattern Symmetry Summary (n=110)

Symmetry Status	Frequency	Most Common Pattern
Symmetrical	50	Loop
Asymmetrical	60	Mixed

Fingerprint symmetry was significantly associated with several demographic and genetic variables. Females had more symmetrical patterns than males ($p=0.037$; Cramér's $V=0.199$, 95% CI: 0.070–0.329), while right-handed individuals showed greater symmetry compared to left-handed ones ($p=0.001$; Cramér's $V=0.326$, 95% CI: 0.201–0.450). Parental consanguinity had a strong association with symmetry ($p<0.001$; Cramér's $V=0.478$), and older age groups, particularly those over 40, showed higher symmetry ($p=0.003$; Cramér's $V=0.357$, 95% CI: 0.234–0.481). The strongest associations were observed for region and ethnicity ($p<0.001$), where all Khyber Pakhtunkhwa residents and Pashtuns exhibited complete symmetry, while Sindhi and Baloch participants were entirely asymmetrical (Cramér's $V=0.852$; 95% CI: 0.783–0.921). These findings highlight the influence of genetic and regional factors on fingerprint symmetry (Table 5).

Table 5: Association of Fingerprint Symmetry with Demographic and Genetic Variables (n=110)

Variables	Category	Symmetrical	Asymmetrical	p-value	Cramér's V	95% CI for Cramér's V
Gender	Male	20	36	0.037	0.199	0.070–0.329
	Female	30	24			
Dominant Hand	Right	33	20	0.001	0.326	0.201–0.450
	Left	17	40			
Parental Consanguinity	Yes	39	18	<0.001	0.478	0.340–0.617 (est.) ¹
	No	11	42			
Age Group	<20	13	23	0.003	0.357	0.234 – 0.481
	21–30	10	15			
	31–40	7	16			
	>40	20	6			
Regions	KPK	34	0	<0.001	0.852	0.783–0.921
	Punjab	16	14			
	Sindh	0	27			
	Balochistan	0	19			
Ethnicity	Pashtun	34	0	<0.001	0.852	0.783–0.921
	Punjabi	16	14			
	Sindhi	0	27			
	Baloch	0	19			

¹Estimated conservatively based on the observed test statistic using the standard error approximation

DISCUSSION

The present study aimed to investigate the association of fingerprint symmetry with various demographic and genetic variables, including gender, age group, ethnicity, region, dominant hand, and parental consanguinity. The findings indicated significant associations in several domains, highlighting the multifactorial influences shaping dermatoglyphic patterns. In this study, loop patterns were found to be the most common, followed by whorls and arches. This aligns with the findings of Iqbal *et al.*, who reported loop dominance (54.6%) among medical students in Peshawar, with no significant gender association [11]. Similarly, Rastogi *et al.*, also confirmed loop predominance in both genders among Indian healthcare workers, further supporting the notion of loops as the most stable and genetically inherited pattern across populations [12]. Gender-wise comparison in our study revealed that males exhibited more asymmetry than females ($p=0.037$), which is comparable to findings from Aziz *et al.*, who also reported gender-based differences in fingerprint morphology in their cross-sectional hospital-based analysis [13]. In contrast, studies by Zeeshan *et al.*, in Sialkot and Buzdar *et al.*, found no significant gender-based variation in fingerprint types, underscoring population-specific differences in dermatoglyphic expression [14, 15]. A strong and highly significant association was found between fingerprint symmetry and dominant hand ($p=0.001$), with left-handed individuals displaying more asymmetry. This result echoes the findings of Rivaldería *et al.*, who demonstrated significant lateralization effects in

fingerprint patterns related to hand dominance, particularly in one-delta and two-delta types [16]. Another notable association was with parental consanguinity ($p<0.001$), where individuals from consanguineous unions showed higher fingerprint symmetry. This supports the idea that genetic factors may influence fingerprint symmetry. While we did not directly assess molecular or chromosomal markers of genetic stability, the inclusion of consanguinity and ethnicity served as reasonable proxies for hereditary influence in this population-based context. Gavrilova *et al.*, and Al Habsi *et al.*, also observed statistically significant links between genetically inherited traits and fingerprint morphology in populations with high rates of consanguineous marriages [17, 18]. The age group variable was also statistically associated with fingerprint symmetry ($p=0.003$). Interestingly, participants above 40 years had the highest rates of symmetry. While most fingerprint studies focus on younger age groups, our finding suggests potential developmental or adaptive influences that warrant further longitudinal research. Similar age-related considerations were reported by Patra *et al.*, who found shifting trends in dermatoglyphics across age categories [19]. When analyzing ethnicity and region, the most significant associations ($p<0.001$) were observed. Khyber Pakhtunkhwa (KPK) residents displayed exclusively symmetrical fingerprints, whereas Sindhi and Baloch individuals demonstrated complete asymmetry. While these regional and ethnic trends were notable, they must be interpreted with caution. The use of convenience

sampling and unequal subgroup sizes may have introduced selection bias, limiting the generalizability of these findings. The observed extremes in symmetry and asymmetry may reflect sample-specific patterns rather than population-wide traits. This limitation has been acknowledged in our study. These findings mirror those of Singh *et al.*, who identified regional variability in fingerprint types across ethnic groups in South Asia, highlighting the influence of both environmental and hereditary factors [20]. Moreover, these regional results are consistent with the multicultural data presented by Rane and Bhadade, where multimodal biometric systems showed accuracy differences based on ethnic fingerprint texture and vein patterns, emphasizing the importance of population-specific biometric databases for effective forensic use [21]. The overall findings also validate the theoretical claims made by Shah, who emphasized the importance of integrating forensic education and population-specific dermatoglyphic data in Pakistan to strengthen biometric and criminal identification systems [22]. Furthermore, our findings expand on the work of Al Habsi *et al.*, who found significant relationships between blood group and fingerprint types in the Omani population, although we did not evaluate blood groups. Our method of analyzing fingerprint symmetry opens additional avenues for research in biometric linkage [18]. The absence of statistically significant differences between right and left hand fingerprint types in our study aligns with the results of international studies, including those by Aziz *et al.*, and Singh *et al.*, suggesting that while certain demographic and genetic factors influence fingerprint symmetry, others like hand pattern (loop, arch, whorl) may not directly correlate with symmetry alone [13, 20].

This study was limited by the use of convenience sampling and unequal subgroup distribution, which may introduce selection bias and limit the generalizability of the findings. Additionally, the lack of molecular or genetic marker analysis restricts deeper understanding of the biological basis of fingerprint symmetry. Future studies should incorporate larger, representative samples and include genetic or molecular analyses to better explore the determinants of fingerprint symmetry.

CONCLUSIONS

It was concluded that fingerprint symmetry is significantly influenced by demographic and genetic factors, including gender, age group, region, ethnicity, dominant hand, and parental consanguinity. In contrast, fingerprint pattern types (loop, whorl, arch) showed no significant association with symmetry. Symmetry was more common in females, right-handed individuals, and those with consanguineous parentage. It was also prevalent among participants from Khyber Pakhtunkhwa and Pashtun ethnicity, while

asymmetry was more frequent in Sindhi and Baloch groups. These findings highlight the role of both hereditary and environmental influences in dermatoglyphic traits. Our study supports the growing body of evidence emphasizing the influence of gender, genetics, consanguinity, and ethnicity on dermatoglyphic patterns. These findings have practical implications for forensic science, especially in developing region-specific biometric databases and refining identification techniques.

Authors' Contribution

Conceptualization: RA

Methodology: RA, DZ, SM, ZAB, TT

Formal analysis: RA, DZ, SS, ZAB, TT

Writing and Drafting: RA, DZ, SS, SM, ZAB, TT

Review and Editing: RA, DZ, SS, SM, ZAB, TT

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



Assessing the Outcomes of Combined Surgical Techniques in Spondylolisthesis: A One Year Retrospective Analysis

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ABSTRACT

Surgical intervention is the treatment of choice in cases of severe pain in spondylolisthesis that doesn't respond to conservative measures. Decompression and fusion surgery is the gold standard surgical procedure for treating lumbar spondylolisthesis with foraminal stenosis, and it can be carried out in a variety of ways. **Objectives:** To investigate the outcomes of combined surgical techniques, including facetectomy along with foraminotomy, to secure the normal alignment of the lumbar spine in patients with spondylolisthesis. **Methods:** This retrospective cross-sectional study included the records of fifty-two patients who underwent facetectomy along with foraminotomy for spondylolisthesis from January 2022 to March 2023. Assessment of demographic information, clinical presentations, and outcomes was conducted. Descriptive statistics were analyzed via IBM SPSS software version 26. **Results:** The Mean age of the participants was 42 ± 15 years. The majority were female, 31(59%), as compared to male. The most frequent level which demonstrated listhesis was L4-L5 23 (45%), followed by L5, S1 18 (34%) and L3, L4 11(21%). In Type 1 listhesis, Full correction was achieved in 100% of cases, while in Type 2 listhesis, 80% of cases achieved correction. Further significant association ($p \leq 0.05$) was found among post-surgical outcomes including pain, functional disability and neurological status. **Conclusions:** It was concluded that facetectomy combined with foraminotomy is associated with improved clinical outcomes in the management of spondylolisthesis, particularly in Type 1 cases. The procedure was linked to pain relief, enhanced functional ability, and improved neurological status. Further longitudinal studies are required to assess long-term efficacy and safety.

INTRODUCTION

Spondylolisthesis, derived from the Greek roots "spondyl" (for vertebrae) and "olisthesis" (for dislocation or slippage), is a clinical entity characterised by the slipping of one vertebra forward over the one below it [1, 2]. Childhood spondylolisthesis is known to occur in 4% and 6% of the time, with the majority of cases being isthmic and occurring between L5 and S1 [3]. Adult incidence rises to 5% to 10%, becoming mostly degenerative, more prevalent in the female population, and commonly affects the L4 to L5 region, then the L5 to S1 region [4]. According to the Myerding classification, the caudal vertebrae represent the amount of vertebral slippage on an X-ray. The Myerding classification of spondylolisthesis has five levels. Grade I

slippage is less than 25%, Grade II slippage ranges between 26% to 50%, Grade III slippage (51% - 75%), Grade IV slippage (76% - 100%), and Grade V slippage is over 100% and is known as spondyloptosis [5]. A prevalent degenerative condition that affects people with low-grade spondylolisthesis at a rate of 10% to 50% is lumbar facet cysts [6]. Surgical intervention is the treatment of choice in cases of severe pain that doesn't respond to conservative measures [7]. Early treatment for Degenerative Spondylolisthesis involved decompression, reduction, fixation, and fusion, much like dysplastic spondylolisthesis. With the advent of spinal instrumentation and the identification of DS as a distinct condition, surgical



treatment advanced mostly in the second half of the 20th century [8]. Decompression and fusion surgery is the gold standard surgical procedure for treating lumbar spondylolisthesis with foraminal stenosis, and it can be carried out in a variety of ways [9]. Surgery for partial facetectomy with or without fusion is still debatable. Fusion improves results in situations of preoperative instability or spondylolisthesis, prevents segmental instability, and lessens adjacent segment degeneration [10]. However, Literature have also reported the destabilizing effects of Facetectomy on the spine [11]. Despite decompression and fusion being the standard treatment for lumbar spondylolisthesis, the role of additional procedures such as partial facetectomy with foraminotomy remains controversial due to conflicting evidence regarding spinal stability and outcomes. Existing literature shows inconsistent findings on whether facetectomy improves or compromises postoperative stability, particularly in patients with foraminal stenosis. This study aims to assess the outcomes of combined surgical techniques, including facetectomy along with foraminotomy, to secure the normal alignment of the lumbar spine in patients with spondylolisthesis.

METHODS

This study conducted a retrospective cross-sectional analysis. The records and data were gathered from January 2022 to March 2023 at Rizwan Medical Center, Peshawar. Ethical Approval was obtained from the Institutional Review Board of the Hospital (Ref no: 305/RMC&GH), and informed consent was obtained from all patients or their legal guardians before surgery and data collection. The study population consisted of fifty-two patients who underwent surgical intervention from January 2022 to March 2023. Inclusion criteria encompassed patients who have undergone facetectomy along with foraminotomy for spondylolisthesis diagnosed by subjective and radiological findings of plain X-ray. Patients with spondylolisthesis due to post-traumatic, post-malignant, osteoporotic, or congenital etiologies were not included in the study. Data were gathered from medical records, surgical logs, and radiological reports of patients who met the inclusion criteria. The demographic information, including age, gender, and relevant medical history, along with preoperative evaluation, including clinical evaluations, and radiological imaging (e.g., X-rays, CT scans, and MRI scans), was gathered. The patient was placed in a prone position on the operating table, and general anesthesia was administered. An incision was made over the affected lumbar area. Through the dissection of soft tissues, the surgical team gained access to the affected vertebrae and their surrounding structures. Once access was

established, facetectomies were performed, according to the specific case and level of spondylolisthesis. This involved the removal of the facet joint, which articulates with adjacent vertebrae, facilitating access to the spinal canal. Following this, a foraminotomy was performed to enlarge the neural foramen, the passageway through which spinal nerves exit the spine. The incision was then closed, often utilizing absorbable sutures or staples. Postoperatively, patients were closely monitored in the recovery area before being transferred to a standard hospital room. Physical therapy and rehabilitation commenced to aid the recovery process, and follow-up visits were scheduled. Postoperative clinical outcomes were assessed using standardized measures such as the Visual Analogue Scale (VAS) for pain intensity, the Oswestry disability index for functional disability scores, and neurological status. These assessments were performed at specified follow-up intervals post-surgery of 8 months. Any perioperative and postoperative complications were documented, including infection, neurological deficits, hardware failure, and wound-related issues. Statistical analysis was done on SPSS version 26.0. Descriptive statistics were reported to summarize the demographic and clinical outcomes data. Frequency and percentages were used to analyze categorical variables, while continuous variables were assessed through mean and standard deviation. A paired sample t-test was used to evaluate the difference between pre- and post-values. A p-value of ≤ 0.050 was considered statistically significant.

RESULTS

The study shows the demographics of patients. A total of 52 individuals were enrolled in the study, ranging in age from 30-54 years, with a mean age of 42 ± 15 years. The sample consisted of 21(41%) male and 31(59%) female in the study population. 4 (7%) of patients presented after surgical management for laminectomy and discectomy. 3 (6%) of patients presented with post-discitis. Degenerative listhesis was the most common clinical presentation, accounting for 17 (33%) of cases. 8 (15%) of patients exhibited a pars defect as part of their clinical presentation (Table 1).

Table 1: Patient characteristics of enrolled participants

Patient Characteristics	Categories	Frequency (%)
Gender	Male	21(41%)
	Female	31(59%)
Age (Years)	Age Range (30-54)	Mean age 42 ± 15 Years
Post-surgical Patients Undergoing Laminectomy and Discectomy	Laminectomy Post-Discitis	4 (7%)
	Discectomy Post-Discitis	3 (6%)

Clinical Presentation	Degenerative listhesis	17(33%)
	Pars defect	8(15%)

The most frequent level which demonstrated listhesis was L4-L5 23 (45%), followed by L5, S1 18 (34%) and L3, L4 11 (21%)(Table 2).

Table 2: Level of Listhesis

Level of Listhesis	Frequency (%)
L4-L5	23(44.2%)
L5-S1	18(34.6%)
L3-L4	11(21.2)

The Sapiro-Wilk test was applied to test for normal distribution. The current study found that the dataset was normally distributed, as its significance value was ($p>0.05$) (Table 3).

Table 3: Shapiro-Wilk Test

Sapiro-Wilk Test	Statistic	Sig
Pain	0.962	0.16
Functional Disability	0.971	0.11
Neurological Status	0.917	0.09

The outcomes of the surgical procedure varied based on the type of spondylolisthesis: In Type 1 listhesis, Full correction was achieved in 100% of cases, while in Type 2 listhesis, 80% of cases achieved correction. Residual listhesis was observed in 10% of the cases of Type II, and 30% of cases were of Type 3 listhesis. Post-operative outcomes are summarized in this study. A significant reduction ($p=0.020$) in pain scores was observed with a mean score from (mean $\pm$ SD (7.8 ± 1.1)) to (3.2 ± 0.9)) in the study population following surgery with 39 (75%) of patients reporting a decrease in pain scores after the procedure, while 8 (15%) of patients experienced no significant change in pain scores and 5 (10%) of patients reported an increase in pain scores post-surgery. After assessing the functional ability of patients, the results showed that 31 (60%) of patients showed a statistically significant functional improvement ($p=0.050$) with a mean score ranged from 62.5 ± 7.3 to 36.4 ± 6.5 in functional disability scores, while 13 (25%) of patients demonstrated no change in functional disability scores. However, 8 (15%) of patients experienced moderate improvement in functional disability scores. The study also evaluated changes in neurological status following the surgical intervention. 44 (85%) of patients showed statistically improved neurological functioning ($p=0.050$) with a mean score ranged from 4.3 ± 1.5 to 8.2 ± 1.0 in neurological status post-surgery while 6(12%) of patients exhibited a moderate improvement in neurological status and 2 (3%) of patients experienced no significant change in neurological status (Table 4).

Table 4: Outcome Measure Score

Outcome Measure	Categories	n (%)	Pre-operative (mean $\pm$ SD)	Post-operative (mean $\pm$ SD)	p-Value
Pain Scores	Significantly Improved	39(75%)	7.8 ± 1.1	36.4 ± 6.5	0.020
	No Change	8(15%)			
	Worsened	5(10%)			
Functional Disability	Significantly Improved	31(60%)	62.5 ± 7.3	3.2 ± 0.9	0.010
	No Change	13(25%)			
	Moderate Improvement	8(15%)			
Neurological Status	Significantly Improved	44(85%)	4.3 ± 1.5	8.2 ± 1.0	0.050
	No Change	2(3%)			
	Moderate Improvement	6(12%)			

Foot drop was observed in 1 patient (2%) while Wrong screw placement was noted in 3 cases (5%) and Tears were observed in 1 case (2%). Wound infection was documented in 1 case (2%)(Table 5).

Table 5: Complications of the Procedure

Complications	Frequency (%)
Footdrop	1(2%)
Wrong Screw Placement	3(5%)
Tears	1(2%)
Wound Infection	1(2%)

DISCUSSION

The findings of this study provide valuable insights into the clinical outcomes of combined surgical intervention for spondylolisthesis in a cohort of 52 patients at Afridi Medical Complex, Peshawar. Congenital dysplasia, excessive stretch, traumatic injury and other etiologies of improper musculoskeletal attachment between adjacent vertebral bodies are the causes of lumbar spondylolisthesis [12]. Based on the cause, Wiltse divided spondylolisthesis into six categories: pathogenic, congenital, degenerative, isthmic, and iatrogenic [13]. The symptoms of lumbar spondylolisthesis aggravate gradually, such as low back muscles ache with lower limb numbness, and discomfort, since the extent of degeneration and injuries are not the same [14, 15]. As a result, many surgeons favour surgical treatment for lumbar spondylolisthesis [16]. Laminectomy is the surgical procedure of choice for treating lumbar spinal stenosis secondary to spondylolisthesis, and it's frequently paired with medial facetectomy and foraminotomy [17]. Current study identified a higher representation of female, 31(59%), within our study cohort. This contrasts with the previous study's results, which involved 4,548 participants in the study, and 2,490 (54.75%) of them were males and 2,058 (45.25%) were female. Our study, reflecting the ongoing pattern of spondylolisthesis,

demonstrates a greater prevalence among female [18]. Research studies and epidemiological data have shown that female are often at a higher risk of developing spondylolisthesis compared to males. This gender difference may be attributed to factors such as differences in spinal anatomy, hormonal influences, and biomechanical factors. The mean age of participants having spondylolisthesis was observed to be 42 years in our study. A study reported that age greater than 50 is more associated with the incidence of spondylolisthesis, as their results depicted the range of 55-59 to be the most common age, having high cases observed in the study group [18]. The prevalence rate may vary, but spondylolisthesis becomes more prevalent as individuals reach their 50s and beyond. The most common type of listhesis reported in our study was degenerative in 17 (33%) of patients. These findings are following the well-established understanding that degenerative changes and pars defects are primary contributors to spondylolisthesis. The results of our study are consistent with a study which illustrated the frequency of degenerative spondylolisthesis to be 30% [19]. Additionally, post-discitis cases 3 (6%) and post-surgical cases 4 (7%) underscore the diverse etiologies of spondylolisthesis. Our study identified L4-L5 23 (45%) as the most frequently affected level of listhesis, followed by L5-S1 18 (34%) and L3-L4 11 (21%). These results are consistent with existing literature, which often reports a higher prevalence of listhesis in the lower lumbar spine, particularly at the L4-L5 and L5-S1 levels [20, 21]. Present study highlighted the postoperative clinical outcomes, including pain reduction and improved functional ability. A significant reduction in pain scores was noted in 75% of patients, which is consistent with the primary goal of surgical intervention to alleviate pain. Moreover, the majority of patients exhibited improved functional ability, with 60% showing significant improvement in functional disability scores. These outcomes underscore the potential benefits of surgical intervention in enhancing patients' quality of life [22]. In terms of neurological status, a substantial improvement was observed in 85% of patients, further supporting the positive impact of surgery on neurological outcomes. Complications following surgery were relatively low in current study. Foot drop occurred in 1(2%) of cases, while wrong screw placement and dural tears were observed in 3(5%) and 1(2%) of cases, respectively. Wound infection was documented in 1(2%) of cases. In a previous study, one case of dural tear was observed as consistent with present study [9]. While complications are inherent risks in surgical procedures [23], current study's low complication rates are encouraging and reflect the dedication to patient safety

during surgical interventions.

This study was limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings. Additionally, reliance on self-reported lifestyle and dietary factors may have introduced recall bias. Further prospective studies are needed to assess long-term efficacy and safety.

CONCLUSIONS

It was concluded that facetectomy combined with foraminotomy is associated with improved clinical outcomes in the management of spondylolisthesis, particularly in Type 1 cases. The procedure was linked to pain relief, enhanced functional ability, and improved neurological status. Further prospective studies are needed to assess long-term efficacy and safety.

Authors' Contribution

Conceptualization: KU

Methodology: KU, RUK

Formal analysis: RUK

Writing and Drafting: KU

Review and Editing: KU, RUK

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



GP73 Level in Patients with Chronic Hepatitis B: Relationship with Liver Biopsy, Levels of ALT, AST and HBV DNA

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ABSTRACT

GP73 is a serum protein that increases with liver disease progression in chronic hepatitis B (CHB) and has been proposed as a marker for liver status monitoring. **Objectives:** To evaluate the correlation between GP73 levels, Histological Activity Index (HAI), and fibrosis stages in CHB patients, assessing its potential as a non-invasive biomarker. **Methods:** A cross-sectional study was conducted over six months (May to October 2024) at the Department of Infectious Diseases, Khairpur Medical College/Civil Hospital Khairpur. A total of 250 CHB patients were enrolled and categorized by fibrosis stages and HAI scores. GP73 concentrations were measured using ELISA. Patients were classified based on fibrosis stage (F0-F4) and HAI scores, determined through liver biopsy, with F0 representing no fibrosis and F4 indicating cirrhosis. Statistical analysis included one-way ANOVA, Kruskal-Wallis test, and correlation analysis. **Results:** GP73 levels increased progressively with fibrosis stages: 5.3 ng/mL in Group 1, 6.1 ng/mL in Group 2, and 7.5 ng/mL in Group 3 ($p=0.001$). GP73 also rose with HAI scores, from 5.0 ng/mL in minimal to 8.0 ng/mL in severe activity groups ($p=0.05$). GP73 showed a moderate correlation with fibrosis stage ($r=0.6$, $p<0.05$) and a strong correlation with HAI ($r=0.75$, $p<0.001$). **Conclusions:** GP73 is a promising non-invasive biomarker for evaluating liver fibrosis and necroinflammation in CHB, warranting further validation in larger studies.

INTRODUCTION

Hepatitis B virus (HBV) infection remains a major global health concern, affecting over 296 million people worldwide [1, 2]. In 2019, it was responsible for an estimated 331,000 deaths, including 192,000 deaths from HBV-related liver cancer, a significant rise from 2010 figures. Chronic hepatitis B (CHB) prevalence is highest in Sub-Saharan Africa and East Asia, where most infections occur perinatally or in early childhood [3]. Despite the availability of effective vaccines and antiviral therapies, gaps in diagnosis, treatment, and prevention continue to drive the disease burden [4, 5]. CHB results from the immune system's failure to clear the virus, leading to chronic inflammation, necrosis, and progressive liver fibrosis, and

eventually cirrhosis and hepatocellular carcinoma (HCC). Necrosis plays a pivotal role in the pathogenesis of Chronic Hepatitis B (CHB), reflecting ongoing hepatocellular injury and contributing to disease progression, fibrosis, and potential liver failure [6, 7]. Early detection of liver damage is crucial for guiding treatment decisions and preventing complications. While liver biopsy remains the gold standard for assessing fibrosis and necroinflammatory activity, its invasiveness and associated risks limit its routine use [8]. Golgi Protein 73 (GP73) is a promising non-invasive biomarker for liver fibrosis and cirrhosis [9]. Studies suggest GP73 levels increase progressively with disease severity, including in conditions like autoimmune



hepatitis, fatty liver disease, and viral hepatitis [10]. However, commonly used liver enzymes like ALT and AST, though indicative of hepatocellular injury, lack sensitivity and correlation with disease severity [11]. The Histological Activity Index (HAI) measures necroinflammation, while the Ishak scoring system stages liver fibrosis. Both remain essential in CHB management. Although HBV DNA levels reflect viral replication, they do not consistently correlate with liver damage. Hence, additional markers are needed to bridge the gap between virological activity and histological changes [12]. Although GP73 has been associated with fibrosis, its relationship with necroinflammation (HAI) and fibrosis stages in CHB patients is not yet well defined.

Despite advances in the management of chronic hepatitis B (CHB), there remains a lack of reliable non-invasive markers that accurately reflect both necroinflammatory activity and fibrosis severity, as commonly used parameters like ALT, AST, and HBV DNA show limited correlation with histological changes. While Golgi Protein 73 (GP73) has shown promise as a marker of liver fibrosis, its relationship with necroinflammation (Histological Activity Index) and fibrosis stages in CHB patients is not well established. Therefore, this study aims to evaluate the association of GP73 levels with HAI and fibrosis stages to assess its potential as a comprehensive non-invasive biomarker in CHB.

METHODS

This cross-sectional study was conducted for six months from May 2024 to October 2024 at the Department of Infectious Diseases, Khairpur Medical College. Written informed consent was obtained from all patients included in the study. The study was conducted by the principles of the Declaration of Helsinki, and ethical approval was obtained from the Institutional Review Board (IRB) of Khairpur Medical College, Khairpur (KMC/RERC/112). A total of $n=250$ participants in fibrosis stages and HAI scores are categorized into groups. The participants were divided into two groups: HBeAg-positive ($n=120$) and HBeAg-negative ($n=130$). The age range was 20–65 years. Fibrosis stages (F0–F4) were determined using liver biopsy, while HAI scores were categorized as mild, moderate, or severe based on histopathological assessment. The sample size was calculated to detect a minimum correlation of $r = 0.18$ between GP73 levels and fibrosis stages at a 95% confidence level and 80% power using the following formula: $n = (Z_{\alpha/2} + Z_{\beta})^2 (0.5 \ln(1+r) - r)^2 = 1.96 Z_{\alpha/2} = 1.96$ (for a significance level of 5%), $Z_{\beta} = 0.84$ (for 80% power), and $r = 0.18$ (the minimum detectable correlation based on conservative estimates). The calculated minimum sample size was approximately 250 participants. HAI grades liver activity from 0–22 based on periportal necrosis (0–10), lobular degeneration (0–4), and portal inflammation (0–4), while the Ishak system provides an inflammation grade (0–18) and fibrosis stage (0–6), offering more detailed

assessment [13]. Inclusion criteria: Positivity for HBsAg for more than 6 months, abnormal ALT level, or normal ALT level, or the presence of advanced liver disease. Physicals, liver function tests (AST, ALT), CBC, and prothrombin time were basic evaluations. Patients were included if they had a history of HBV DNA $\geq 2,000$ IU/mL within the past three months. Minor variations below this threshold at the time of sampling were accepted to account for natural viral fluctuations. By ultrasound and AFP testing, liver cancer was excluded. Exclusion criteria were HDV, HCV, and/or HIV co-infections. Other causes of chronic diseases of the liver. Patients with a history of liver cancer or those having conditions that make it difficult to accurately assess CHB. Biochemical Parameters were ALT, AST, gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), bilirubin, albumin, full blood count, and prothrombin time. HBV DNA: Quantified by PCR. GP73 Levels were measured by ELISA using the RayBio® Human G0LM1/GP-73 ELISA kit. The normal reference range for ALT (Alanine Aminotransferase) is 7–56 U/L, and for AST (Aspartate Aminotransferase) is 10–40 U/L, with values exceeding these ranges considered elevated. For HBV DNA levels, a viral load of $\geq 2,000$ IU/mL was used as the clinically significant cutoff, by established international guidelines for chronic hepatitis B management. GP73 levels, measured using an ELISA kit, were interpreted based on previously published studies and manufacturer recommendations, with levels above 70 ng/mL considered elevated and indicative of significant liver pathology. HBeAg status was determined using ELISA testing. GP73 is a valuable biomarker with growing clinical relevance in liver diseases. It has shown higher sensitivity and specificity than AFP in diagnosing hepatocellular carcinoma (HCC), with cutoff levels typically ranging from 8.5 to 10 ng/mL. GP73 levels also correlate with liver fibrosis severity, making it useful in staging chronic liver disease. Liver biopsy was performed using the Menghini technique with 16-gauge Hepafix® needles. Histological grading and staging were conducted using the Ishak scoring system, which classifies fibrosis on a scale from 0 (no fibrosis) to 6 (cirrhosis). Based on this system, patients were categorized into three groups: Group 1 (fibrosis stages 0–1), Group 2 (stages 2–4), and Group 3 (stages 5–6). This classification allowed us to stratify patients by the severity of fibrosis for analytical purposes. The use of the Metavir system, which ranges only from F0 to F4. The use of the Ishak system was now explicitly stated and justified within the scientific context. The scored specimens were graded for necro-inflammatory activity and fibrosis using the Ishak system. Patients were grouped by fibrosis stages: Stage 0–1: Group 1; Stage 2–4: Group 2; Stage 5–6: Group 3. The data were analyzed using SPSS version 21.0. Spearman's rank correlation was used to make a correlation between GP73 and other variables. Normality was tested using the Shapiro-Wilk test, and since the data were non-normally distributed, for non-parametric tests (Kruskal-Wallis and Mann-Whitney U) for appropriate group comparisons,

$p < 0.050$ was considered significant.

RESULTS

HBeAg-positive patients had a significantly lower mean age than HBeAg-negative patients ($p = 0.020$). Male were predominated in the HBeAg-positive group ($p = 0.001$), while female was more common in the HBeAg-negative group ($p = 0.001$). ALT ($p = 0.030$), AST ($p = 0.040$), and HBV DNA levels ($p = 0.001$) were significantly higher in HBeAg-positive patients, indicating greater liver activity and viral load. No BMI difference was noted ($p = 0.150$). GP73 levels were slightly lower in HBeAg-positive cases ($p = 0.045$). HAI scores were higher in HBeAg-negative patients ($p = 0.038$), while fibrosis stages were greater in HBeAg-positive patients ($p = 0.045$) (Table 1).

Table 1: Patients' Characteristics by HBeAg Status (n=250)

Variables	Total (n=250)	HBeAg (+) (n=120)	HBeAg (-) (n=130)	p-value
Age (Years, Mean $\pm$ SD)	40.5 $\pm$ 12.3	38.2 $\pm$ 10.5	42.7 $\pm$ 13.2	0.020*
Gender (Male, n (%))	160 (64%)	90 (75%)	70 (54%)	0.001**
Gender (Female, n (%))	90 (36%)	30 (25%)	60 (46%)	0.001**
ALT (U/L, Median [IQR])	55 [45-68]	60 [50-72]	50 [40-65]	0.030*
AST (U/L, Median [IQR])	47 [38-59]	50 [40-63]	45 [35-55]	0.040*
BMI (kg/m ² , Mean $\pm$ SD)	25.8 $\pm$ 3.2	26.1 $\pm$ 3.4	25.5 $\pm$ 3.1	0.150
HBV DNA (IU/mL, Median [IQR])	8000 [2000-20,000]	12,000 [5000-30,000]	4000 [1000-10,000]	0.001**
GP73 (ng/mL)				
Mean $\pm$ SD	6.2 $\pm$ 2.4	5.8 $\pm$ 2.3	6.5 $\pm$ 2.5	0.045
Median	5.8	5.6	6.0	
HAI Score (mean)	8.5 $\pm$ 4.2	7.9 $\pm$ 4.5	9.0 $\pm$ 3.8	0.038
Fibrosis Stage (mean)	6.5 $\pm$ 3.2	7.2 $\pm$ 3.0	5.9 $\pm$ 3.4	0.045

On the basis of the Histological Activity Index (HAI) scores in 250 chronic hepatitis B patients, most were considered to be in moderate (34%) and severe (14%) activity group, suggesting a high prevalence rate of advanced liver disease. Fewer patients were in the minimal (24%), mild (28%), moderate (34%), and severe (14%) activity categories (Figure 1).

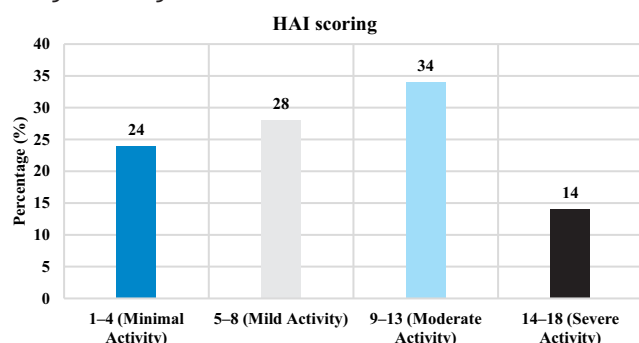


Figure 1: HAI Scoring Analysis

A distribution of fibrosis stage with more patients in Group 2 (2-4) than in Group 1 (0-1) and Group 3 (5-6). There is a statistically significant difference on these stages (Figure 2).

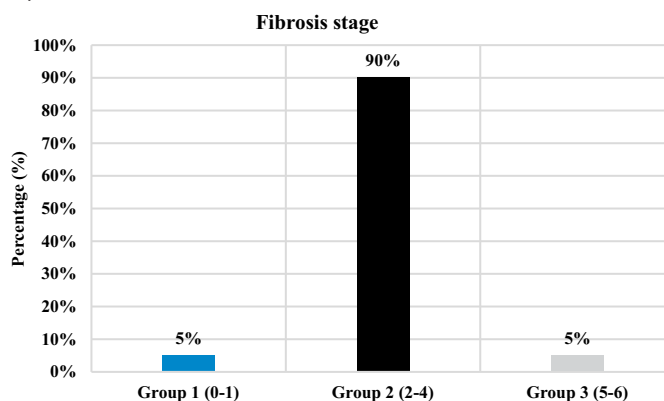


Figure 2: Fibrosis Stage Distribution

GP73 levels showed significant variation across different HAI scores and fibrosis stages. As disease activity worsened, GP73 levels increased, with minimal activity (HAI 1-4) averaging 5.0 ng/mL and severe activity (HAI 14-18) reaching 8.0 ng/mL (Kruskal-Wallis, $p = 0.050$). Similarly, GP73 rose with fibrosis severity: 5.3 ng/mL in stage 0-1, 6.1 ng/mL in stage 2-4, and 7.5 ng/mL in stage 5-6 (One-way ANOVA, $p = 0.001$) (Table 2).

Table 2: Correlation Between Golgi Protein 73 Levels and Liver Fibrosis Staging Using the Ishak Scoring System

Groups	n	Mean Gp73 (ng/mL)	Median	Min	Max	p-value
HAI Score Range						
Minimal Activity (1-4)	50	5.0 $\pm$ 1.9	4.8	1.0	7.2	0.050
Mild Activity (5-8)	100	6.0 $\pm$ 2.0	6.0	2.0	8.5	0.050
Moderate Activity (9-13)	75	6.8 $\pm$ 2.5	6.5	3.0	9.5	0.050
Severe Activity (14-18)	25	8.0 $\pm$ 3.0	8.2	5.5	12.0	0.050
Fibrosis Stage						
Group 1 (0-1)	25	5.3 $\pm$ 2.1	5.0	1.0	8.5	0.001
Group 2 (2-4)	40	7.5 $\pm$ 2.3	6.0	1.5	9.0	0.001
Group 3 (5-6)	185	6.4 $\pm$ 2.0	7.5	5.5	10.0	0.001

GP73 levels were significantly associated with higher fibrosis stages and HAI scores ($p < 0.050$) (Figure 3).

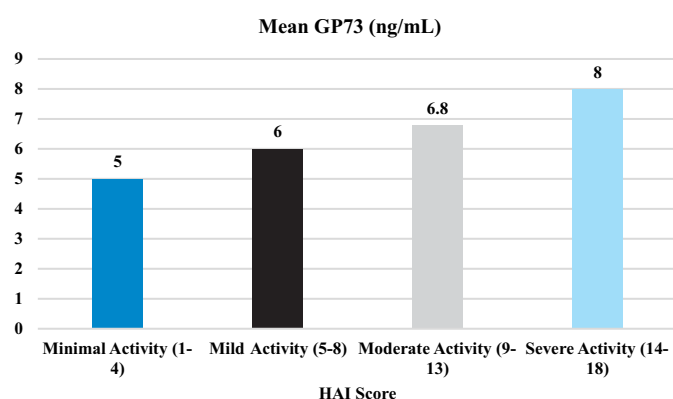


Figure 3: Compare GP73 with Different Activities of HAI Score

DISCUSSION

Chronic hepatitis B virus (HBV) infection increases the risk of cirrhosis and hepatocellular carcinoma (HCC) due to both host and viral factors. The primary goal of treatment is to halt disease progression, thereby improving survival and quality of life. Accurately determining the severity of liver damage is crucial for guiding treatment decisions [14]. When routine blood tests and HBV markers are insufficient, non-invasive tools or liver biopsies are often required. This highlights the need for reliable blood-based biomarkers to reduce reliance on invasive procedures. In this context, we evaluated clinical and biochemical differences between HBeAg-positive and HBeAg-negative patients, identifying GP73, a glycoprotein produced by hepatocytes, as a potential marker for liver disease severity in chronic hepatitis B (CHB). HBeAg status was a secondary analysis and not the primary focus of the study [15]. Our study demonstrated a significant difference in age distribution, with younger patients being predominantly HBeAg-positive ($p=0.020$). This aligns with Wang *et al.*, and Duan *et al.*, who noted that HBeAg positivity is more common in younger CHB patients due to the natural course of the disease, where seroconversion often occurs with age, marking a transition from the immune-tolerant to the immune-active phase [16, 17]. Additionally, male were more frequently HBeAg-positive (75%) compared to female (46%, $p=0.001$), consistent with previous research indicating male are at higher risk of severe disease progression due to the effects of sex hormones on immune regulation and viral replication dynamics [18]. Moreover, HBeAg-positive patients exhibited significantly higher ALT and AST levels ($p=0.030$ and 0.040), reflecting greater liver inflammation. This finding supports earlier studies reporting that higher viral replication in HBeAg-positive patients contributes to more active immune-mediated hepatocyte damage [19]. Elevated ALT and AST levels result from viral replication within hepatocytes, accumulation of viral proteins, and subsequent immune-induced cytopathic effects leading to membrane

disruption and enzyme leakage into the bloodstream [20]. High HBV DNA levels increase with HBeAg positivity and correlate strongly with liver inflammation in this test group. Persistent hepatocyte injury is a result of active, continuing viral replication and perpetuation of immune system activation. Immune recognition of viral proteins, HBeAg, HBcAg, and HBsAg, presented on the hepatocyte surface, adds to primary immune-mediated damage. ALT is localized mainly in the cytoplasm of hepatocytes, where it acts as a specific marker of acute liver damage; in contrast, AST, which exists in the cytoplasm and mitochondria, is increased in response to more severe or protracted hepatocyte injury (deeper cell damage). Patients with HBeAg positivity are in the immune clearance phase of HBV infection, accompanied by ongoing immunological targeting of HBV-infected cells [21]. The consequence is peak liver inflammation at the time when immune cells infiltrate the liver and leading to dramatically increased ALT and AST levels. There are generally lower levels of these enzymes in HBeAg-negative patients compared to HBeAg-positive patients, reflecting reduced viral replication and consequently, less pronounced immune-mediated hepatocyte destruction. In HBeAg-negative patients, there could, however, be ongoing low-level viral activity or residual immune responses that cause chronic liver inflammation as well [22]. In current study, GP73 levels were significantly higher in the HBeAg-negative group to the HBeAg-positive group; there was a trend of lower HBV DNA in HBeAg-negative patients (mean 5 ± 2.5 ng/mL). The previous study reported that the higher GP73 in HBeAg-positive patients; lower GP73 levels were found in HBeAg-positive patients. On the other hand, the higher levels of GP73 in the HBeAg negative individuals in our series could reflect a more advanced stage of disease since their HAI scores and fibrosis stage were also greater. Additionally, correlation analysis showed that GP73 levels had a positive correlation with HAI scores and fibrosis stages, which progressed as liver disease worsens. Mean GP73 levels were, for example, 5.0 ng/mL in minimal activity (HAI 1-4) and 8.0 ng/mL in severe activity (HAI 14-18, $p=0.050$). Similarly, increasing GP73 levels were correlated with fibrosis stage progression ($p=0.001$) from stage 0-1 to stage 5-6. It showed the use of GP73 as a reliable noninvasive biomarker for the assessment of liver fibrosis and inflammation [23]. Fibrosis stage analysis revealed that HBeAg-positive patients had more advanced fibrosis. However, compared with HBeAg-negative patients, the mean stage was 5.9 ± 3.4 ($p=0.045$), which is significantly lower than that of HBeAg-positive patients (mean stage: 2 ± 3.0). These findings are consistent with the previous study in which HBeAg positivity was associated with fibrotic progression through prolonged viral activity and

liver damage. In our study, GP73 levels correlate positively with both HAI scores and fibrosis stages, supporting GP73 as a biomarker for liver disease progression. GP73 can be used to diagnose stages of fibrosis and cirrhosis. GP73 is a better biomarker for subclinical liver damage compared to traditional markers such as ALT and AST. In our study, GP73 levels dichotomized patients according to mild to severe disease activity ($p=0.050$), and early vs late fibrosis stages ($p=0.001$). It was found that these findings support the notion of GP73 as a potential adjunct to current diagnostic tools for monitoring disease progression in CHB patients, because GP73 measurement can be done noninvasively [24]. Current findings suggest personalized management strategies for chronic HBV patients according to their HBeAg status, GP73 levels, and histological activity. Aggressive antiviral treatment might be considered in HBeAg-positive patients to prevent fibrosis. HBeAg-negative patients with elevated GP73 levels and HAI scores should be followed closely for cirrhotic and HCC risk. This study was limited by its relatively small sample size and single-center design, which may limit the generalizability of the findings. Additionally, the cross-sectional nature of the study and lack of longitudinal follow-up restricted assessment of GP73 dynamics and long-term disease progression. Further studies are needed to assess GP73 as a dynamic predictive biomarker in response to antiviral therapy. Adding GP73 to routine tests (HBV DNA and liver enzymes) for an expanded risk stratification of HBV patients is warranted.

CONCLUSIONS

It was concluded that GP73 levels are increased with higher HAI scores and more advanced fibrosis stages, suggesting that it is a noninvasive biomarker in liver disease progression. These results have an important contribution toward the body of literature supporting the use of GP73 as a useful clinical tool for the management of chronic hepatitis B infection, which may help improve patient care moving forward.

Authors' Contribution

Conceptualization: RKR

Methodology: SA, AHP, SAP

Formal analysis: SA, AA

Writing and Drafting: AHP, SAP, AQM

Review and Editing: RKR, SA, AHP, SAP, AQM

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



Clinical Outcomes and Frequency of Electroencephalographic Abnormalities in Patients with First Unprovoked Seizure in a Tertiary Care Hospital: A Cross-Sectional Study

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ABSTRACT

Epilepsy is a common medical condition that has widespread neurobiological, cognitive, psychological, and social consequences. Recurrent seizures are a common feature of this illness. Individuals experiencing their first unprovoked seizure generally present with Electroencephalographic (EEG) abnormalities, which might reflect a broad range of underlying neurophysiological changes. Identifying and measuring these abnormalities is critical for differentiating between epileptic and non-epileptic seizures, determining suitable treatment techniques, and predicting future seizure risk. **Objective:** To determine the frequency of abnormal EEG in patients presenting after first unprovoked seizures. Early detection of these abnormalities will better guide for better management and to predict recurrence. **Methods:** The study was a six-month cross-sectional retrospective held at the Punjab Institute of Neurosciences, Lahore, Pakistan from January 2024 to June 2024. This study employed the non-probability consecutive sampling method. The study included 95 patients who met the inclusion and exclusion criteria. Previous medical data included a complete patient history, clinical examination, and EEG results. Data were then analyzed using SPSS version 21.0. **Results:** Out of 95 patients, 52.63% were male and 47.37% were female, averaging 52.6 ± 5.6 years. A total of 46 individuals (48.42%) had abnormal EEG irrespective of age, gender, length of symptoms, and awareness of symptoms. **Conclusion:** This study concluded that EEG abnormalities are highly frequent among individuals following their first unprovoked seizure.

INTRODUCTION

Epilepsy affects up to 1% of the global population. It is the second most prevalent neurological disease after stroke which is affecting around 50 million individuals globally, mostly in poor countries. It impacts 5 to 10 persons per 1,000 worldwide, with Pakistan having around 1.38 million cases [1]. It is known as a persistent tendency to develop spontaneous seizures, which can have cognitive, social, and psychological consequences. It can develop at any age,

it usually appears in early childhood or beyond the age of 60, and the type of seizures differs depending on the part of the brain affected; however, most seizures are well controlled with antiepileptic medicines and patients have regular lives [2]. Seizures are brief episodes of abnormal brain activity. Most people experience them at some point in their lifetime [3]. Unprovoked seizures are defined as seizures that occur in the absence of any underlying causes or more than



seven days after an acute injury or insult [4]. A First unprovoked seizure is a disturbing experience for both patients and their families and raises anxiety about recurrence of seizure. Correct diagnosis after a first unprovoked seizure is important to distinguish it from other conditions to identify the cause, and for optimal treatment management [5]. Although all initial unprovoked seizures were formerly treated, recent studies have demonstrated that the risk of recurrence is not assured. Moreover, the treatment options are now based on the individual's risk of recurrence and the impact on life quality [6]. The first stage in diagnosing epilepsy is to take a complete history from patients and witnesses to evaluate if the first unprovoked seizure is epileptic or not, followed by investigations such as EEG or MRI [7]. EEG is an important tool for diagnosing and managing epilepsy, particularly after a first unprovoked seizure, since it identifies epileptiform activity, measures the risk of recurrence, and gives direction for treatment options. EEG is unlikely to detect the possibility of a subsequent seizure after the first unprovoked seizure. However, it can aid in the identification of seizure tendencies, especially in individuals under 25 [8]. Early EEG (within 24 hours) and EEG in sleep-deprived or ambulatory patients improve diagnostic accuracy and predict recurrence of seizures [9]. While EEG should be conducted immediately following the incident, although it may not be available in emergencies. Sleep-deprived or repeat EEGs can improve diagnosis accuracy in unclear circumstances [10]. Patients with a First Single Unprovoked Seizure (FSUS) face diagnostic challenges in assessing the risk of recurrence and need for anti-seizure medication [11]. EEG is critical for the early diagnosis and treatment of unprovoked seizures, especially non-convulsive status epilepticus and mild seizure activity. Its capacity to detect early electrical disruptions in the brain allows for earlier intervention, which dramatically improves prognosis and guides therapy in critical care and epilepsy management [12]. Understanding the distinct seizure patterns of aged individuals, especially in the context of neurodegenerative alterations and vascular risk factors, is critical for appropriate diagnosis and therapy. Future research should look at bigger cohorts and incorporate longitudinal follow-ups to understand the impact of age-related variables like stroke and dementia in the emergence of secondary epilepsy. This intelligence will assist healthcare practitioners to modify treatment techniques, enhance patient outcomes, and allocate resources more effectively. Furthermore, developments in EEG methods, such as extended monitoring and video-EEG integration, may improve the identification and diagnosis of mild seizure activity, particularly in the older population. Despite the clinical importance of Epilepsy and the use of Electroencephalography in evaluating first unprovoked

seizures, there remains limited local evidence regarding the frequency of abnormal EEG findings and their association with patient outcomes. This gap creates uncertainty in clinical decision-making, particularly in initiating anti-seizure therapy after a first episode. The objective of this study was to determine the clinical outcomes and frequency of abnormal EEG in patients with first unprovoked seizures. Early diagnosis of these abnormalities will better guide therapeutic options, such as starting anti-epileptic drugs, which may help avoid further recurrence.

METHODS

This cross-sectional, retrospective study was carried out at the Department of Neurology, Punjab Institute of Neurosciences, Lahore, Pakistan, after the approval of IRB No. (1902/IRB/PINS/approval/2024). The sample size was calculated using the WHO calculator, taking into account a 95% confidence level, 10% relative precision, and an expected 57.6% frequency of abnormal EEG in first-seizure patients. Participants were chosen via non-probability sequential sampling. The study included both males and females aged 25 to 70 years who had their first seizure activity, as per operational definitions and were willing to participate. Exclusion criteria included an incomplete history, unwitnessed seizures, and a history of underlying disorders such as brain lesions, fever, prior encephalitis, or traumatic brain damage. Providing informed consent, 95 individuals who fulfilled the inclusion and exclusion criteria were enrolled from the pre-existing records in the electrophysiology laboratory at Punjab Institute of Neurosciences. Patient information was entered into a pre-designed form, thorough histories and examination data entered. EEG findings of each patient were entered on the same form. All subjects were treated under hospital practice, and their information was kept anonymous. The data were entered into SPSS version 21.0 for analysis. The statistical analysis was carried out with SPSS version 21.0. Quantitative data such as age was presented as mean $\pm$ SD, whereas qualitative data (gender, duration of symptoms, and symptom awareness) were provided as frequencies and percentages. Data were stratified by age, gender, and seizure length, and effect modifiers were identified using chi-square testing. A p-value < 0.5 was considered statistically significant.

RESULTS

A total of ninety-five patients participated in this study. In this study, 43.16% of patients were between the ages of 25-50 years while 56.84% of patients were between the ages of 51-70 years. The mean age of patients was 52.6 $\pm$ 5.6 years. Regarding gender distribution, 52.63% of patients were male while the remaining 47.37% of patients were female.

Table 1: Demographic Characterization of the Study Population (n=95)

Age and Gender Distribution	Number of Patients Frequency (%) / Mean $\pm$ SD
Age (Years)	
25-50	41 (43.16)
51-70	54 (56.84)
Mean $\pm$ SD	52.6 $\pm$ 5.6 Years
Gender	
Male	50 (52.63)
Female	45 (47.37)
Total	95 (100)

With regards to the frequency of abnormal EEG, 48.42% of patients had abnormal EEG whereas the remaining patients had normal EEG. Approximately 80% of patients experienced symptoms for less than one minute, whereas 20% experienced symptoms for more than one minute.

Table 2: Frequency of Abnormal EEG and Duration of Symptoms (n=95)

Frequency of Abnormal EEG and Duration of Symptoms	Number of patients Frequency (%)
Abnormal EEG	
Yes	46 (48.42)
No	49 (51.58)
Symptom Duration	
≤ 1 minute	76 (80)
> 1 minute	19 (20)
Total	95 (100)

When this data stratified by age group, 20 patients discovered out of 41 (48.78%) in the 25-50 year age group had abnormal EEG, whereas 26 patients out of 54 (48.14%) in the 51-70 year group had abnormal EEG. The Chi-square was 0.0037, with a p-value of 0.951, indicating that it was not significant. When this data stratified by gender, 24 male patients found out of 50 total male patients, or 48%, had abnormal EEG, whereas 22 female patients out of 45 total female patients, or 48.88%, had abnormal EEG, with a Chi-square of 0.0075 and a p-value of 0.931, indicating non-significance. On further stratification of data according to the duration of disease, it was seen that 37 patients out of 76 i.e. 48.6% with symptoms duration < 1 minute had abnormal EEG compared to 9 patients out of 19 i.e. 47.36% with symptoms duration > 1 minute had abnormal EEG with Chi-square of 0.010 and p-value of 0.918 i.e. non-significant. Further analysis of the data based on awareness of symptoms revealed no significant correlation between symptom awareness in epileptic patients with abnormal EEG findings and those with normal EEG results, as evidenced by a p-value of 0.678.

Table 3: Stratification of Patients with Abnormal EEG (n=95)

Variables	Abnormal EEG (Yes)	Abnormal EEG (No)	Total	Chi-Square Test	p-Value
Age (Years)					
25-50	20	21	41	0.0037	0.951
51-70	26	28	54		
Gender					
Male	24	26	50	0.0075	0.931
Female	22	23	45		
≤1 minute	37	39	76	0.010	0.918
>1 minute	9	10	19		
Awareness of Symptoms					
Yes	38	42	80	0.172	0.678
No	8	7	15		
Total	46	49	95		

DISCUSSION

Epilepsy-related seizures are defined by transient signs and symptoms caused by alterations in brain activity [13]. Electroencephalography (EEG) is routinely performed in patients presenting with first-ever seizures to see if there is any abnormal wave pattern [14]. Current study "Clinical Significance and Frequency of Electroencephalographic Abnormalities in Patients with First Unprovoked Seizure in a Tertiary Care Hospital: A Cross-Sectional Study" was conducted at Neurology department Punjab Institute of Neurosciences Lahore. This study found that abnormal EEG was observed in 48.42% of individuals who experienced their first seizure. These findings are consistent with other investigations. According to one study done in Japan, 55.2% of patients had abnormal EEG after their first seizure [15]. In one Australian research, aberrant EEG was seen in 77% of individuals experiencing their first seizure [16]. In another research done in Malaysia, 55% of patients with clinical features indicative of epilepsy were identified with abnormal EEG [17]. One research done at the Mayo Clinic's neurology department in the United States reported that aberrant EEG tracing was present in 12-50% of adult patients [18]. One study conducted in Canada to assess the role of EEG in patients presenting to the first seizure clinic showed that EEG was abnormal in 41% of patients after the first seizure [19]. Another study conducted in New York showed that EEG was abnormal in 42% of patients [20]. Another study conducted in Singapore showed that in patients who had their first seizure, EEG was abnormal in 29.4% of patients [21]. A study conducted in Israel showed that when EEG was performed after the first ever seizure, it was positive in 69% of patients [22]. The same results were found in a study performed at Heidelberg University Germany where standard EEG was abnormal in 70.7% after first-ever seizure [23]. On stratification of data according to age, any significant correlation was not found between abnormal EEG in different age groups after the first seizure activity

i.e. p value was 0.951 (non-significant). In one study conducted in China, abnormal EEG was significant in patients with first-ever seizures [24]. A study conducted in India recommends performing an EEG in all patients presenting with a first seizure [25]. There are significant clinical implications of the findings in this study. An abnormal EEG result was seen in nearly half of the patients in this study presenting with a first unprovoked seizure emphasizes the utility of EEG in identifying those at higher risk for recurrent seizures, helping in the diagnosis of epilepsy. Early detection of EEG abnormalities will guide clinicians in making timely decisions about management and monitoring strategies, improving patient outcomes. Additionally, EEG abnormalities were not associated with age, EEG can be considered a useful diagnostic tool in all age groups. This study supplements the existing literature by providing localized data from Punjab Institute of Neurosciences in Lahore, addressing an existing gap regarding data of EEG abnormalities in Pakistan's Population.

The limitation of the study is that the data on EEG findings after first unprovoked seizure from Pakistan was limited, and these findings are consistent with studies from South Asian region, showing similar EEG abnormality rates. This study contributes to the existing literature that EEG should be performed following a first seizure, aiding in its status as a routine procedure in epilepsy diagnosis. The findings of this study provide an outline for further evaluation of the predictive utility of EEG in patients presenting with first seizure, especially among diverse groups. Future research should probe into whether distinguished EEG patterns are linked with recurring seizures or epilepsy subtypes, thus helping in prognosis and individualized management approaches. In addition, this study encourages multi-centre and prospective studies to create uniform protocols for utilizing EEG in first-seizure cases, which may lead to more widely accepted guidelines.

CONCLUSIONS

In conclusion, EEG abnormalities are prevalent in individuals experiencing their first unprovoked seizure. These findings align with the international research and reveals that abnormal EEG pattern was seen in 48.4% of patients. This study emphasizes the clinical significance of EEG as a useful tool for determining the risk of seizure recurrence and likely development to epilepsy. Thus improved EEG practice may contribute to better individualized management for patients with seizure disorder.

Authors' Contribution

Conceptualization: RM

Methodology: MM, MTR, AN

Formal analysis: SH, AN, TH

Writing, review and editing: RM, MM, MTR, SH, TH

Review and Editing: RM, MM, MTR, AN, SH, TH

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



Impact of Structured Early Clinical Exposure on Confidence and Competence among Undergraduate Health Science Students in Islamabad

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ABSTRACT

Transitioning from classroom to clinical settings can be overwhelming for undergraduate health sciences students. Early Clinical Exposure (ECE) has been proposed to enhance confidence and competence during early training, yet its impact remains under-evaluated in local contexts.

Objective: To assess the effect of structured early clinical exposure on the self-reported confidence and perceived competence of undergraduate medical, dental, and nursing students. **Methods:** This quasi-experimental pretest-posttest study was conducted from November 2024 to April 2025 at Rawal Institute of Health Sciences, Islamabad. A total of 71 students from 3rd, 4th, and final year were enrolled through convenience sampling. Participants completed a validated self-assessment questionnaire before and after a structured ECE session, which included classroom orientation, ward rotations, bedside interaction, and debriefing. The tool was pilot tested and showed strong internal consistency (Cronbach's alpha = 0.86). Paired t-tests and chi-square tests were used for analysis ($p < 0.05$). **Results:** Post-intervention scores showed significant improvements across all five domains of clinical confidence, including history taking, communication, examination skills, case presentation, and anxiety management ($p < 0.001$). Gender was significantly associated with comfort in ward settings and understanding hospital hierarchy. No significant differences were observed across academic years. **Conclusions:** Structured early clinical exposure significantly enhanced students' clinical confidence and preparedness across domains. Integrating ECE into undergraduate curricula can foster smoother transitions into clinical environments.

INTRODUCTION

In recent years, there has been a growing emphasis on integrating clinical experiences early in medical and health sciences education [1]. Traditional curricula often delayed clinical exposure until the later years, leaving students underprepared for real-world patient interactions [2]. This delay not only affected their clinical confidence but also widened the gap between theoretical learning and practical application. Early clinical exposure (ECE) emerged as a promising educational approach to bridge

this gap by introducing students to patient care settings during the pre-clinical or early clinical years [3]. ECE allowed students to observe, interact, and reflect within the clinical environment under structured guidance [4]. It offered opportunities to apply basic science knowledge in real-life contexts, develop professional behavior, and become familiar with hospital systems and team dynamics. Numerous international studies demonstrated that early exposure enhanced communication skills, promoted



patient-centered attitudes, and improved confidence in performing clinical tasks. For example, a study conducted at Burapha University in Thailand reported that ECE improved second-year students' confidence and understanding of hospital roles, while Kalusopa et al., in (2023) observed enhanced integration of theoretical knowledge and practical care in early neonatal nursing exposure in Zambia [5, 6]. However, the impact of such interventions in local and regional contexts, such as India, Nepal, and Pakistan, remained underexplored. For instance, a study conducted in a North Indian medical college found that early exposure significantly reduced student anxiety, while another study from a Pakistani institution reported improved self-efficacy in clinical communication following ECE interventions [7, 8]. In Pakistan, many medical and dental colleges still followed traditional didactic models, offering limited opportunities for early hospital engagement [9]. As a result, students often felt anxious and unprepared when they first entered the wards in their senior years. There was, therefore, a growing need to investigate whether structured early clinical experiences could improve student preparedness and confidence before formal clinical rotations began.

This study aimed to evaluate the effect of early clinical exposure on the self-reported confidence and perceived competence of undergraduate students at a health sciences institute in Islamabad. Specifically, it sought to answer the research question: *Does structured early clinical exposure significantly enhance the clinical confidence and perceived competence of undergraduate students in pre-final and final years?* The study addressed a critical gap in the literature by providing evidence from a local setting and examined how early clinical exposure could support a smoother transition into clinical practice.

METHODS

This was a quantitative, quasi-experimental pre-post-test study designed to assess the impact of structured Early Clinical Exposure (ECE) on the confidence and self-perceived competence of undergraduate health science students. The study was conducted at Rawal Institute of Health Sciences, Islamabad, over six months, from November 2024 to April 2025. Ethical approval was obtained from the Institutional Review Board (IRB) of Rawal Institute of Health Sciences, under Reference No. RIHS/IRB/29/2024. The study titled "Impact of Early Clinical Exposure on Medical Students' Confidence and Competency" was approved for one year. Informed written consent was obtained from all participants, who were informed of their right to withdraw from the study at any stage without penalty. Participation was entirely voluntary. The principles outlined in the Declaration of Helsinki were strictly followed. All collected data were used solely for research purposes, and participant anonymity and

confidentiality were rigorously maintained throughout. The sample size was calculated using G*Power software (version 3.1.9.7) for a paired-sample t-test. With an effect size (Cohen's d) of 0.8, a power of 80%, and an alpha of 0.05, the minimum required sample was 64 participants. To allow for potential dropouts, the final sample was increased to 71 students. The effect size estimation was based on a prior interventional study by AkbariRad et al., in (2023), which reported comparable gains in self-reported confidence following structured clinical exposure [10]. Participants were recruited via convenience sampling. Eligible students were those enrolled in the 3rd, 4th, or final year of MBBS, who had no prior structured clinical exposure and who voluntarily agreed to participate with written informed consent. First and second-year students were excluded from this study as they had not yet entered the clinical phase of their curriculum and lacked the necessary foundational clinical knowledge and hospital orientation. The study focused on 3rd, 4th, and final-year students who had sufficient academic background and readiness to engage in structured clinical exposure and meaningfully reflect on their confidence and competency in patient care settings. Students who had participated in pilot ECE sessions, external hospital rotations, or who submitted incomplete questionnaires were excluded. The study used a single-group pre-post design. Initially, participants completed a pre-intervention questionnaire assessing confidence in five clinical domains: (a) taking patient history, (b) communicating with patients, (c) performing general physical examination, (d) presenting cases to seniors, and (e) managing clinical anxiety. Responses were rated on a 5-point Likert scale ranging from 1 (not confident at all) to 5 (very confident). The questionnaire was adapted from previously validated tools used in studies evaluating early clinical exposure and student readiness [11, 12]. The ECE intervention included: A structured classroom orientation on hospital protocols and clinical communication. A guided hospital tour introducing key clinical departments. Supervised small-group ward rotations in medical and surgical units. Real-time bedside exposure with patient interaction. A concluding debriefing and reflection session with faculty. After one week, the same students completed a post-intervention questionnaire with identical items for comparison. The questionnaire was pilot tested on 10 students (excluded from the main sample) for clarity and structure. Content validity was reviewed by two senior faculty members. Internal consistency was assessed using Cronbach's alpha, which yielded a value of 0.86, indicating strong reliability. All responses were entered and analysed using IBM SPSS Statistics version 25.0. Descriptive statistics were used to summarize demographic data and confidence scores. A paired sample t-test was conducted to compare pre- and post-exposure confidence means. Chi-square tests examined associations between demographics (gender, academic year, clinical exposure) and perceived

competencies. Effect sizes were reported using Phi coefficient or Cramer's V, and one-way ANOVA was applied to compare post-confidence scores across academic years. Levene's test was used to assess homogeneity of variance, and the Shapiro-Wilk test confirmed data normality. A p-value of <0.05 was considered statistically significant. Missing data were addressed using listwise deletion.

RESULTS

The study included 71 students, with a fairly even age distribution between 18–20 years (42.3%) and 21–23 years (43.7%). Slightly more females (54.9%) participated than males (45.1%). Representation was balanced across academic years. Notably, 87.3% of students had no prior clinical exposure, highlighting the relevance of evaluating early clinical exposure in this cohort, Table 1.

Table 1: Demographic Characteristics of Participants (n=71)

Variables	Category	Frequency (%)
Age Group	18–20 Years	30 (42.3)
	21–23 Years	31 (43.7)
	>23 Years	10 (14.1)
Gender	Male	32 (45.1)
	Female	39 (54.9)
Year of Study	3 rd Year	24 (33.8)
	4 th Year	22 (31.0)
	Final Year	25 (35.2)
Previous Clinical Exposure	Yes	9 (12.7)
	No	62 (87.3)

All five domains of clinical confidence showed statistically significant improvement following the intervention ($p < 0.001$). The largest gains were observed in history taking and general examination skills. Communication, case presentation, and anxiety management also improved markedly, indicating a broad and consistent impact of early clinical exposure on self-perceived competence, Table 2.

Table 2: Comparison of Confidence Levels Before and After Clinical Exposure (n=71)

Domain of Confidence	Pre-Exposure Mean $\pm$ SD	Post-Exposure Mean $\pm$ SD	p-Value
Taking patient history	2.67 $\pm$ 0.56	3.99 $\pm$ 0.54	$p < 0.001$
Communicating with patients	2.62 $\pm$ 0.37	4.01 $\pm$ 0.40	$p < 0.001$
Performing general examination	2.59 $\pm$ 0.52	3.99 $\pm$ 0.48	$p < 0.001$
Presenting cases to seniors	2.25 $\pm$ 0.55	3.77 $\pm$ 0.54	$p < 0.001$
Handling clinical anxiety	2.39 $\pm$ 0.45	3.66 $\pm$ 0.49	$p < 0.001$

Chi-square analysis showed no significant associations between background variables and most competencies. However, gender was significantly associated with comfort in the ward ($p = 0.021$, $\Phi = 0.329$) and understanding of hospital hierarchy ($p = 0.036$, $\Phi = 0.307$), suggesting gender-specific differences in adapting to the clinical

environment. Other factors, including year of study and prior exposure, showed no meaningful associations, Table 3.

Table 3: Summary of Chi-Square Test Results and Strength of Association (n=71)

Competency	Variables	Chi-square	p-Value	Phi/Cramer's V
Link theory to practice	Gender	3.93	$p = 0.140$	0.235 (small)
	Year of Study	4.30	$p = 0.367$	0.174 (weak)
	Previous Clinical Exp.	1.74	$p = 0.419$	0.156 (weak)
	Confidence Category	0.11	$p = 0.949$	0.039 (v. weak)
Conduct physical exams	Gender	1.71	$p = 0.425$	0.155 (weak)
	Year of Study	3.82	$p = 0.431$	0.164 (weak)
	Previous Clinical Exp.	2.76	$p = 0.251$	0.197 (weak)
	Confidence Category	0.19	$p = 0.908$	0.052 (v. weak)
Comfortable in ward	Gender	7.70	$p = 0.021$	0.329 (moderate)
	Year of Study	2.87	$p = 0.580$	0.142 (weak)
	Previous Clinical Exp.	2.28	$p = 0.320$	0.179 (weak)
Understand hospital hierarchy	Gender	6.68	$p = 0.036$	0.307 (moderate)
	Year of Study	7.33	$p = 0.120$	0.227 (weak)
	Previous Clinical Exp.	1.83	$p = 0.402$	0.160 (weak)

Post-intervention confidence levels were comparable between male and female students. Although a higher proportion of females (28.2%) reported high confidence compared to males (21.9%), the difference was not statistically significant ($p = 0.542$), suggesting that the intervention benefited both genders similarly, Table 4.

Table 4: Gender-wise Change in Confidence Score (Post-Exposure) (n=71)

Confidence Category	Male Frequency (%)	Female Frequency (%)	p-Value (Chi-square)
High confidence (≥ 4.0)	7 (21.9)	11 (28.2)	$p = 0.542$
Moderate confidence (3.0–3.9)	25 (78.1)	28 (71.8)	
Total	32 (100)	39 (100)	

Post-exposure confidence scores were slightly higher among 4th-year students (mean = 3.913), followed closely by 3rd-year students (3.905), with final-year students slightly lower (3.833). However, these differences were not statistically significant ($p = 0.257$), indicating consistent benefits of early clinical exposure across academic levels, Table 5.

Table 5: Comparison of Post-Exposure Confidence Scores Across Years of Study (n=71)

Year of Study	Mean $\pm$ SD	p-Value (ANOVA)
3rd Year	3.905 $\pm$ 0.178	$p = 0.257$
4th Year	3.913 $\pm$ 0.200	
Final Year	3.833 $\pm$ 0.172	

As shown in Figure 1, post-intervention confidence scores were relatively consistent across all academic years. The

median score was similar for 3rd, 4th, and final-year students, suggesting that structured early clinical exposure was equally beneficial regardless of academic level. Slightly greater variability was noted among 4th-year students, as reflected by a wider interquartile range and the presence of outliers. These findings align with the ANOVA results, which indicated no statistically significant difference in post-confidence scores between academic years ($p = 0.257$). This boxplot illustrates the distribution of average self-reported post-exposure confidence scores among 3rd, 4th, and final-year undergraduate students. Median values appear comparable across all three cohorts, with slightly higher interquartile variability observed in the 4th-year group. Outliers are present in the 4th-year data, suggesting individual differences in response to early clinical exposure. Overall, the distribution indicates a consistent positive impact of the intervention across academic years.

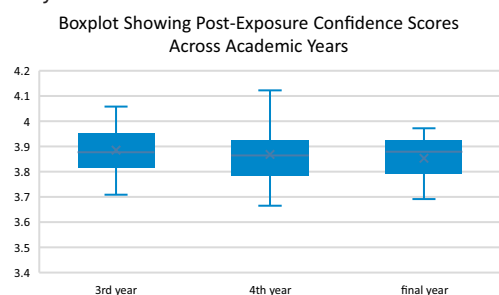


Figure 1: Boxplot Showing Post-Exposure Confidence Scores Across Academic Year

DISCUSSION

The findings of this study demonstrated that structured Early Clinical Exposure (ECE) significantly improved undergraduate students' confidence across multiple domains. Notable gains were observed in patient history taking, physical examination, communication, case presentation, and anxiety management. These results reinforced the value of even short-term, well-structured clinical exposure in enhancing students' readiness for real-world responsibilities [13]. Similar improvements have been reported in the literature. Liu et al., in (2022), Velou et al., in (2020), and Klumpp et al., in (2025) found that structured ECE programs enhanced students' self-reported competence, particularly in basic clinical and communication skills [2, 14, 15]. Other studies from regional contexts, including Reddi et al., in (2025), Yu et al., in (2021), and Maheshwari (2023), also emphasized the value of bedside exposure in bridging the gap between theory and practice [16-18]. The consistency of these outcomes across diverse educational systems supports the broader applicability of ECE interventions. This study also revealed significant gender-based differences. Female students reported greater comfort in ward settings and a better

understanding of hospital hierarchy. These findings are consistent with those of Farajpour et al., in (2024), who noted higher self-assurance among female students in collaborative learning environments [19]. However, no significant differences were observed across academic years, suggesting that ECE benefited students equally regardless of seniority similar to findings by Kachuei et al., in (2024) and Klumpp et al., in (2025), who reported enhanced self-efficacy across all levels [15, 20].

While the overall findings were encouraging, several limitations must be acknowledged. The study was conducted at a single institution with a modest sample size, which may affect generalizability. The reliance on self-reported data introduces potential bias, as responses may reflect perceptions rather than actual performance. Additionally, the gender-wise comparison (Table 4) included small subgroups (e.g., only 7 males and 11 females in the high-confidence category), which may have limited the power of the chi-square analysis. The short follow-up period also captured only immediate changes in confidence and did not assess long-term outcomes. Future studies should involve multi-institutional designs, include objective measures such as OSCE scores, and examine the sustainability of ECE impacts over time.

CONCLUSIONS

This study demonstrated that structured early clinical exposure significantly improved undergraduate students' confidence and perceived competence across technical, interpersonal, and emotional domains. Notably, gender differences were observed in comfort within ward settings and understanding of hospital hierarchy. These findings support the integration of structured ECE into early medical training to ease the transition into clinical practice. This study recommended that health sciences curricula adopt early, structured clinical modules to enhance student readiness. Future studies should use larger, multi-institutional samples and incorporate objective assessments such as OSCEs to validate long-term impacts.

Authors' Contribution

Conceptualization: SA

Methodology: SA

Formal analysis: KA, WR, HG

Writing and Drafting: KA, BH, ZQ, WR, HG, SA

Review and Editing: KA, BH, ZQ, WR, HG, SA

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 Hypoalbuminemia in Acute Ischemic Stroke Patients Presenting at Tertiary Care Hospital, Karachi

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ABSTRACT

Stroke is regarded as the second most commonly reported death worldwide. The effect of albumin is mainly in the early reperfusion phase of acute ischemic stroke. **Objective:** To determine the frequency of hypoalbuminemia in patients with acute ischemic stroke. **Methods:** This cross-sectional observational study was carried out for six months (from April 2024 to October 2024) at the Department of Medicine, Al-Tibri Medical College, Karachi. 196 patients newly diagnosed with stroke patients presented within 24 hours were included, while patients with renal impairment, liver disease, etc., were excluded. SPSS version 24.0 was used for data analysis. Demographical data were reported with post-stratification chi-square applied, keeping p -value < 0.05 as statistically significant. **Results:** A total of 196 patients with acute ischemic stroke were included in this study. The mean age in our study was 44.14 ± 4.49 years. 146 (74.5%) were male and 50 (25.5%) were female. Out of 196 acute ischemic stroke patients, 90 (45.9%) and 106 (54.1%) had and did not have hypoalbuminemia. **Conclusions:** It was concluded that a significant frequency of hypoalbuminemia was observed among patients presenting with acute ischemic stroke. However, association with stroke severity could not be established. Therefore, patients presenting with ischemic stroke ought to be screened for serum albumin levels when presenting to the hospital. In addition, patients with low serum albumin levels must be considered high risk and should be managed accordingly.

INTRODUCTION

Stroke, the second most common cause of mortality, is regarded as a critical health problem, having high prevalence with worsening health outcomes [1]. Around 16.9 million people globally report experiencing a stroke at least once in their lives. The frequency of ischemic stroke is higher in underdeveloped and developing countries than in developed countries [2]. Over 85% of strokes are of the ischemic variety. The incidence of ischemic stroke is ever-increasing [3]. Severity and prevalence of stroke have become a burden to the already compromised healthcare system [4]. Stroke is a multi-factorial disease including biological, non-modifiable, genetic, modifiable, and environmental factors [5]. Low albumin in the blood, or hypoalbuminemia, is emerging as a serious stroke risk

factor. Even a small change in albumin levels can worsen a patient's course, make symptoms stronger, and affect eventual recovery [6]. Several studies link low albumin directly with poorer stroke outcomes. When albumin stays within the normal range, patients tend to progress faster and face lower in-hospital death rates [7]. In contrast, weak albumin levels point to a higher chance of having another stroke, catching infections, dying during the hospital stay, and facing other related problems [8]. Furthermore, low albumin levels in blood tend to have poor prognostic value in intracerebral hemorrhages [9]. In stroke patients, hypoalbuminemia worsens the ischemic stroke [10]. In one of the studies, including 112 patients with ischemic stroke, the aim was to find an association between



hypoalbuminemia and in-hospital outcome. It was reported that 87.7% of patients who died during hospital stay were found to have hypoalbuminemia. In addition, the association between ischemic stroke and hypoalbuminemia was substantially higher in non-survivors ($p=0.001$) [11]. With regards to local data, the frequency of hypoalbuminemia in ischemic stroke patients was reported to be around 42% and 41.6% in research done in KPK and Lahore [12, 13]. Nonetheless, no local research has quantitatively reported and assessed hypoalbuminemia and its association with stroke severity. In another study, the frequency of hypoalbuminemia was reported to be around 43.84 %. Survival was recorded in approximately 32.5% of patients, while 75.8% of patients who did not survive were found to have hypoalbuminemia [14]. The elevated serum albumin levels are related to haemoconcentration, and a reduction in its levels is associated with chronic inflammatory diseases, malnutrition, etc., that represent negative acute phase proteins [15]. Another study reported that around 19% of stroke patients who are hospitalized report hypoalbuminemia [16]. Although numerous studies have explored the clinical outcomes and risk factors associated with acute ischemic stroke, there is limited research specifically examining the frequency and implications of hypoalbuminemia in this patient population. Most existing literature focuses broadly on the prognostic role of serum albumin levels without offering targeted, region-specific data or addressing variations across different healthcare settings.

Furthermore, while hypoalbuminemia is known to influence recovery and mortality rates, its exact prevalence and contributory mechanisms in acute ischemic stroke patients remain under-reported and poorly understood. This gap highlights the need for focused investigations to better define the frequency of hypoalbuminemia in stroke patients and its potential impact on clinical outcomes, enabling more effective management strategies. This study aims to determine the frequency of hypoalbuminemia in patients with acute ischemic stroke.

METHODS

This cross-sectional observational study using non-probability consecutive sampling was carried out at the Department of Medicine, Al-Tibri Medical College (IRB No. ATMC/IERC/13th/01-2023/11) for a period of six months (from April 2024 to October 2024). The sample size for the study was calculated using the WHO software for sample size calculation. Keeping prevalence of hypoalbuminemia at 43.84 % as reported in a study, with 95 % confidence level and margin of error = 7%, the sample size came out to be 196 [14]. Therefore, after ethical approval from the Institutional Review Committee, 196 ischemic stroke patients were

included in the study. Newly diagnosed stroke patients of either gender and between 30-60 years of age, presenting within 24 hours, confirmed through CT-scan showing hypodense area were included in the research while patients with malnutrition, SLE, psychological condition, post-traumatic stress, significant hyponatremia ($\text{Na} < 130$ meq), central nervous system disease (multiple sclerosis or head trauma), impaired renal function, chronic liver disease and chronic obstructive pulmonary disease as well as patients that did not consent for the study were excluded. Patients above 60 years were excluded to minimize confounding factors that are more prevalent in older populations, such as multiple comorbidities (e.g., chronic kidney disease, malignancies, chronic infections) and age-related physiological changes that independently affect serum albumin levels. Including these patients could obscure the relationship between hypoalbuminemia and acute ischemic stroke by introducing additional variables that influence albumin metabolism. The focus on a relatively younger cohort allows for a clearer assessment of hypoalbuminemia's frequency and its direct association with stroke, without the complexities associated with advanced age-related systemic conditions. After ethical approval, data collection was initiated. Before data collection, informed consent was sought from each patient. A self-designed questionnaire was used for collecting baseline demographical data, patients' history, and examination and laboratory findings. A CT scan was done by a minimum of five years of experience. Scans showing a hypodense area were labeled as ischemic stroke and included in the study. For the blood sample, 5 ml of blood was drawn from the peripheral vein using aseptic technique and a 10 cc disposable syringe. Serum albumin was measured using the blood sample. Patients having serum albumin < 3.5 mg/dl were labeled as hypoalbuminemic [17]. Demographics included age, gender, BMI, hypertension, diabetic status, anemia, dyslipidemia, smoking status, socio-economic status, and history of ischemic heart disease. Data were analyzed using SPSS version 24.0. For numbers, the study reported averages and standard deviations; for categories, we simply showed counts and percentages. To see if low albumin levels and ischemic stroke were linked, research ran a chi-square test was run, and p -values under 0.05 were considered meaningful.

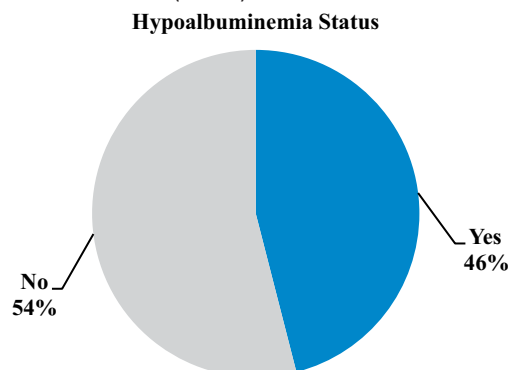
RESULTS

196 patients with ischemic stroke were included in the study from the Department of Medicine of the hospital. The minimum age of included patients was 38, while the maximum was 58, with a mean of 44.14 ± 4.49 years. 146 (74.5%) patients were male, while 50 (25.5%) were female. Other variables and their values have been recorded (Table 1).

Table 1: Baseline Demographics of Patients Included in the Study (n=196)

Variables	Mean $\pm$ SD
Age (Years)	44.14 $\pm$ 4.49
Duration of Disease (Years)	1.72 $\pm$ 0.24
Albumin	1.89 $\pm$ 0.33
GCS	09 $\pm$ 2.35
Height (cm)	158 $\pm$ 7.28
Weight (kg)	78.7 $\pm$ 9.87
BMI (kg/m ²)	26.72 $\pm$ 1.56
SBP (mmHg)	141 $\pm$ 9.81
DBP (mmHg)	92 $\pm$ 7.22
Cholesterol (mg/dl)	196.7 $\pm$ 12.88
Triglycerides (mg/dl)	144.7 $\pm$ 10.43
LDL (mg/dl)	123.8 $\pm$ 9.06
HDL (mg/dl)	41.61 $\pm$ 4.03

Amongst ischemic stroke patients, 70 (35.7%) patients were found to have ischemic heart disease while 126 (64.3%) did not. 90 (45.9%) of patients were reported to have hypoalbuminemia, while 106 (54.1%) did not (Figure 1).

Figure 1: Graphical Representation of Distribution of Hypoalbuminemia Status (n=196)

Among ischemic heart disease patients with hypoalbuminemia, 45 (64.3%) of patients were reported to have hypoalbuminemia, while 25 (35.7%) did not. Among patients without a history of ischemic heart disease, 45 (35.7%) were found to have hypoalbuminemia, whilst 81 (64.3%) did not. A significant p-value of <0.001 was observed between the two groups (Table 2).

Table 2: Relation of Hypoalbuminemia with history of Ischemic Heart Disease (IHD) (n=196)

History of IHD	Hypoalbuminemia		p-Value
	Yes	No	
Yes (n=70)	45 (64.3%)	25 (35.7%)	<0.001
No (n=126)	45 (35.7%)	81 (64.3%)	

DISCUSSION

Despite all the new tests and treatments doctors now have, strokes still kill and cripple millions of people each year. The problem hits hardest in low-income and middle-income countries, where resources are often scarce. In our group

of heart patients, nearly 50% had low albumin levels, a finding that echoes earlier work by Haq and others, who saw hypoalbuminemia show up in 30 percent of stroke cases [18]. Dziedzic's team reported a similar figure of 45.5% [16]. Every study, including ours, found a strong link between low albumin and ischemic strokes, with p-values below 0.05. On average, we measured albumin at only 1.89 0.33 gm/dl. Another report shows that stroke patients who did poorly had slightly higher readings, 2.02 0.67 gm/dl, while those who recovered well had 3.08 0.61 gm/dl [19]. Because albumin levels drop during stress, low serum values may warn doctors that a new stroke is coming or that a current one will be harder to treat [20]. Patients with hypoalbuminemia end up facing worse symptoms and more infections. Hypoalbuminemia, or low albumin in the blood, commonly shows up in people who have an ischemic stroke, and doctors often link it to worse outcomes over time [21]. In a study done in Egypt, every stroke patient who died was found to have hypoalbuminemia. Yet among those who left the hospital, 92.5% had normal albumin levels and only 7.5% still showed low albumin [22]. This shows that serum albumin directly links to how well stroke patients do in the short term. In a study by Abubakar and colleagues, doctors looked at 75 people who had ischemic strokes and found that those with a better outlook had an average albumin level of 3.03 g/dL, while patients with a poor prognosis averaged only 2.08 g/dL (p<0.001) [19]. Because of the many tests done, scientists now believe low albumin levels, or hypoalbuminemia, really do link to a higher chance of having an ischemic stroke. For these reasons, doctors say every stroke patient should get a simple albumin blood test as soon as they arrive at the hospital. When the test shows low albumin, the care team should treat that person as high-risk and adjust the stroke plan right away.

This study was limited by a relatively small sample size and single-center design, which may affect the generalizability of the findings. Additionally, the observational nature of the study and lack of control for confounding factors such as nutritional status, comorbidities, and acute inflammatory response may have influenced serum albumin levels. Future studies should include larger, multi-center cohorts with adjustment for confounders to better evaluate the prognostic role of serum albumin in ischemic stroke.

CONCLUSIONS

It was concluded that many people who arrive at the hospital with an acute ischemic stroke also have low albumin levels in their blood. Yet, the researchers could not link those low levels to how severe the stroke turned out to be. Because of this, every patient with ischemic stroke should have their serum albumin tested as part of the initial work-up. If the test shows the albumin is low, the patient

deserves extra attention and care that matches this possible high-risk sign.

Authors' Contribution

Conceptualization: HA

Methodology: HA, BN

Formal analysis: HA

Writing and Drafting: HZ, AK, AM, NUH

Review and Editing: HA, HZ, BN, AK, AM, NUH

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



Effect of Thrombocytopenia in Pregnancy and Their Maternal Outcome

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ABSTRACT

Gestational thrombocytopenia is a common hematological disorder during pregnancy that can significantly impact maternal health, depending on its severity. **Objective:** To assess the effects of thrombocytopenia severity on key maternal outcomes, including antepartum and postpartum hemorrhage, and placental abruption. **Methods:** In this prospective study, 192 pregnant women diagnosed with thrombocytopenia were analyzed at the Department of Obstetrics and Gynecology, Tertiary Care Hospital, Bahawalpur, from March 07, 2023, to September 06, 2023. We evaluated the severity of thrombocytopenia, maternal age, platelet count, and gestational age, examining their associations with maternal health outcomes using chi-square and correlation analysis. **Results:** No significant correlation was found between thrombocytopenia severity and maternal age ($p=0.467$). Severe thrombocytopenia was strongly associated with increased risks of antepartum hemorrhage (100% of cases), postpartum hemorrhage, and placental abruption ($p<0.001$ for both). Additionally, a moderate positive correlation was observed between platelet count and gestational age ($r=0.478$, $p<0.001$), indicating a potential link between the progression of pregnancy and changes in thrombocytopenia severity. **Conclusions:** It was concluded that severe gestational thrombocytopenia markedly increases maternal risks, underscoring the importance of diligent monitoring and management. The findings advocate for early detection and proactive interventions to enhance maternal outcomes in thrombocytopenic pregnancies.

INTRODUCTION

Thrombocytopenia, defined as a platelet count below $150,000/\mu\text{L}$, is the second most common hematological abnormality in pregnancy after anemia. It affects approximately 7% to 12% of pregnant women, with gestational thrombocytopenia accounting for the majority of cases. While gestational thrombocytopenia is generally mild and resolves spontaneously after delivery, it is crucial to differentiate it from more serious causes such as preeclampsia, HELLP syndrome, immune thrombocytopenic purpura (ITP), and thrombotic microangiopathies, which can lead to significant maternal and fetal morbidity and mortality [1, 2]. In clinical practice, distinguishing benign gestational thrombocytopenia from more serious etiologies is based on the timing of onset, degree of thrombocytopenia, and absence of systemic symptoms. Gestational thrombocytopenia typically

presents in the late second or third trimester with mild reductions in platelet count (usually $>70,000/\mu\text{L}$), lacks associated hypertension, liver dysfunction, or hemolysis, and resolves spontaneously postpartum without requiring specific therapy [2, 3]. In contrast, serious causes such as preeclampsia, HELLP syndrome, and ITP are often associated with more profound thrombocytopenia, systemic signs (e.g., elevated liver enzymes, hypertension, hemolysis), and may require active medical intervention or early delivery. Patients in this study were carefully evaluated through clinical history, laboratory assessments, and exclusion of systemic disease to ensure appropriate classification of thrombocytopenia severity and etiology. The severity of thrombocytopenia plays a pivotal role in determining maternal outcomes. Mild thrombocytopenia is often asymptomatic; however,



moderate to severe thrombocytopenia significantly increases the risk of adverse outcomes such as antepartum hemorrhage (APH), postpartum hemorrhage (PPH), and placental abruption [3]. A study conducted in Ethiopia reported that pregnant women with moderate to severe thrombocytopenia had higher incidences of cesarean sections, APH, PPH, wound hematoma, intrauterine fetal death, preterm delivery, and intrauterine growth restriction compared to those with mild thrombocytopenia [4]. Placental abruption, a severe obstetric complication, has also been linked to low platelet counts. In a prospective study involving 96 thrombocytopenic pregnant women, 21.8% developed placental abruption, 14.6% suffered from PPH, and 7.3% required intensive care unit admission, while the maternal mortality rate was noted at 2.1% [5]. Another recent study emphasized that severe thrombocytopenia was more prevalent among primigravidae and associated with increased adverse outcomes, highlighting the importance of severity grading in clinical practice [6]. Immune thrombocytopenic purpura (ITP), an autoimmune disorder causing accelerated platelet destruction, presents additional challenges in pregnancy. Women with ITP are at an elevated risk of significant bleeding during delivery, and their neonates are susceptible to thrombocytopenia due to the trans-placental transfer of antiplatelet antibodies [7]. This condition necessitates careful monitoring and multidisciplinary management to prevent severe bleeding complications. Even mild thrombocytopenia before cesarean delivery has been identified as a risk factor for PPH. A retrospective cohort study reported that women with mild thrombocytopenia had a threefold increase in PPH risk compared to those with normal platelet counts [8]. This finding underscores the importance of monitoring platelet levels, even when thrombocytopenia appears clinically insignificant. Preventive strategies to reduce postpartum hemorrhage risk in thrombocytopenic pregnant women include routine monitoring of platelet counts throughout pregnancy and optimizing delivery planning. For women with moderate to severe thrombocytopenia, multidisciplinary management involving obstetricians, anesthesiologists, and hematologists is recommended. Prophylactic platelet transfusions are considered when counts fall below critical thresholds, especially before cesarean delivery or anticipated bleeding events [9]. Additionally, active management of the third stage of labor, including uterotonic administration and readiness with blood products, further mitigates PPH risk. The study adhered to these standard preventive protocols to ensure safe delivery outcomes. The correlation between

thrombocytopenia severity and poor maternal outcomes such as APH, PPH, and placental abruption emphasizes the need for timely diagnosis and appropriate management. Early identification of at-risk women and proactive obstetric care can substantially improve maternal and neonatal outcomes. Comprehensive assessment strategies, including routine platelet count monitoring and individualized care plans based on thrombocytopenia severity, are essential components of obstetric care [9, 10]. Although various studies have examined gestational thrombocytopenia, most are limited either by sample size or lack of stratification by severity. Furthermore, there is little consensus on the threshold for intervention and limited local data regarding how varying degrees of thrombocytopenia affect maternal outcomes in our population. Additionally, few studies comprehensively explore antepartum hemorrhage and placental abruption about thrombocytopenia severity. This study aims to fill this gap by evaluating the association between thrombocytopenia severity and key maternal outcomes, including antepartum hemorrhage, postpartum hemorrhage, and placental abruption in a well-characterized cohort of pregnant women. By identifying risk patterns across severity levels, this research aims to improve early diagnosis, risk stratification, and intervention planning.

METHODS

This prospective cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Tertiary Care Hospital, Bahawalpur, from March 07, 2023, to September 06, 2023. Ethical approval (Letter No: EC-2-2023) was obtained from the Institutional Review Board of CMH Bahawalpur, and informed consent was taken from all participants before data collection. The sample size was calculated using Open Epi version 3.01, a free and open-source epidemiological statistics tool. The calculation was based on a prior study by Qureshi et al., which reported a 14.6% incidence of postpartum hemorrhage (PPH) among pregnant women with thrombocytopenia [11]. Using a 95% confidence level, a 5% margin of error, and a population proportion (p) of 0.146, the required sample size was determined to be 192 participants. The formula used by Open Epi is: $n = (Z^2 \times p \times (1-p)) / d^2$. Where: n=required sample size, Z=Z-score for 95% confidence (1.96), p=expected proportion (0.146) and d=precision or margin of error (0.05). Inclusion criteria were pregnant women aged 18–45 years, with thrombocytopenia (platelet count $<150,000/\mu\text{L}$) confirmed via complete blood count (CBC), diagnosed during routine antenatal visits. Exclusion criteria included: Pre-existing hematological disorders (e.g., ITP, aplastic anemia), known autoimmune diseases, chronic liver

disease, known malignancies, and patients who declined participation or had incomplete records. A non-probability consecutive sampling technique was used. All pregnant women who met the inclusion criteria and presented to the Obstetrics and Gynecology Department during the study period were enrolled until the desired sample size was achieved. This approach minimized selection bias by ensuring that each eligible case was included in the analysis in the order of presentation. To ensure accurate differentiation between benign gestational thrombocytopenia and other pregnancy-related causes of thrombocytopenia, such as preeclampsia, HELLP syndrome, and thrombotic microangiopathies, all patients underwent a comprehensive multi-step clinical and laboratory evaluation. This included a detailed medical and obstetric history, serial blood pressure monitoring, urinalysis for proteinuria, liver function tests, renal function tests, and peripheral blood smear review. Women with elevated blood pressure ($\geq 140/90$ mmHg), significant proteinuria, elevated liver enzymes, evidence of hemolysis, or signs suggestive of systemic disease were thoroughly assessed for preeclampsia, HELLP syndrome, or other hematological disorders. Patients diagnosed with any secondary cause of thrombocytopenia were excluded from the study. Furthermore, any patient who developed features of hypertensive disorders or other systemic complications later in pregnancy was also excluded from the final analysis. This rigorous approach ensured that the study population was limited to women with isolated gestational thrombocytopenia, minimizing diagnostic overlap. Data were collected through a standardized, pre-tested proforma that included demographic details (age), clinical parameters (gestational age at diagnosis, platelet count), and maternal outcomes (incidence of APH, PPH, and placental abruption). Platelet count severity was stratified as: Mild: 100,000-150,000/ μ L, moderate: 50,000-99,999/ μ L and Severe: <50,000/ μ L. Data analysis was performed using SPSS Version 26.0. Descriptive statistics (means, standard deviations, frequencies, and percentages) were used to summarize participant characteristics. To evaluate associations between categorical variables, such as thrombocytopenia severity (mild, moderate, severe) and maternal outcomes (presence or absence of PPH, APH, or placental abruption), the Chi-square test was applied. Specifically, cross-tabulations were created comparing the distribution of each maternal outcome across the thrombocytopenia severity groups. The Chi-square test then determined whether these distributions differed significantly, identifying whether increasing severity of thrombocytopenia was associated with a higher frequency of adverse maternal outcomes. Additionally, Pearson correlation analysis was used to explore the relationship between continuous variables,

namely platelet count and gestational age, as well as platelet count and maternal age. The rationale for using Pearson correlation was to determine whether a linear relationship existed between the degree of thrombocytopenia and either gestational progression or maternal demographic factors. This helped assess whether declining platelet counts correlated with advancing gestation or maternal age, which could influence clinical decision-making. Together, these methods allowed for a two-pronged approach: Chi-square testing assessed whether the categorical grouping of thrombocytopenia severity correlated with adverse outcomes. Pearson correlation identified potential linear trends in platelet counts with continuous variables such as gestational age. At this stage, no additional statistical models were applied because the primary objective was to explore bivariate associations. However, recognizing the potential influence of confounding variables (e.g., maternal age, gestational age), we plan to conduct logistic regression analysis in future or larger datasets to validate these findings and adjust for possible confounders. For the current study, results were considered statistically significant at $p < 0.05$.

RESULTS

The study analyzed 192 participants. The average age was 30.20 years with a standard deviation of 7.985, indicating a diverse age range. The mean platelet count was 193,292.96 platelets per microliter, showing substantial variation among participants as suggested by a standard deviation of 101,167.246. The gestational age at diagnosis averaged 26.51 weeks with a standard deviation of 3.400, reflecting diagnoses made primarily in the mid to late second trimester. The distribution of thrombocytopenia severity across different age groups reveals varying patterns. In the Young Adult group (18-25 years), thrombocytopenia was categorized as mild in 27 cases (42.19%), moderate in 25 cases (39.06%), and severe in 12 cases (18.75%) out of a total of 64 cases. This indicated a relatively even spread of severity among the younger age group. For the Adult group (26-35 years), there was a noticeable shift towards milder forms of thrombocytopenia, with 38 cases (57.58%) recorded as mild, while moderate and severe cases are comparatively less frequent at 18 (27.27%) and 10 (15.15%) respectively, out of 66 total cases. This suggests that thrombocytopenia tends to present less severely as the age within this cohort increases. The Middle Age group (36-45 years) shows a distribution of 28 cases (45.16%) with mild thrombocytopenia, 22 cases (35.48%) moderate, and 12 cases (19.35%) severe, out of a total of 62 cases. This pattern is somewhat similar to that observed in the Young Adult group, indicating that the severity of thrombocytopenia does not significantly taper off with

advancing age in this cohort. A p-value of 0.467 indicates no statistically significant association between age groups and thrombocytopenia severity, suggesting that observed variations across age groups do not differ meaningfully on a statistical basis (Table 1).

Table 1: Association of Age Group with Severity of Thrombocytopenia

Age Group	Severity of Thrombocytopenia, n (%)			Total	p-Value
	Mild	Moderate	Severe		
Young Adult (18-25 Years)	27 (42.19%)	25 (39.06%)	12 (18.75%)	64	0.467
Adult (26-35 Years)	38 (57.58%)	18 (27.27%)	10 (15.15%)	66	
Middle Age (36-45 Years)	28 (45.16%)	22 (35.48%)	12 (19.35%)	62	

The data illustrated a distinct pattern where Antepartum Hemorrhage (APH) was exclusively associated with severe thrombocytopenia, with all 34 cases of APH occurring in this group (100%). There were no occurrences of APH in the mild or moderate thrombocytopenia groups. This highlights a critical and significant relationship between the severity of thrombocytopenia and the likelihood of experiencing APH, as supported by a p-value < 0.001. This indicates a statistically significant association, where the severity of thrombocytopenia appears to be a determinant factor in the occurrence of APH (Table 2).

Table 2: Association of Antepartum Hemorrhage with severity of Thrombocytopenia

Antepartum Hemorrhage	Severity of Thrombocytopenia, n (%)			Total	p-Value
	Mild	Moderate	Severe		
No	93 (58.86%)	65 (41.14%)	0 (0%)	158	<0.001
Yes	0 (0%)	0 (0%)	34 (100%)	34	
Total	93 (48.44%)	65 (33.85%)	34 (17.71%)	192	

The analysis of the relationship between the severity of thrombocytopenia and the incidence of postpartum hemorrhage (PPH) reveals a statistically significant correlation (p-value = 0.007). The data demonstrate that as the severity of thrombocytopenia progresses from mild to severe, there is a notable shift in the incidence and severity of PPH. Specifically, the proportion of patients experiencing no PPH declines markedly from 49 (52.69%) in mild cases to only 6 (17.65%) in severe cases. Conversely, the frequencies of mild PPH increase from 26 (27.96%) in mild thrombocytopenia to 13 (38.24%) in severe, and similar trends are observed in moderate and severe PPH, which rise from 14 (15.05%) and 4 (4.30%) in mild cases to 9 (26.47%) and 6 (17.65%) in severe cases, respectively. This progression underscores the clinical importance of closely monitoring and managing thrombocytopenia in pregnant patients to reduce the risks associated with more severe outcomes of PPH (Table 3).

Table 3: Association of PPH with severity of Thrombocytopenia

Postpartum Hemorrhage	Severity of Thrombocytopenia, n (%)			Total	p-Value
	Mild	Moderate	Severe		
No PPH	49 (52.69%)	21 (32.31%)	6 (17.65%)	76	<0.001
Mild PPH	26 (27.96%)	24 (36.92%)	13 (38.24%)	63	
Moderate PPH	14 (15.05%)	12 (18.46%)	9 (26.47%)	35	
Severe PPH	4 (4.30%)	8 (12.31%)	6 (17.65%)	18	
Total	93 (100%)	65 (100%)	34 (100%)	192	

The association between the severity of thrombocytopenia and the occurrence of placental abruption is highlighted by a statistically significant link (p-value < 0.001). The data clearly show that placental abruption is uniquely associated with severe thrombocytopenia, with all instances (n = 9, 26.47%) occurring in this group, while no cases of placental abruption are observed in the mild or moderate thrombocytopenia groups. Notably, among those with severe thrombocytopenia, approximately one-quarter experience placental abruption, contrasting sharply with the absence of this complication in the milder categories. This significant association underscores the critical need for monitoring thrombocytopenia severity in pregnant patients to preemptively manage and mitigate the risk of severe outcomes such as placental abruption (Table 4).

Table 4: Association of Placental Abruption with Severity of Thrombocytopenia

Placental Abruption	Severity of Thrombocytopenia, n (%)			Total	p-Value
	Mild	Moderate	Severe		
No	93 (100%)	65 (100%)	25 (73.53%)	183	<0.001
Yes	0 (0%)	0 (0%)	9 (26.47%)	9	
Total	93 (100%)	65 (100%)	34 (100%)	192	

The correlation analysis provides insights into the relationships among age, platelet count, and gestational age at diagnosis. The correlation between the age of the patient and platelet count was found to be very weak and not statistically significant ($r = 0.004$, $p = 0.953$, 95% CI: -0.137 to 0.145), indicating that maternal age has no meaningful linear association with platelet count in this cohort. Similarly, the correlation between maternal age and gestational age at diagnosis demonstrated a weak negative trend ($r = -0.137$, $p = 0.058$, 95% CI: -0.270 to 0.003), suggesting that older patients may tend to be diagnosed earlier in pregnancy; however, the association did not reach statistical significance and the confidence interval includes zero, implying uncertainty about the direction or strength of this relationship. In contrast, a moderate and statistically significant positive correlation was observed between platelet count and gestational age at diagnosis ($r = 0.478$, $p < 0.001$, 95% CI: 0.345 to 0.592). This indicates that higher platelet counts were more frequently observed at later gestational ages, supporting the possibility that

gestational thrombocytopenia tends to present or worsen earlier in pregnancy and then stabilize or improve in the later stages. The confidence interval here does not include zero, reinforcing the robustness of this association. These findings provide a more precise understanding of how thrombocytopenia may evolve during pregnancy and offer useful insights for monitoring trends in platelet levels throughout gestational progression (Table 5).

Table 5: Correlation Analysis

Variable Pairs	Pearson Correlation (r)	P-Value	n	95% CI for r	Interpretation
Age of Patient and Platelet Count	0.004	0.953	192	-0.137 to 0.145	Very weak positive correlation, not significant
Age of Patient and Gestational Age at Diagnosis	-0.137	0.058	192	-0.270 to 0.003	Weak negative correlation, not significant
Platelet Count and Gestational Age at Diagnosis	0.478	<0.001	192	0.345 to 0.592	Moderate positive correlation, statistically significant

DISCUSSION

The investigation into the implications of gestational thrombocytopenia on maternal outcomes reveals intricate relationships between the severity of thrombocytopenia and various adverse maternal events. Our findings extend and corroborate previous research, establishing severe thrombocytopenia as a critical predictor of increased maternal risk. This discussion integrates and contrasts our findings with seminal studies in the field, enhancing our understanding and management of this prevalent condition. Our study's observation that severe thrombocytopenia markedly increases the incidence of placental abruption and postpartum hemorrhage aligns with Qureshi et al., who documented significant maternal complications in thrombocytopenic pregnancies, including a 21.8% incidence of placental abruption and a 14.6% incidence of postpartum hemorrhage. This alignment underscores the importance of proactive management in severe cases to prevent such adverse outcomes [11]. Similarly, Bai et al., found that gestational thrombocytopenia was the most common cause of thrombocytopenia in their cohort [12]. This supports our findings and highlights the frequent, albeit often benign, occurrence of this condition in pregnancies, necessitating vigilant clinical monitoring. Further echoing our results, Roy et al., reported that the incidence of thrombocytopenia varies across its severity, influencing clinical outcomes [13]. Current study also noted that as thrombocytopenia severity increases, so does the incidence of complications such as antepartum and postpartum hemorrhages. The

clinical implications noted in Abro et al., resonate with our findings, where severe thrombocytopenia was significantly linked to adverse feto-maternal outcomes, emphasizing the necessity for multidisciplinary management strategies to mitigate associated risks [14]. Taş et al., reported significant perinatal complications associated with severe thrombocytopenia, including lower birth weights and earlier deliveries, a pattern also discernible in our study, which suggests that severe thrombocytopenia may predispose to earlier and more complicated deliveries [15]. Mumtaz et al., observed that thrombocytopenia significantly elevated the risk of severe maternal outcomes like placental abruption and the need for blood transfusions, findings that are consistent with our observations of increased complications with progressing thrombocytopenia severity [16]. Sumathi et al., and A Dar et al., provide further context to our results, highlighting the broader spectrum of thrombocytopenia's impact on maternal health and reiterating the critical nature of its management within obstetric care [17, 18]. Harde et al., discuss the complications associated with thrombocytopenia in Indian pregnant women, noting a high correlation with conditions like preeclampsia and infectious causes, which is a crucial consideration that aligns with our findings on the complexity of managing thrombocytopenia [19]. Finally, Chauhan et al., emphasize the prevalence and management complexities of thrombocytopenia in Indian women, highlighting the need for tailored management strategies based on severity, similar to the implications derived from our study [20].

This study did not differentiate between various underlying causes of thrombocytopenia (e.g., gestational vs. pathological), which may have influenced the severity and associated maternal outcomes. Additionally, detailed assessment of management strategies (such as timing of intervention or transfusion protocols) was not included, which could impact the observed complications. Future studies should stratify thrombocytopenia by etiology and evaluate standardized management approaches to better guide risk-based obstetric care.

CONCLUSIONS

It was concluded that this study evaluated the effects of thrombocytopenia severity on key maternal outcomes, specifically antepartum hemorrhage, postpartum hemorrhage, and placental abruption. The findings demonstrate that increasing thrombocytopenia severity is significantly associated with a higher risk of these adverse maternal events. Early identification and accurate classification of thrombocytopenia severity are essential for guiding clinical monitoring and implementing timely interventions to improve maternal safety and outcomes.

Authors' Contribution

Conceptualization: HM

Methodology: SZC

Formal analysis: SU

Writing and Drafting: NH

Review and Editing: HM, SU, SZC, NH

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



Age and Gender Specific Associations between Hyperuricemia and Hypertension: A Cross-Sectional Study in Karachi

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ABSTRACT

Hyperuricemia is increasingly linked to hypertension and various metabolic disorders.

Objectives: To investigate the relationship between hyperuricemia and various anthropometric indices among individuals newly diagnosed with hypertension, with an emphasis on identifying potential age- and gender-specific patterns. **Methods:** The cross-sectional study enrolled 370 newly diagnosed hypertensive adults (230 male and 140 female), aged 18 years and above, using stratified sampling. Anthropometric data, blood pressure, and serum uric acid levels were recorded. Serum uric acid (SUA) levels above 7 mg/dL in males and above 6 mg/dL in females were used to define hyperuricemia. SPSS version 22.0 was used for statistical analysis. Independent t-tests, Pearson's correlation, Chi-square tests, and ANOVA were applied to analyze the data, with a significance level of $p < 0.05$. **Results:** The research found a 27.5% prevalence of hyperuricemia, significantly higher in male (33.9%) than female (17.1%) ($p < 0.001$). Male had significantly elevated systolic BP ($p = 0.043$), waist circumference ($p < 0.001$), and serum uric acid levels ($p < 0.001$). Serum uric acid showed positive correlations with systolic BP ($p = 0.001$), diastolic BP ($p = 0.007$), BMI ($p < 0.001$), waist circumference ($p < 0.001$), and age ($p = 0.024$). Hyperuricemic individuals had significantly higher age, BP, BMI, and waist circumference (all $p < 0.01$). Females with hyperuricemia were older ($p = 0.04$) and more frequently in the >50 age group ($p = 0.036$). **Conclusions:** It was concluded that male showed a higher prevalence of hyperuricemia, while older age was a significant factor for females. These findings suggest the importance of monitoring serum uric acid as an early marker for cardiovascular and metabolic risks, particularly in populations at risk based on gender and age.

INTRODUCTION

Hypertension is a persistent elevation in blood pressure, though diagnostic thresholds may vary slightly across guidelines. According to the European Society of Cardiology/European Society of Hypertension (ESC/ESH, 2018), hypertension is defined as blood pressure equal to or exceeding 140/90 mmHg. In contrast, the American College of Cardiology/American Heart Association (ACC/AHA, 2017) considers blood pressure values of 130/80 mmHg or higher as indicative of hypertension, based on interpretations

from various clinical studies [1, 2]. It remains a major global public health challenge, as it contributes significantly to cardiovascular mortality [3]. Epidemiological data obtained from Pakistan reveal that hypertension affects around 26% of adults, with the condition being more prevalent in urban regions than in rural areas [4]. Uric acid is formed as a result of the breakdown of endogenous cellular components and the metabolism of dietary purines [5]. Initial scientific findings demonstrated that elevated

uric acid levels are involved in causing hypertension by contributing to vascular dysfunction and increased blood pressure [6]. Several pathophysiological pathways have been proposed, including oxidative stress, endothelial dysfunction, and activation of the renin-angiotensin-aldosterone system (RAAS) [7]. Hypertension causes vascular damage by exerting harmful effects on blood vessels, and a rise in uric acid is similarly associated with vascular injury. SUA contributes to oxidative stress primarily by activating NADPH oxidases, which are major enzymes responsible for producing reactive oxygen species in vascular tissues. It also suppresses the activity of endothelial nitric oxide synthase, resulting in a decrease in nitric oxide. This reduction impairs vasodilation, increases vasoconstriction, and results in endothelial dysfunction [8]. Epidemiological studies suggest that uric acid levels above 7 mg/dL in men and 6 mg/dL in women are considered hyperuricemia, and are associated with a 1.5 to 2-fold increased risk of developing hypertension [9]. Though this link appears to vary by age and gender, with a study reporting stronger correlations in younger women [10]. In contrast, a Chinese study found the association to be more prominent in adult men and older women [11]. Pre-menopausal females usually have lower SUA levels in comparison to men, primarily due to the uricosuric effect of estrogen [12]. A longitudinal study has identified hyperuricemia as a risk factor for hypertension and a cause of metabolic syndrome across all age groups [13]. Although growing evidence suggests a link between elevated serum uric acid levels and hypertension, findings remain inconsistent across different populations, age groups, and genders, with limited context-specific data available from Pakistan. This lack of clarity restricts a comprehensive understanding of the role of uric acid in hypertension and its interaction with anthropometric factors. Therefore, this study aims to examine the association between serum uric acid levels, blood pressure, and anthropometric indices in newly diagnosed hypertensive patients in Karachi.

METHODS

This is a cross-sectional analytical study aimed at examining the associations between hyperuricemia and hypertension among newly diagnosed hypertensive individuals in Karachi. The research took place during three months (December 2024 to February 2025) at Fazaia Ruth Pfau Medical College. Ethical approval was obtained from the Ethical Review Committee of Fazaia Ruth Pfau Medical College under protocol number FRPMC-IRB-2024-69, following the ethical standards of the Declaration of Helsinki and its subsequent amendments. This research included 370 newly diagnosed hypertensive participants who met the demographic criteria of being 18 years or older, with both male and female represented. This study utilized

Open Epi software to determine its sample size since this program remains common across epidemiological research. The assessment used the 95% confidence level formula together with a 5% margin of error for proportion estimation. The Karachi adult population contains approximately 26% of hypertension cases [14]. The researchers chose participants through stratified sampling, which included both genders and different age groups. The investigation included healthy adults newly diagnosed with hypertension between 18 and 60 years old, with no history of kidney disease, diabetes, stroke, cardiovascular conditions, metabolic disorders, or the use of medications affecting blood pressure or serum uric acid levels. Participants were also required to provide informed consent in the local language. The study excluded participants who were smokers, pregnant or breastfeeding, used antihypertensive or antihyperuricemic drugs, had a history of gout or cardiovascular issues, kidney disease, diabetes, lipid disorders, or any other ongoing health conditions. Individuals who were unable to provide informed consent or those with recent acute illness or infection were also excluded. The study involved the collection of demographic, anthropometric, and biochemical data. The participants underwent evaluation early in the day following a minimum 12-hour fasting period. Participants provided their demographic characteristics, including age and gender, together with medical status and lifestyle patterns, including physical activity levels and dietary patterns, by following a structured questionnaire. The investigation used three anthropometric measurements for height and weight assessment by a Secastadiometer, while weight measurements were acquired by an electronic digital weighing machine. Body mass index was generated from height measured in meters squared and weight in kilograms. Waist circumference was calculated to 1 cm using a tape placed at the mid-position between the lower margin of the last rib and the iliac crest. A body mass index (BMI) of 30 kg/m² or higher was taken, while central obesity was identified by a waist circumference of more than 94 cm in men and 80 cm in women. Researchers measured hypertension twice through the OMRON 907 automated sphygmomanometer during a minimum five-minute rest period. The two blood pressure readings were averaged to use in analysis where hypertension was indicated by a systolic pressure of 140 mmHg or higher and/or a diastolic pressure of at least 90 mmHg. The Mindray BS-200E biochemical analyzer measured serum uric acid levels from blood samples obtained through venipuncture. The research data were explored by GraphPad Prism version 8.0.2 through a system of recording options. The research presented data as mean $\pm$ standard deviation (SD), together with categorical data displayed through simple percentages. The Shapiro-Wilk

test was used to assess normality before applying parametric tests such as the t-test and ANOVA. To assess differences between groups, the researchers employed the t-test and one-way analysis of variance (ANOVA) for continuous variables, and the chi-square test for categorical variables. Pearson's correlation analysis was used to explore the relationships between age, BMI, blood pressure, and serum uric acid levels. A p-value of 0.05 or less was considered statistically significant. Consent was secured from the study individuals before their inclusion in the study. Data confidentiality assurances were provided to study participants before the researchers performed complete dataset anonymization before analysis. All participants received information about their freedom to join the research study voluntarily and their ability to leave with no negative repercussions.

RESULTS

The research included 370 study participants, comprising 230 male and 140 female, for analysis. Normality of the data was assessed using the Shapiro-Wilk test, confirming that all continuous variables were normally distributed. The results indicated that all variables, including age, systolic and diastolic blood pressure, body mass index (BMI), waist circumference, and serum uric acid levels, were normally distributed, with p-values greater than 0.050. Specifically, the p-values for age ($p=0.065$), systolic BP ($p=0.082$), diastolic BP ($p=0.091$), BMI ($p=0.073$), waist circumference ($p=0.086$), and serum uric acid ($p=0.079$) all exceeded the 0.050 threshold, confirming the assumption of normality. The study displays the essential demographic information for all study participants. The research included both male and female individuals, with a mean age of 38.7 ± 11.6 years for males and 39.2 ± 12.1 years for females. Men exhibited higher systolic blood pressure levels, reaching 136.4 ± 13.9 mmHg, compared to female, who registered 132.7 ± 15.3 mmHg ($p=0.043$). The waist circumference findings demonstrated significant gender differences, with men measuring 94.8 ± 10.6 cm and women 88.7 ± 11.4 cm ($p<0.001$). Male participants also maintained higher uric acid concentrations, averaging 6.8 ± 1.1 mg/dL, while female participants had lower levels at 5.5 ± 1.0 mg/dL (Table 1).

Table 1: General Features of Research Participants($n=370$)

Features	Males ($n=230$)	Females ($n=140$)	p-Value
Age (Years)	38.7 ± 11.6	39.2 ± 12.1	0.842
Systolic BP (mmHg)	136.4 ± 13.9	130.7 ± 15.3	0.043*
Diastolic BP (mmHg)	84.2 ± 11.3	85.9 ± 12.1	0.248
BMI (kg/m^2)	26.4 ± 4.2	27.3 ± 5.1	0.070
Waist Circumference (cm)	94.8 ± 10.6	88.7 ± 11.4	$<0.001^{**}$
Serum Uric Acid (mg/dL)	6.8 ± 1.1	5.5 ± 1.0	$<0.001^{**}$

** Indicates $p<0.010$ (high statistical significance), * Indicates

$p<0.050$ (statistical significance)

Results present that among the 370 participants, 78 male (33.9%) and 24 female (17.1%) were found to have hyperuricemia. The analysis of the study subjects showed that the prevalence of hyperuricemia reached 27.5% (Table 2).

Table 2: Prevalence of Hyperuricemia by Gender

Hyperuricemia Criteria	Males ($n=230$)	Females ($n=140$)	Total ($n=370$)
SUA >7.0 mg/dL (M), >6.0 (F)	78 (33.9%)	24 (17.1%)	102 (27.5%)

Findings present a positive statistical relationship between SUA and systolic BP ($r=0.18$, $p=0.001$), diastolic BP ($r=0.14$, $p=0.007$), BMI ($r=0.21$, $p<0.001$), and waist circumference ($r=0.27$, $p<0.001$). The research data revealed a statistically significant age-related relationship ($r=0.12$, $p=0.024$) between SUA values (Table 3).

Table 3: Correlation of Serum Uric Acid (SUA) with Clinical Parameters($n=102$)

Parameters	Pearson's r	p-value
Age (Years)	0.12	0.024*
Systolic Blood Pressure (mmHg)	0.18	0.001**
Diastolic Blood Pressure (mmHg)	0.14	0.007**
BMI (kg/m^2)	0.21	$<0.001^{**}$
Waist Circumference (cm)	0.27	$<0.001^{**}$

** Indicates $p<0.010$ (high statistical significance) and * Indicates $p<0.050$ (statistical significance)

The study indicates that individuals with hyperuricemia ($n=102$) had a significantly higher mean age (42.1 ± 10.8 years) compared to those without hyperuricemia (38.5 ± 12.0 years) ($p=0.008$). Furthermore, those with hyperuricemia had significantly higher systolic BP (139.6 ± 13.2 mmHg vs. 131.2 ± 14.8 mmHg, $p<0.001$), diastolic BP (87.1 ± 11.2 mmHg vs. 83.2 ± 11.7 mmHg, $p=0.003$), BMI (28.6 ± 4.9 kg/m^2 vs. 26.4 ± 4.6 kg/m^2 , $p<0.001$), and waist circumference (95.2 ± 10.9 cm vs. 89.1 ± 11.4 cm, $p<0.001$) (Table 4).

Table 4: Age Group Distribution of Male and Female with Hyperuricemia(HU)

Age Group (Years)	Males with HU ($n=78$)	Females with HU ($n=24$)	p-value (M vs. F)
18-30	9 (11.5%)	3 (12.5%)	0.932
31-40	28 (35.9%)	2 (8.3%)	0.018*
41-50	20 (25.6%)	8 (33.3%)	0.821
>50	17 (21.8%)	11 (45.8%)	0.036*

** Indicates $p<0.010$ (high statistical significance) and * Indicates $p<0.050$ (statistical significance)

Results present a comparative analysis of clinical parameters between hyperuricemic males and females. Among these parameters, only age showed a statistically significant difference, with females being older (44.3 ± 11.1 years) than males (40.8 ± 10.2 years) ($p=0.04$) (Table 5).

Table 5: Comparative Analysis of Clinical Parameters between Male and Female

Parameters	Male (n=78)	Female (n=24)	p-value
Age (Years)	40.8 ± 10.2	44.3 ± 11.1	0.040*
Systolic BP (mmHg)	140.0 ± 13.2	138.0 ± 13.2	0.300
Diastolic BP (mmHg)	86.4 ± 11.0	87.8 ± 11.5	0.480
BMI (kg/m ²)	28.1 ± 4.8	29.0 ± 5.1	0.360
Waist Circumference (cm)	96.5 ± 11.0	93.9 ± 10.7	0.170

** Indicates $p < 0.010$ (high statistical significance) and * Indicates $p < 0.050$ (statistical significance)

DISCUSSION

The level of link between high uric acid levels and elevated blood pressure exists with diverse changes in individuals, which include demographic characteristics like gender and age. Research shows that a rise in uric acid increases the risk of hypertension and heart diseases, but the exact cause-and-effect links remain under discussion [15]. The mechanistic link between elevated SUA and hypertension may involve uric acid-induced activation of the renin-angiotensin system and promotion of vascular inflammation. These pathways are thought to contribute to increased arterial resistance, which raises systolic BP [16]. This study investigated the gender and age associations between hyperuricemia and hypertension among healthy adults in Karachi. Our findings revealed that male had significantly higher mean serum uric acid (SUA) levels (6.8 ± 1.1 mg/dL) compared to female (5.5 ± 1.0 mg/dL), and a higher prevalence of hyperuricemia was also observed among male (33.9%) versus female (17.1%). Moreover, hyperuricemia emerged as an independent predictor of increased systolic blood pressure in male, whereas no such association was observed in female. Similarly, the previous literature also reported gender disparities in SUA levels. Men diagnosed with hyperuricemia (and mainly at middle-aged stages) exhibited elevated hypertension risks compared to men without the condition, but women showed no such link between hyperuricemia and hypertension. Additionally, the research showed that hyperuricemia functions independently as a risk factor to increase blood pressure levels in male patients but not in female patients [17]. A survey study from China found that serum uric acid (SUA) concentrations were greater in males compared to females. In men, increased SUA levels showed a positive correlation with hypertension. Among women, elevated SUA was significantly linked to both hypertension and diabetes. After controlling for possible confounders, SUA continued to be identified as an independent determinant of high blood pressure in male [18]. The ELSA-Brasil cohort research presented that the mean level of serum uric acid reached 6.3 mg/100 ml for men and 4.7 mg/100 ml for women, which demonstrates increased SUA in male patients. The prevalence of hyperuricemia increased more frequently among elderly women than elderly men, who showed similar SUA levels [19]. Another

study found that postmenopausal women had significantly higher SUA levels compared to premenopausal women, possibly owing to the loss of estrogen's uricosuric effect [20]. Moreover, a sex- and age-adjusted analysis in 2021 showed that hyperuricemia affected 13.6% of the population, but women had a notably lower rate of 2.6% than men at 24.3% based on serum levels exceeding 420mmol/L. She et al., revealed that the elderly female population (≥ 60 years old) experienced higher HUA prevalence than middle-aged and younger women based on their findings [21]. This increase in prevalence in women after menopause supports the finding in our study that female over 50 years had a higher prevalence of hyperuricemia (45.8%) compared to male (21.8%), suggesting that postmenopausal women experience an increase in uric acid due to the loss of estrogen's protective effects [22]. Additionally, She et al., also reported that the occurrence of HUA in males was significantly higher in the 2019 group across all age groups, with young men (20–39 years) showing the maximum prevalence [21]. This trend is reflected in our study, where male aged 31–40 years had a considerably greater incidence of hyperuricemia (35.9%) compared to female (8.3%) in the same age group. In this study, serum uric acid (SUA) was linked with age, systolic and diastolic blood pressure, body mass index (BMI), and waist circumference (WC). These findings are in line with results from a study conducted in Ghana, which also observed significant positive relationships between SUA and factors such as age, BMI, and WC, particularly among women over the age of 45 [23]. Furthermore, a broad-based research performed in China revealed that elevated body mass index (BMI) and waist circumference (WC) were significantly linked to a greater risk of developing new-onset hyperuricemia in individuals with hypertension [24]. The research from the United States established that the combination of hyperuricemia and overweight/obesity significantly increased the occurrence of hypertension, suggesting a synergistic effect between elevated SUA levels and increased body weight. Additionally, a longitudinal study from the Gusu cohort demonstrated that obesity precedes hyperuricemia, which in turn partially mediates the development of hypertension. The mediation analysis indicated that hyperuricemia accounted for a portion of the effect of obesity on both systolic and diastolic blood pressure, highlighting the intermediary role of elevated uric acid levels in the progression from obesity to hypertension [25].

This study was limited by its cross-sectional design, which restricts the ability to establish a causal relationship between serum uric acid levels and hypertension. Additionally, important lifestyle and dietary factors such as purine intake, physical activity, and medication use were not fully assessed, which may have influenced uric acid levels and blood pressure. Future studies should use longitudinal designs with detailed assessment of lifestyle, hormonal status, and metabolic factors to better

understand the gender- and age-specific role of hyperuricemia in hypertension.

CONCLUSIONS

It was concluded that the gender- and age-specific variations observed in serum uric acid levels underline the importance of considering demographic factors in managing hyperuricemia. Given the increased risk of hypertension, particularly in men and postmenopausal women with hyperuricemia, early detection and targeted interventions are crucial for mitigating long-term cardiovascular risks. Upcoming research ought to focus on exploring the pathways linking hyperuricemia to hypertension and assessing the effectiveness of personalized treatment strategies based on gender and age.

Authors' Contribution

Conceptualization: YB

Methodology: AJ, FA, UN

Formal analysis: UN, SZA, NL

Writing and Drafting: YB, AJ, FA, SM

Review and Editing: YB, AJ, FA, UN, SZA, SM, NL

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



Mandibular Symphyseal Height Determination in Various Vertical Patterns

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ABSTRACT

The mandibular symphysis is a crucial anatomical structure influencing facial aesthetics and harmony. Its morphology is pivotal in determining optimal lower incisor positioning, especially in borderline orthodontic cases requiring meticulous treatment planning. **Objective:** To determine and compare symphyseal dimensions in different vertical patterns of skeletal class I cases. **Methods:** The study was designed as a cross-sectional study. Data was analyzed using SPSS 25, with mean and standard deviations used for quantitative variables and frequency and proportions for qualitative data. Statistical significance was assessed using chi-square tests for gender and ANOVA for symphysis height and vertical facial patterns, with a P-value ≤ 0.05 considered significant. **Results:** Male subjects with Hypodivergent ($\downarrow$ D), Normodivergent (ND) and Hyperdivergent ($\uparrow$ D) profiles showed no statistically significant difference in Id-Me, whereas female subjects showed statistically significant difference in Id-Me between ($\downarrow$ D) and ($\uparrow$ D) subjects. Additionally, a notable sex difference was observed in Id-Me, with significant variations between males and females. In contrast, the differences in LI between males and females were found to be statistically non-significant ($P > 0.05$). **Conclusion:** This article reflected that males show longer chin than females.

INTRODUCTION

The mandibular symphysis is a critical anatomical structure within the mandible, encompassing the lower incisors and anterior chin [1, 2]. Morphologically, it comprises two distinct regions: the dentoalveolar symphysis, which is comprised of the alveolar processes and lower anterior teeth, and the basal symphyseal area [1, 2]. The symphysis plays a pivotal role in achieving facial harmony and aesthetics, and its evaluation is essential in orthodontic treatment planning, particularly in cases requiring precise lower incisor positioning [3]. The

dimensions of the dentoalveolar symphysis, specifically its thickness and length, are crucial considerations in orthodontic treatment planning, particularly when planning incisor movements such as protraction or retraction [4, 5]. This is due to the limited accommodative capacity of the symphysis for the lower incisors. Failure to account for these dimensions may result in iatrogenic complications, including fenestrations, dehiscence, gingival recession, and mobility [5, 6]. In orthodontic camouflage cases, with or without extractions, careful

consideration of tooth movement boundaries is crucial during treatment planning. Specifically, the inclinations of the lower incisors can significantly influence post-treatment stability, underscoring the importance of precise planning in orthodontic therapy [7, 8, 10]. These compensations can manifest sagittally through proclination or retroclination of the incisors, or vertically through modifications in symphysis length or incisor eruption [9, 11, 12]. Whenever the maxilla or mandible deviates from the normal skeletally defined growth pattern, dental compensation occurs to camouflage the discrepancy and establish a normal incisor relationship [8, 13-15]. Research by Handleman has demonstrated that patients with high vertical facial patterns exhibit reduced alveolar width compared to those with normal and low facial heights, highlighting the complex interplay between skeletal and dental relationships in malocclusion [16-21]. Traditional cephalometric analysis is a cornerstone in orthodontics, facilitating the evaluation of diverse facial profiles through various linear and angular measurements on intraosseous landmarks. These measurements enable the quantification of anteroposterior jaw and incisal positions, providing valuable insights for treatment planning [13, 16, 17]. Achieving normal occlusion in patients with varying facial patterns relies heavily on dental compensations. Conversely, insufficient dentoalveolar compensation can lead to malocclusions [18]. Thus, accurate alignment of the incisors in both the upper and lower jaws is vital for successful treatment strategy, diagnostic evaluation, long-term durability, and superior results following treatment [19]. A significant correlation exists between the morphology of the symphysis and lower facial height. Specifically, individuals with increased lower facial height tend to exhibit a narrower and more elongated symphysis, suggesting a strong association between these two anatomical parameters [20]. Therefore, the shape and assessment of symphysis in growing individuals may be predictive of adult lower facial height, hence determining overall developing facial pattern in adults [20, 21].

In light of the limited availability of local data and the acknowledged importance of mandibular symphysis in orthodontic treatment, this study seeks to explore the comparison of vertical dimensions of the mandibular symphysis in different vertical patterns of Class I malocclusions within the Pakistani population. By doing so, it aims to determine the anatomical limitations that may influence lower incisor movement and contribute to more stable and effective orthodontic treatment outcomes. The objective of the study was to determine and compare symphyseal dimensions in different vertical patterns of skeletal class I cases.

METHODS

The study was conducted over a duration of six months, from January 2016 to June 2016, as a cross-sectional study (IRB Reference #: FMH-03/02/2025-IRB-1599) in the dental outpatient department of Fatima Memorial Hospital, College of Medicine and Dentistry. The sample size was determined using the World Health Organization's (WHO) formula/calculator. Based on an expected mean symphysis height of 32 mm with a standard deviation of 0.39 mm in patients with skeletal Class I malocclusion, a total sample size of 90 subjects was calculated. This calculation was performed at a 95% confidence level with a desired precision (d) of 0.13 [22]. Participants included in the study were aged between 12 and 30 years and were skeletal class I patients of Pakistani descent presenting to the outpatient department for orthodontic treatment, with an ANB angle between 0 and 4 degrees. Only those with a clinically symmetric face were selected. Exclusion criteria comprised a history of prior orthodontic treatment, any previous maxillofacial surgery, and evidence of root resorption on orthopantomogram (OPG), gingival recession, periodontal problems, or the presence of missing or supernumerary teeth. Vertical facial patterns were classified according to the Go-Gn-SN angle, with high angle defined as $\geq 37^\circ$, normal angle as $28-36^\circ$, and low angle as $\leq 27^\circ$. The Id-Menton measurement was defined as the distance in millimeters from the midpoint of the anterior alveolus of the lower incisor to the menton point, while LI referred to the linear distance in millimeters of bone inferior to the apex of the lower incisor, measured according to Handleman's criteria. Demographic data was recorded for all participants. A non-probability consecutive sampling technique was employed. The skeletal Class I subjects were further stratified into three subgroups based on their vertical growth patterns, as determined by cephalometric analysis. Symphyseal dimensions were subsequently measured on lateral cephalograms for each subgroup. To ensure accuracy and reliability, the symphysis height measurements obtained in this study were reevaluated and confirmed by the supervisor. This quality control measure helped to minimize errors and ensure the precision of the data. The collected data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 25. Quantitative variables, such as age, were summarized using means and standard deviations. Qualitative data, including gender and vertical patterns, were presented as frequencies and proportions. A comprehensive statistical analysis was conducted, incorporating both descriptive and inferential statistics as warranted. To identify significant differences in symphyseal dimensions between groups, various statistical tests were employed. Specifically, categorical variables such as gender were analyzed using chi-square tests, while analysis of variance (ANOVA) was applied to

continuous variables, including symphyseal dimensions, symphysis height, vertical facial patterns, and ANB angle to assess differences between groups (Hypodivergent ($\downarrow$ D), Normodivergent (ND) and Hyperdivergent ($\uparrow$ D)). Statistical significance was set at a p-value of 0.050 or less

RESULTS

This study comprised a total of 90 Skeletal Class I cases. The study population had a Mean Age (MA) of 18.34 years, with a Standard Deviation (SD) of 3.45 years. Frequency distribution of facial divergence according to SN-MP and MMA showed that 43 subjects were (ND), 25 were ($\downarrow$ D) and 22 were ($\uparrow$ D). The percentages for (ND), ($\downarrow$ D) and ($\uparrow$ D) were 47.78%, 27.78% and 24.44% respectively. The (MA) LI of the subjects were 19.66 ± 3.06 mm. The (MA) ID-Me of the subjects were 29.57 ± 3.09 mm [Table 1]. The (MA) and (SD) of LI in ($\downarrow$ D) subjects were 19.28 ± 3.26 mm. The (MA) and (SD) of LI in (ND) subjects were 19.56 ± 2.56 mm. The (MA) and (SD) of LI in ($\uparrow$ D) subjects were 20.27 ± 3.71 mm [Table 1]. The (MA) and (SD) of ID-Me in ($\downarrow$ D) subjects were 28.98 ± 3.71 mm. The (MA) and (SD) of ID-Me in (ND) subjects were 29.53 ± 2.8 mm. The (MA) and (SD) of ID-Me in ($\uparrow$ D) subjects were 30.36 ± 2.8 mm [Table 1].

Table 1: Descriptive Statistics of Id-Me and LI, Between Genders in Various Vertical Profiles

Causes	Gender	Mean $\pm$ SD	SN-MP	Mean $\pm$ SD
Inferior to Apex (LI)	Male	20.28 ± 2.82	($\downarrow$ D)	19.28 ± 3.26
			(ND)	19.56 ± 2.56
	Female	19.14 ± 3.17	($\uparrow$ D)	20.27 ± 3.71
			Total	19.66 ± 3.06
Anterior Alveolus to menton (ID-Me)	Male	30.70 ± 2.96	($\downarrow$ D)	28.98 ± 3.71
			(ND)	29.52 ± 2.80
	Female	28.63 ± 2.90	($\uparrow$ D)	30.36 ± 2.82
			Total	29.57 ± 3.09

Analysis of variance (ANOVA) showed LI, ID-Me between ($\downarrow$ D), (ND) and ($\uparrow$ D) subjects were statistically insignificant [Table 2].

Table 2: Analysis of Variance among Groups (ANOVA)

Variables	Group 1 Hypodivergent (Mean $\pm$ SD)	Group 2 Normodivergent (Mean $\pm$ SD)	Group 3 hyperdivergent (Mean $\pm$ SD)	ANOVA p-Value
LI	19.280 ± 3.2630	19.569 ± 2.5625	20.272 ± 3.7184	0.526
ID-Me	28.980 ± 3.7122	29.523 ± 2.8050	30.363 ± 2.8249	0.310

Lower Incisor (LI) measurements between groups were statistically insignificant in both males and females. ($P > 0.050$). The analysis revealed that the ID-Me measurement did not exhibit significant variations among males across the ($\downarrow$ D), (ND), and ($\uparrow$ D) groups, yielding statistically insignificant results ($P > 0.050$). Similarly, females demonstrated comparable results for ID-Me, with statistically insignificant differences ($P > 0.050$) [Table 3].

Table 3: Comparative Statistics for LI and Id-Me between Genders

Variables	Gender	Categories	Sum of Squares	Mean Square	Significance
Inferior to Apex (LI)	Male	Between Groups	3.915	1.958	0.791
		Within Groups	316.109	8.319	
		Total	320.024	-	
	Female	Between Groups	40.410	20.205	0.135
		Within Groups	444.590	9.665	
		Total	485.000	-	
Anterior Alveolus to menton (ID-Me)	Male	Between Groups	0.883	0.442	0.953
		Within Groups	350.105	9.213	
		Total	350.988	-	
	Female	Between Groups	39.673	19.836	0.093
		Within Groups	364.715	7.929	
		Total	404.388	-	

Further analysis using independent T-tests showed that ID-Me measurements varied significantly between males and females ($P < 0.050$). However, the comparison of symphysis dimensions, specifically lower incisor (LI) measurements, between males and females were statistically insignificant ($P > 0.05$) [Table 4].

Table 4: Independent t-test for Variables

Variables	Male (Mean $\pm$ SD)	Female (Mean $\pm$ SD)	t-value	p-Value
LI	20.280 ± 2.8285	19.142 ± 3.1787	1.777	0.079
ID-Me	30.707 ± 2.9622	28.632 ± 2.9025	3.346	0.001*

DISCUSSION

Research found that roughly 70% of the population possessed a mesomorphic facial morphology, whereas the remaining 30% were divided fairly evenly between brachyfacial and dolichofacial types. Notably, a significant gender-based difference was observed, with long facial types being more prevalent among females and short facial types more common among males. Furthermore, their study demonstrated that symphysis height was significantly greater in individuals with long facial types, a finding that held true for both males and females [1]. Our study revealed that (ND) were about 48% whereas, ($\downarrow$ D) and ($\uparrow$ D) were 51% (27.78% and 24.44% respectively). Mandibular symphysis in males displayed gender dimorphism with longer chin. Shortest symphyseal length was present in females with ($\downarrow$ D) pattern. Evangelista K et al., reported significant findings from their research, indicating that symphysis height was 10% greater in males and was strongly associated with vertical skeletal pattern and gender [4]. Collectively, these factors accounted for 43.6% of the variation observed. Moreover, the investigation disclosed that the basal symphysis exhibited sexual dimorphism, with males displaying a significantly larger structure. Additionally, the morphology of the basal symphysis underwent a transformation with increasing age, characterized by a downward shift and reduction in

vertical dimension. Notably, sagittal and vertical skeletal patterns demonstrated the correlation with alveolar symphysis, whereas gender and age influenced the vertical position of the symphysis. Our study showed statistically significant difference between males and females for Id-Me that varied significantly between genders. The mean for Id-Me in males was 30.7 ± 2.9 , whereas for females was 28.6 ± 2.9 respectively. Males therefore showed a longer symphysis than females in our study. Khan E et al., concluded that the mean symphysis vertical dimension of participants was 49.9 ± 4.7 . Symphysis vertical dimension in males was 48.20 ± 6.17 and 50.78 ± 3.52 in females, which was statistically significant at p value 0.029 [8]. This was contrary with our research showing 30.7073 and 28.6327 in males and females respectively showing increased vertical dimensions for males. Notably, our findings diverge from previous research conducted by Gininda and colleagues, which demonstrated a greater lower anterior dimension in females than males among South African adults with skeletal Class I pattern [17]. Khan et al., previously demonstrated that symphysis morphology is influenced by vertical facial patterns, with ($\uparrow$ D) subjects exhibiting narrower and more elongated symphyses, and ($\downarrow$ D) subjects displaying wider and shorter symphyses [23]. The authors reported that the mean vertical heights of 28.73 ± 3.88 mm, 29.13 ± 2.64 mm, and 27.87 ± 2.75 mm for (ND), ($\uparrow$ D), and ($\downarrow$ D) groups, respectively. Our study's findings support these observations, with mean vertical heights of 29.5233 mm, 30.3636 mm, and 28.9800 mm recorded for (ND), ($\uparrow$ D), and ($\downarrow$ D) groups, respectively. Orthodontists must carefully consider symphysis dimensions during treatment planning for orthodontic camouflage or surgical interventions to minimize the risk of iatrogenic complications, including fenestrations and dehiscence. This consideration is crucial due to the limited adaptive capacity of the mandibular symphysis to accommodate the lower dentition, which can compromise treatment outcomes and patient prognosis. The primary limitation of this investigation was that the measurements were based on 2-dimensional cephalometric radiographs. The study was conducted in our local hospital setup; therefore, results cannot be generalized for other populations. The inclusion criteria of skeletal class I patients eliminated the bias that could have made a difference in effect of dentoalveolar anatomy and symphysis dimensions.

This study was limited by the use of two-dimensional cephalometric radiographs, which may not accurately represent the true three-dimensional morphology of the mandibular symphysis. Additionally, the single-center setting and inclusion of only skeletal Class I patients limit the generalizability of the findings to broader populations. Future studies should utilize three-dimensional imaging

techniques (e.g., CBCT) and include diverse skeletal patterns to provide a more comprehensive assessment of symphysis morphology.

CONCLUSIONS

This study revealed a statistically significant sex-related difference in the mandibular symphysis among the Pakistani population, wherein males demonstrate a significantly longer chin length compared to females. Females ($\downarrow$ D) showed a short symphysis than (ND) and ($\uparrow$ D) subjects.

Authors' Contribution

Conceptualization: SA, NAC

Methodology: SA, AA, MA

Formal analysis: AA, MA, QK, KH, SB

Writing and Drafting: SA, AA, KH, SB

Review and Editing: SA, AA, MA, QK, KH, SB, NAC

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



Changes in Physiological and Biochemical Parameters in Women During the Spontaneous Menstrual Cycle and Following Oral Contraceptives

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ABSTRACT

Oral contraceptive pills (OCPs) are widely used for birth control and management of various gynaecological conditions. While their primary mechanism is to regulate the reproductive cycle, they are known to exert broader systemic effects. However, comparative data on physiological, hormonal, and metabolic parameters between OCP users and women with natural menstrual cycles remain limited. **Objectives:** To evaluate and compare selected physiological signs, reproductive hormones, and metabolic indicators among women experiencing natural menstrual cycles and those on OCPs. **Methods:** A comparative cross-sectional study was conducted involving 80 women aged 18–40 years, divided into two equal groups: natural cycle (n=40) and OCP users (n=40). Data were collected on demographic details, vital signs, and laboratory measures including estrogen, progesterone, LH, FSH, SHBG, TSH, testosterone, HDL cholesterol, and fasting glucose. Statistical analysis was performed using SPSS version 26.0. **Results:** Significant differences were observed in estrogen, progesterone, LH, and SHBG levels, with OCP users showing notably altered hormonal profiles. OCP users also had higher systolic blood pressure and HDL cholesterol, while glucose levels were slightly elevated. No significant differences were found in prolactin, FSH, or haemoglobin. **Conclusions:** It was concluded that OCP use is associated with measurable changes in several physiological, hormonal, and metabolic parameters. These findings highlight the importance of routine monitoring in long-term users and support individualized contraceptive counselling based on clinical risk profiles.

INTRODUCTION

The menstrual cycle is a coordinated physiological event controlled by the Action of several hormones like estrogen, progesterone, luteinizing hormone, and follicle-stimulating hormone (LH and FSH, respectively) [1]. For women with menstruating cycles, these hormones exhibit a precise pattern, controlling ovulation along with the changes in endometrial tissue. With the advent of combined oral contraceptive pills (OCPs), these hormonal patterns are intentionally disrupted to suppress ovulation

and control the menstrual cycle [2]. OCPs have been prescribed for contraception and also for the treatment of menstrual irregularities, acne, polycystic ovary syndrome (PCOS), and dysmenorrhea [3]. Commonly used OCPs have an effect beyond the reproductive system, which includes alterations in cardiovascular parameters (blood pressure and pulse), endocrine changes (SHBG and testosterone), and metabolism, including lipid profile and glucose control. There are many studies evaluating the impact of OCPs on



individual hormones or risk markers, but there is scant information analysing the multi-observational framework of physiology, dynamics, and metabolism side-by-side in a single population [4, 5]. Moreover, variations in study design, population characteristics, and duration of OCP use have led to inconsistent findings, particularly regarding effects on TSH, prolactin, or HDL cholesterol. There is also a paucity of data from South Asian populations where hormonal contraceptive use patterns and baseline physiological profiles may differ due to genetic, dietary, or environmental factors. These gaps underscore the need for well-controlled studies that examine the collective impact of OCP use across multiple domains in comparison to natural cycles [6].

This study aimed to compare physiological (vital signs), hormonal (estrogen, progesterone, LH, FSH, etc.), and metabolic (HDL, glucose) parameters between women with natural menstrual cycles and those using oral contraceptive pills. This study generates comprehensive local data and provides a clearer understanding of the systemic effects of OCP use.

METHODS

This was a comparative cross-sectional study conducted at Health Net Hospital, Hayatabad, Peshawar, from 11 August 2022 to 11 February 2023. Ethical clearance for this study was granted by the Ethics Review Committee of Health Net Hospital, Peshawar, under reference number 3098/HNH/HR. All participants gave written informed consent before data collection began. The study involved 80 premenopausal women, who were divided into two equal groups. Group 1 (natural menstrual cycle group): women with regular menstrual cycles and no history of hormonal contraceptive use for the past six months. Group 2 (OCP users group): Women using combined oral contraceptive pills for at least three consecutive months. In the OCP group, participants were required to have used combined oral contraceptive pills continuously for at least three months before enrolment. OCP use was confirmed through participant interview and verification of pill packaging or prescription details (brand name, dosage, and start date). Only users of monophasic combined OCPs were included to ensure consistency. For the natural menstrual cycle group, participants confirmed no use of hormonal contraceptives (oral, injectable, implant, or patch) within the past six months. This was verified through a detailed contraceptive history questionnaire to exclude any recent or ongoing hormonal intervention. A non-probability purposive sampling method was used. The required sample size for this comparative study was determined using the standard formula for comparing two independent means. Sample size was calculated using the formula: $n = [2 \times (Z_{\alpha/2} + Z_{\beta})^2 \times \sigma^2] / \Delta^2$ Where: $Z_{\alpha/2} = 1.96$ for 95% confidence level, $Z_{\beta} = 0.84$ for 80% power, $\sigma = 35$ (standard deviation of estrogen levels based on Wang et al., 2016) [7],

$\Delta = 25$ (expected mean difference in estrogen levels), substituting: $n = [2 \times (1.96 + 0.84)^2 \times 1225] / 625 = 30.73$ per group. Thus, the minimum required sample size was approximately 31 participants per group. To enhance statistical robustness and account for potential dropouts or missing data, the sample size was increased to 40 participants per group, resulting in a total of 80 women. This number aligns with existing literature and ensures adequate power to detect clinically meaningful differences in hormonal and physiological parameters. Inclusion criteria included women aged 18–40 years, having a body mass index (BMI) between 18.5 and 29.9 kg/m², Regular menstrual cycles (for group 1), and currently using OCPs for more than 3 months (for group 2). Exclusion criteria included history of endocrine disorders (e.g., PCOS, thyroid disease), use of hormonal therapy other than OCPs, chronic illnesses such as diabetes or hypertension, smoking, or alcohol consumption. Data collection was divided into three main components: clinical evaluation, laboratory investigations, and questionnaire-based history. Participants completed a pretested questionnaire that recorded demographic details (age, education, marital status), age at menarche, menstrual regularity, contraceptive history, duration of OCP use, and reported side effects. Vital signs were recorded by trained nursing staff using calibrated instruments: Pulse rate: measured at rest using a digital pulse oximeter. Blood pressure: measured twice in a seated position using a digital sphygmomanometer. Body temperature was recorded orally using a clinical thermometer. Respiratory rate was counted manually over one minute. Anthropometric measurements, height and weight, were recorded to calculate BMI using the formula: $BMI = \text{Weight (kg)} \div \text{Height (m)}^2$. Venous blood samples (5–7 mL) were collected early morning after an overnight fast (8–10 hours). All samples were processed in the institutional diagnostic lab within 2 hours of collection. The following parameters were assessed: hormonal profile, estrogen (E2), progesterone, LH, FSH, prolactin, and TSH. All parameters were measured using electrochemiluminescence immunoassay (ECLIA) technology on the Cobas e411 analyzer (Roche Diagnostics). Additional hormonal and metabolic markers, SHBG and total testosterone, were analyzed via enzyme-linked immunosorbent assay (ELISA). HDL cholesterol and fasting blood glucose (FBG) were measured using standard automated biochemistry analyzers (Hitachi 902). The selection of hormones and metabolic markers (estrogen, progesterone, LH, FSH, TSH, SHBG, testosterone, HDL cholesterol, and fasting glucose) was based on their known physiological relevance and prior evidence indicating their sensitivity to hormonal contraceptive use. These markers represent key pathways influenced by OCPs, including the hypothalamic-pituitary-gonadal axis, thyroid regulation, androgen metabolism, and cardiometabolic risk profiles. To minimize variability due to natural hormonal fluctuations, blood samples for women in the natural

menstrual cycle group were collected during the early follicular phase (day 5–7 of the cycle). For OCP users, samples were taken during days 5–7 of the active pill phase to ensure hormonal stability and comparability between groups. All testing kits and reagents were within quality control expiry dates, and internal quality assurance protocols were followed. All biochemical assays were performed by trained laboratory technicians who were blinded to participant group assignment to prevent measurement bias. The questionnaire was reviewed by two subject experts and pilot tested on a subset of 10 participants for clarity and face validity. Cronbach's alpha was used to assess internal consistency, yielding a value of 0.81, indicating good reliability. The instruments used for physiological and biochemical measurement were calibrated before each data collection day to ensure consistency. All data were entered and analyzed using SPSS version 26.0. Descriptive statistics were used to summarize participant characteristics. Variables included in the analysis were demographic and categorical variables, marital status, education level, age group, BMI category, menstrual regularity, OCP duration, and side effects. Continuous variables were Pulse rate, systolic and diastolic blood pressure, body temperature, respiratory rate, serum estrogen, progesterone, LH, FSH, prolactin, TSH, SHBG, testosterone, HDL cholesterol, and fasting blood glucose. The Shapiro-Wilk test was applied to assess normality for each continuous variable within both groups.

Table 1: Demographic Characteristics of Participants (n=80)

Variables	Categories	Natural (n=40)	OCP Users (n=40)	Total (n=80)	p-value	Cramér's V	Strength
Marital Status	Married	24 (60.0%)	20 (50.0%)	44 (55.0%)	0.369	0.101	Weak
	Unmarried	16 (40.0%)	20 (50.0%)	36 (45.0%)			
Education Level	High School	12 (30.0%)	10 (25.0%)	22 (27.5%)	0.356	0.161	Weak
	Graduate	18 (45.0%)	14 (35.0%)	32 (40.0%)			
	Postgraduate	10 (25.0%)	16 (40.0%)	26 (32.5%)			
Age Group	< 20	6 (15.0%)	4 (10.0%)	10 (12.5%)	0.710	0.093	Very weak
	20–29	30 (75.0%)	33 (82.5%)	63 (78.8%)			
	30–39	4 (10.0%)	3 (7.5%)	7 (8.8%)			
BMI Category	Normal	32 (80.0%)	15 (37.5%)	47 (58.8%)	0.001	0.435	Moderate
	Overweight	8 (20.0%)	24 (60.0%)	32 (40.0%)			
	Obese	0 (0.0%)	1 (2.5%)	1 (1.3%)			

Age at menarche was similar between groups ($p>0.05$), with the majority falling between 12–14 years. Menstrual regularity data were only applicable to the natural cycle group, where 90% reported regular cycles. Among OCP users, half had used contraceptives for 6–12 months. Nearly half reported side effects, with nausea being common. Group-exclusive variables were excluded from significance testing (Table 2).

Table 2: Menstrual and Contraceptive History of Participants

Variables	Categories	Natural Cycle (n=40)	OCP Users (n=40)	Total (n=80)	p-value
Age at Menarche	<12 Years	14 (35.0%)	15 (37.5%)	29 (36.3%)	0.415
	12–14 Years	13 (32.5%)	17 (42.5%)	30 (37.5%)	
	>14 Years	13 (32.5%)	8 (20.0%)	21 (26.3%)	

Since the majority of the variables followed a normal distribution ($p>0.05$), comparisons between groups were performed using the independent samples t-test. For categorical variables, the Chi-square test was used, and where applicable, Cramér's V was calculated to determine the strength of association. Cohen's d was computed for variables that showed statistically significant differences to quantify effect size (small: $d=0.2$, medium: $d=0.5$, large: $d=0.8$ or above). A multiple linear regression model was employed to determine the independent predictors of serum estrogen levels, with variables such as group assignment (natural vs. OCP), age, and BMI entered as predictors. A $p<0.05$ value was considered statistically significant throughout all analyses.

RESULTS

The distribution of age, BMI, marital status, and education level was compared between women following natural menstrual cycles and those using oral contraceptives. Most participants were aged 20–29 years, with no significant difference in age distribution between groups ($p=0.710$, Cramér's $V=0.093$, very weak association). BMI showed a significant difference ($p=0.001$), with a moderate association (Cramér's $V=0.435$); more OCP users were overweight. Marital status and education level did not differ significantly between groups ($p=0.369$ and 0.356 , respectively), indicating weak associations (Table 1).

Menstrual Regularity*	Regular	36 (90.0%)	—	36 (45.0%)	—
	Irregular	4 (10.0%)	—	4 (5.0%)	—
OCP Duration†	<6 months	—	10 (25.0%)	10 (12.5%)	—
	6–12 months	—	20 (50.0%)	20 (25.0%)	
	>12 months	—	10 (25.0%)	10 (12.5%)	
Side Effects Reported‡	Yes	—	18 (45.0%)	18 (22.5%)	—
	No	—	22 (55.0%)	22 (27.5%)	

Results showed detailed comparison of physiological,

hormonal, and metabolic parameters between women with natural menstrual cycles and those using oral contraceptive pills (OCPs). OCP users showed a significantly higher pulse rate (79.32 ± 6.75 bpm) compared to the natural cycle group (74.71 ± 5.57 bpm; $p=0.001$, Cohen's $d=0.74$). Similarly, systolic blood pressure was higher among OCP users (120.33 ± 6.32 mmHg vs. 111.51 ± 8.93 mmHg; $p<0.001$, $d=1.14$), as was diastolic blood pressure (77.42 ± 6.05 mmHg vs. 72.05 ± 4.46 mmHg; $p<0.001$, $d=1.01$). No significant differences were observed in body temperature (98.35 ± 0.64 °F vs. 98.13 ± 0.55 °F; $p=0.095$) or respiratory rate (17.57 ± 1.40 vs. 16.92 ± 1.64 breaths/min; $p=0.061$). Hormonal analysis revealed that OCP users had significantly lower estrogen levels (106.60 ± 38.36 pg/mL) compared to those with natural cycles (186.41 ± 45.82 pg/mL; $p<0.001$, $d=1.89$), progesterone (5.01 ± 1.98 ng/mL vs. 12.07 ± 4.44 ng/mL; $p<0.001$, $d=2.05$), and LH (4.70 ± 1.55 mIU/mL vs. 8.16 ± 2.90 mIU/mL; $p<0.001$, $d=1.49$). Differences in FSH (7.27 ± 2.39 vs. 8.11 ± 2.86 mIU/mL; $p=0.161$), prolactin (15.54 ± 5.18 vs. 15.35 ± 3.64 ng/mL; $p=0.856$), and haemoglobin (12.29 ± 1.21 vs. 12.43 ± 1.14 g/dL; $p=0.599$) were not statistically significant. However, TSH was slightly elevated in OCP users (2.89 ± 0.94 µIU/mL) compared to the natural group (2.33 ± 0.92 µIU/mL; $p=0.010$, $d=-0.60$). In terms of metabolic and additional hormonal markers, OCP users had significantly higher SHBG levels (71.9 ± 17.3 nmol/L vs. 49.7 ± 10.6 nmol/L; $p<0.001$, $d=1.55$) and HDL cholesterol (58.0 ± 10.5 mg/dL vs. 52.2 ± 8.1 mg/dL; $p=0.007$, $d=0.619$), but lower total testosterone (38.3 ± 4.8 ng/dL vs. 43.2 ± 6.6 ng/dL; $p<0.001$, $d=0.849$). Fasting blood glucose was also modestly but significantly elevated in the OCP group (90.5 ± 6.6 mg/dL vs. 86.3 ± 7.7 mg/dL; $p=0.011$, $d=0.586$). These results indicate that OCP use has a measurable influence on cardiovascular, hormonal, and metabolic functions in women (Table 3).

Table 3: Comparison of Physiological, Hormonal, and Metabolic Parameters Between Natural Cycle and OCP Users

Parameters	Natural Cycle (Mean ± SD)	OCP Users (Mean ± SD)	p-value	Cohen's d / Effect Size
Physiological Parameters				
Pulse Rate (bpm)	74.71 ± 5.57	79.32 ± 6.75	0.001	0.74 (Medium)
Systolic BP (mmHg)	111.51 ± 8.93	120.33 ± 6.32	<0.001	1.14 (Large)
Diastolic BP (mmHg)	72.05 ± 4.46	77.42 ± 6.05	<0.001	1.01 (Large)
Body Temperature (°F)	98.13 ± 0.55	98.35 ± 0.64	0.095	—
Respiratory Rate	16.92 ± 1.64	17.57 ± 1.40	0.061	—
Hormonal Parameters				
Estrogen (pg/mL)	186.41 ± 45.82	106.60 ± 38.36	<0.001	1.89 (Large)

Progesterone (ng/mL)	12.07 ± 4.44	5.01 ± 1.98	<0.001	2.05 (Large)
LH (mIU/mL)	8.16 ± 2.90	4.70 ± 1.55	<0.001	1.49 (Large)
FSH (mIU/mL)	8.11 ± 2.86	7.27 ± 2.39	0.161	—
Prolactin (ng/mL)	15.35 ± 3.64	15.54 ± 5.18	0.856	—
TSH (µIU/mL)	2.33 ± 0.92	2.89 ± 0.94	0.010	-0.60 (Very small)
Hemoglobin (g/dL)	12.43 ± 1.14	12.29 ± 1.21	0.599	—
Metabolic and Additional Hormones				
SHBG (nmol/L)	49.7 ± 10.6	71.9 ± 17.3	<0.001	1.55 (Large)
Total Testosterone (ng/dL)	43.2 ± 6.6	38.3 ± 4.8	<0.001	0.849 (Large)
HDL Cholesterol (mg/dL)	52.2 ± 8.1	58.0 ± 10.5	0.007	0.619 (Moderate)
Fasting Blood Glucose (mg/dL)	86.3 ± 7.7	90.5 ± 6.6	0.011	0.586 (Moderate)

Linear regression revealed that oral contraceptive use significantly predicted lower estrogen levels ($\beta = -82.92$, $p<0.001$). Age and BMI did not contribute significantly to the model ($p>0.4$). The model accounted for nearly 49% of the variance in estrogen ($R^2=0.486$), reinforcing the independent impact of OCP use on estrogen suppression (Table 4).

Table 4: Linear Regression Analysis Predicting Estrogen Levels

Variables	β Coefficient (B)	95% Confidence Interval	p-value
Oral Contraceptive Use	-82.92	-104.37 to -61.48	<0.001
Age (Years)	-1.00	-3.50 to 1.49	0.425
Body Mass Index (kg/m ²)	2.03	-3.15 to 7.22	0.437
Constant (Intercept)	244.30	112.55 to 376.04	<0.001

DISCUSSION

This study compared key physiological, hormonal, and metabolic parameters between women undergoing natural menstrual cycles and those using oral contraceptive pills (OCPs). The findings revealed several statistically significant differences, indicating that OCPs exert considerable effects on systemic health markers. Starting with physiological parameters, pulse rate, systolic blood pressure, and diastolic blood pressure were all significantly higher in OCP users. These findings align with those of Collomp et al., who reported increased cardiovascular reactivity among OCP users due to synthetic estrogen components [8]. Similarly, a study by D'Souza et al., showed that oral contraceptives may elevate blood pressure by promoting fluid retention and altering vascular tone [9]. This trend is clinically important, as even modest elevations in blood pressure can increase long-term cardiovascular risk [10]. The hormonal profile from this study indicates a marked suppression of endogenous estrogen, progesterone, LH, and FSH among OCP users. These findings relate to the previously established theory that OCPs suppress gonadotropin secretion to avoid

ovulation [11]. A similar degree of hormonal suppression is documented by Khan *et al.*, who showed substantial decreases in FSH and LH after three months of OCP use [12]. Notably, OCP users had slightly elevated TSH levels, which Jamil *et al.*, and Leonard *et al.*, reported, proposing that alterations in thyroxine-binding globulin by estrogen may modulate feedback regulation of thyroid hormones on the thyroid [13, 14]. SHBG levels were significantly elevated in the OCP group, consistent with the literature that attributes this to hepatic stimulation by synthetic estrogens [9]. Elevated SHBG may bind more circulating androgens, thereby reducing their bioavailability. This may explain the slightly lower total testosterone levels seen in OCP users in our sample, which mirrors the findings of Pereira *et al.*, who observed reduced androgenicity with combined oral contraceptive use [15]. Metabolic changes were also evident. HDL cholesterol levels were significantly higher among OCP users, possibly reflecting the influence of ethinylestradiol, known to improve lipid profiles [16]. At the same time, a modest but significant increase in fasting blood glucose was observed, which was consistent with findings by Ihalainen *et al.*, that OCPs can slightly impair insulin sensitivity in predisposed individuals [11]. This dual effect on lipids and glucose suggests a nuanced metabolic impact of hormonal contraceptives. Menstrual regularity and timing of menarche did not differ significantly between groups, though previous studies have reported mixed results. For instance, Krog *et al.*, found that age at menarche can influence OCP initiation [17], while Blake *et al.*, emphasized that modern low-dose OCPs typically result in regular withdrawal bleeding patterns [18]. Our study supports the notion that menstrual regularity is primarily altered before OCP use rather than as a consequence of it. The regression analysis further confirmed that oral contraceptive use was a strong negative predictor of estrogen levels, even after adjusting for age and BMI. This supports the endocrine-disrupting potential of synthetic hormones, as shown in experimental and clinical work by Löfberg *et al.*, [19]. Although BMI did not significantly predict estrogen levels in our sample, prior research Boamah-Kaali *et al.*, has shown that higher adiposity may alter hormone metabolism, indicating the need for further stratified analyses [20]. The observed hormonal suppression and metabolic shifts underline the importance of individualized contraceptive counselling, especially for women with pre-existing endocrine or metabolic concerns. As noted by Ahmed *et al.*, understanding physiological responses to hormonal contraceptives helps in tailoring methods that align with a woman's health profile and reproductive goals [21]. This study's strength lies in its detailed profiling across multiple

physiological and biochemical domains. However, being cross-sectional, it cannot establish causality.

This study was limited by its cross-sectional design, which restricts causal interpretation, and the lack of longitudinal follow-up to assess long-term hormonal and metabolic changes. Future longitudinal studies are needed to assess long-term changes and reversibility after discontinuation of OCPs, as suggested by Myers *et al.*, [1].

CONCLUSIONS

This study highlights significant differences in cardiovascular, hormonal, and metabolic parameters between women with natural menstrual cycles and those using oral contraceptives. OCP users exhibited elevated pulse and blood pressure, suppressed endogenous reproductive hormones, altered SHBG and testosterone levels, and modest changes in lipid and glucose metabolism. These findings emphasize the systemic effects of oral contraceptives and underscore the importance of individualized assessment and counseling before initiation. Aligning with the objective, the study provides a clearer understanding of how OCP use modulates internal physiology, guiding clinicians toward safer, more informed contraceptive choices.

Authors' Contribution

Conceptualization: SA, FK, NF

Methodology: SA, FK, SY, RK

Formal analysis: FK, NF, SN, RK

Writing and Drafting: SA, NF, SN, SY

Review and Editing: SA, FK, NF, SN, SY

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



Minimal Hepatic Encephalopathy in Patients with Cirrhosis Using Psychometric Hepatic Encephalopathy Score Tests

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ABSTRACT

Minimal hepatic encephalopathy (MHE) is defined as changes in cognitive ability, electrophysiology, and homeostasis of neurotransmission and blood flow in the cerebrum. It is observed in patients with chronic liver disease and cirrhosis who do not have clinical features of overt hepatic encephalopathy. The International Society for Hepatic Encephalopathy and Nitrogen recommend the Psychometric Hepatic Encephalopathy Score (PHES) to easily detect and treat these patients. **Objectives:** To calculate the frequency of MHE amongst patients with cirrhosis of the liver based on the Psychometric Hepatic Encephalopathy Score. **Methods:** This cross-sectional study was conducted at the Department of Medicine, Al Tibri Medical College, Karachi. A total of 235 patients with cirrhosis of the liver with normal mental status were included. Patients were given 5 printed sheets of paper, one each for the number connection test A and test B, line tracing, serial dotting test and digit symbol test. A score of two or less was labelled as minimal hepatic encephalopathy. Chi-square test was applied for checking the association, and a p-value ≤ 0.05 was considered significant. **Results:** There were 62.13% male and 37.87% female. The mean age was 45.47 ± 13.28 years. The mean duration of cirrhosis was 5.54 ± 3.7 years. Most of the patients (53.6%) successfully performed four and five PHES tests, while 22.13% patients successfully performed three tests. 15.32% and 8.94% were successfully performed two and one PHES test, respectively. Minimal hepatic encephalopathy was observed in 24.68% cases. **Conclusions:** It was concluded that the PHES is easily detected and can treat minimal hepatic encephalopathy.

INTRODUCTION

Around 33 % of liver cirrhotic patients suffer from its major complication, i.e. hepatic encephalopathy (HE). Since HE causes significant reductions in the quality of life, it tends to impact the socio-economic status of people. In addition, a high rate of mortality is associated with HE [1, 2]. In the management of HE, scientific bodies such as the European Association for the Study of Liver and the American Association for Liver Diseases laid out the management guidelines [3]. HE is classified according to two factors, the clinical setting in which the symptoms take place [4].

Encephalopathy of liver cirrhosis is similar in characteristics to acute hepatic failure, however, with some unique features as well. Three main types of HE symptoms can occur in patients with cirrhosis: episodic encephalopathy (precipitant-induced), which is seldom observed in hospitals, wherein the superimposed event remains the pivotal factor. The second is persistent encephalopathy (chronic) reported in patients undergoing surgery for portocaval shunt, having extended portosystemic shunts or having TIPS (Trans jugular



Intrahepatic Portosystemic Shunt) in place. The third type is the minimal encephalopathy (subclinical), reflecting altered cognition amongst patients that exhibit normal clinical mental state [5]. The initial or first phase of clinical HE is the minimal HE occurring in a range of 30 to 84 % of cirrhotic patients [6]. Minimal HE patients show defective neuro-cognition in terms of coordination, attention, vigilance, reaction time, fine motor abilities and memory [7]. In the absence of any recognizable symptoms of HE, the mildest of minimal HE form characteristically includes subtle deficits in psychomotor and cognitive [8]. Minimal HE (MHE) patients report higher prevalence of road traffic accidents, higher chances of development of episodic overt HE and poorer quality of life, thus imposing a considerable socio-economic burden on both family and overall healthcare systems [9]. Generally, minimal HE is linked to a poor prognosis and possibly as an independent survival predictor. Mostly alcoholics, elderly populations are more prone to developing minimal HE, who might already have a history of overt HE with hepatic dysfunction coupled with esophageal varices [10]. PHES questionnaire encompasses five exams (pencil and paper) viz: Connection of Numbers Test- A and B (NCT- A/B) and (SDT), Line Drawing Test (LDT) and Serial Dotting Test (SDT) and Digit Symbol Test (DST). Each and every test evaluates separate neurocognitive abilities [11]. Clinicians can conveniently use PHES across various cultures. Nonetheless, PHES test results might or tend to be influenced by educational levels, age and gender [12]. Moreover, a study reported that around 30-50 % hepatic cirrhosis patients demonstrate minimal HE after testing by PHES or critical flicker frequency (CFF), which is a type of neurophysiological technique. This represents the first stage of the spectrum of HE [13, 14]. By using a simple Psychometric Hepatic Encephalopathy Score, it is possible to easily detect and treat these patients. Early detection and treatment not only improve cognition and psychomotor deficits and quality of life.

Till date, there has been no study conducted in Pakistani population regarding prevalence of minimal HE and there is a need to have a data regarding such patients and rationale is to know the magnitude of these patients with minimal hepatic encephalopathy requiring early recognition and treatment which will avoid development of overt HE thus reducing the economic burden. This study aimed to determine the frequency of MHE in patients with cirrhosis of the liver using the PHES.

METHODS

A cross-sectional descriptive study was carried out on outpatients visiting the Department of Medicine, Al Tibri Medical College and Hospital, Karachi, from January to July 2024 (ERC Approval Number- ATMC/IERC/13th (01-

2023)/23). The sample size was calculated by using the WHO sample size calculator by assuming an expected prevalence of minimal hepatic encephalopathy of 25%, a confidence level of 95%, and a margin of error (precision) of 5% [6]. A total of 235 patients of either gender aged 18 to 70 years suffering liver cirrhosis and normal mental status were included. After explaining the study's protocol, informed consent was obtained. A non-probability consecutive sampling was used. Patient with overt encephalopathy, altered mental status with Glasgow coma scale of less than 15, abnormal EEG record, had history of TIPS or shunt surgery, had any known neurological disease and with electrolyte imbalance (Blood sugar >250mg/dl or <50 mg/dl, Urea >50mg/dl, Creatinine >2.0 mg/dl, Sodium >150 mEq or <130 mEq, and Potassium >4.5 mEq or <3.0 mEq) were excluded. Minimal HE was defined as failure to perform two (2) of the Five (5) psychomotor hepatic encephalopathy score (PHES) tests (One point was given to each test performed successfully) [12]. The patients were shown a paper having numbered circles totaling 25 at random. The task was connecting circles starting from 1 and ending on 25, with a time limit of 30 seconds. The patients were shown a paper with 26 circles, having 13 numbered circles and 13 circles with alphabets (A to L) at random. It was a matter of associating the numbers and letters alternately, i.e. Interchanging 1-A-2-B-3-C and so on in 1 minute. The patients were advised to follow the pattern of the 5mm broad path as fast as he could without crossing the boundaries. Tracing should be completed in 10 minutes. The patients were requested to fill in the center of circles on a sheet of paper, which had 100 circles. The task was to complete in 1 minute. The Digit symbol was administered wherein the participant was presented with several double-boxes in a sheet of paper with the numbers furnished on the upper area. One way to draw a symbol related to this number in the lower side of the boxes. There were nine fixed pairs of numbers and symbols which were placed at the top of the test sheet to be referred. The exercise would have entailed making accurate ticking in at least 50 boxes within 90 seconds. Cirrhosis was declared Hepatic disorder of any cause more than 6 months with a decompensation phenomenon as regards presence of any three of the following clinical and laboratory elements i.e. Jaundice (yellow discoloration of sclera with bilirubin level >2 mg/dl), PT >2 seconds over control or INR >1.3, Albumin <3gm/dl, Platelets <100000/cmm, and Ascites, Splenomegaly, Hepatic encephalopathy, Presence of varices on Upper GI endoscopy, presence of fibrosis and nodule formation in liver. A consultant neurologist examined all the patients to assess their mental status and GCS. Each of the patients was provided with 5 pieces of printout papers, each one being Number connection test A,

Number connection test B, Line tracing (trail drawing test), Serial dotting test and Digit symbol test (PHES test). The results were customized in the pre-approved Performa. SPSS version 25.0 was used to compare the data collected. Statistical calculations were done. Chi-square test has been used to test the association of minimal hepatic encephalopathy with gender, age and ASA class. Fisher's exact test was implemented, where the minimum criteria of count did not apply in the method of meeting the standard of applying a chi-square test. A p-value of 0.05 or less was assumed to be significant.

RESULTS

The mean age of study subjects was 45.47 ± 13.28 years (95%CI: 43.77 to 47.18). The age was also evaluated in patients with/without MHE. The results showed that the mean age was 46.62 ± 13.57 years among patients with MHE, and it was 45.09 ± 13.20 years among patients without MHE. The average duration of cirrhosis pain was 5.54 ± 3.7 years. Duration of cirrhosis was 5.46 ± 3.69 years and 5.56 ± 3.71 years, respectively, among patients with or without MHE (Table 1).

Table 1: Descriptive Statistics of Age and Cirrhosis (n=235)

Variables	Overall	With MHE	Without MHE
Age (Years)			
Mean $\pm$ SD	45.47 ± 13.28	46.62 ± 13.57	45.09 ± 13.20
95%CI (LB - UB)	43.77 - 47.18	43.05 - 50.19	43.13 - 47.05
Median (IQR)	47.0 (21.0)	48.0 (20.25)	46.0 (21.0)
Range	52.0	51.0	52.0
Minimum	18.0	18.0	18.0
Maximum	70.0	69.0	70.0
Duration of Cirrhosis (Years)			
Mean $\pm$ SD	5.54 ± 3.70	5.46 ± 3.69	5.56 ± 3.71
95%CI (LB - UB)	5.06 - 6.02	4.49 - 6.43	5.01 - 6.11
Median (IQR)	5.0 (5.0)	5.0 (6.0)	5.0 (4.5)
Range	19.0	14.0	19.0
Minimum	1.0	1.0	1.0
Maximum	20.0	15.0	20.0

It was also observed that overall, 146 male and 89 females were included. It was observed that the age of 37 patients was ≤ 30 years, 50 were between 31-40 years, 60 between 41-50 years, 56 between 51-60 years' age group, and the age of 32 patients was 61-70 years. As far as the duration of cirrhosis was concerned, it was evaluated that 151 patients had cirrhosis since <5 years, 58 patients for 5-10 years, and 26 had cirrhosis for 10 years (Table 2).

Table 2: Frequency Distribution of Gender, Age, Duration of Pain, and Confounders (n=235)

Variables	Frequency (%)
Gender	Male 146 (62.13%)
	Female 89 (37.87%)

Age Group (Years)	≤ 30	37 (15.74%)
	31-40	50 (21.28%)
	41-50	60 (25.53%)
	51-60	56 (23.83%)
	61-70	32 (13.62%)
Duration of Cirrhosis (Years)	< 5	151 (62.46%)
	5-10	58 (24.68%)
	> 10	26 (11.06%)

The results showed that 8.94% of patients successfully performed one PHES test, 15.32% successfully performed two PHES tests, 22.13% successfully performed three PHES tests, 31.06% successfully performed four PHES tests, and 22.55% performed five PHES tests (Figure 1).

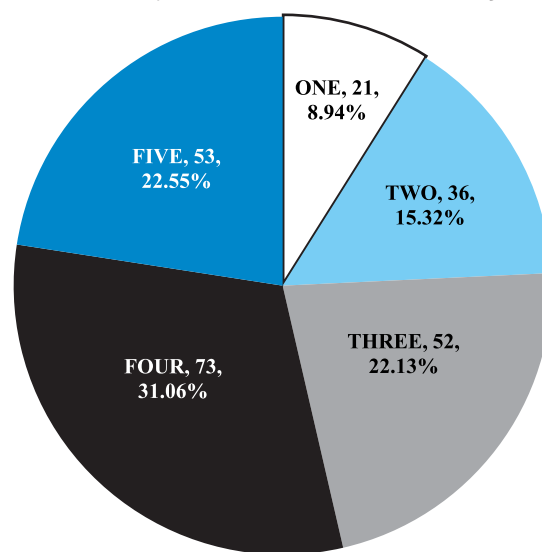


Figure 1: Percentage of Successfully Performed ONE PHES Test (n=235)

The outcome, i.e. Minimal HE using psychometric hepatic encephalopathy score, showed 24.68% patients had MHE with a 95% CI of 19.60% to 30.57% (Figure 2).

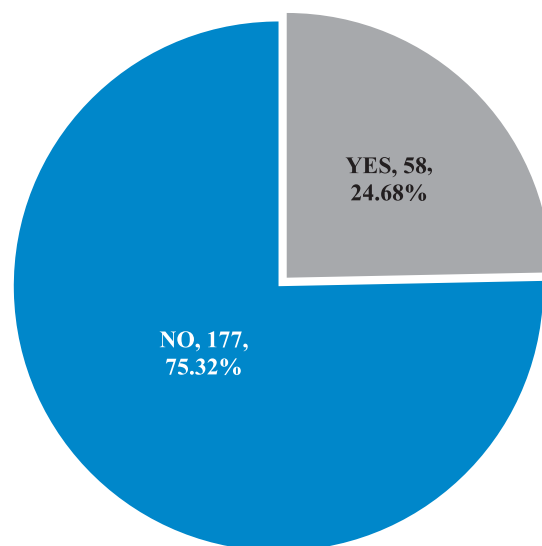


Figure 2: Percentage of MHE (n=235)

The association of MHE using the PHES was evaluated with gender, age, and duration of cirrhosis. Results demonstrated no significant association of MHE with gender ($p=0.52$), age ($p=0.48$), and duration of cirrhosis ($p=0.85$) (Table 3).

Table 3: Association of Minimal Hepatic Encephalopathy with Gender, Age, and Duration of Cirrhosis ($n=235$)

Variables		Minimal Hepatic Encephalopathy		Total	p-Value	Odds Ratio	95 % CI
		Yes (n=58)	No (n=177)				
Gender (Years)	Male	34 (23.3%)	112 (76.7%)	146	0.526**	0.82	0.45-1.51
	Female	24 (27%)	65 (73%)	89			
Age Group (Years)	≤30	8 (21.6%)	29 (78.4%)	37	0.480**	1.45	0.49-4.30
	31-40	8 (16%)	42 (84%)	50		1.00	-
	41-50	18 (30%)	42 (70%)	60		2.25	0.88-5.74
	51-60	15 (26.8%)	41 (73.2%)	56		1.92	0.74-5.02
	61-70	9 (28.1%)	23 (71.9%)	32		2.05	0.7-6.05
Duration of Cirrhosis	<5	39 (25.8%)	112 (74.2%)	151	0.859**	1.21	0.59-2.47
	5-10	13 (22.4%)	45 (77.6%)	58		1.00	-
	>10	6 (23.1%)	20 (76.9%)	26		1.04	0.35-3.12

**Not Significant at 0.050 level

DISCUSSION

In a study, the prevalence of Minimal HE was varied and was found in around 20 to 84% patients having cirrhosis [15]. Minimal HE is described as defects in cognition in cirrhotic patients and/or shunting of porto-systemic, which is diagnosed post overt HE exclusion and alternate neuropsychological impaired diagnoses are made [16]. Various neuropsychological techniques are utilized for diagnosing deficits in cognition among cirrhotic patients. Such included extended neuropsychological assessments, computerized testing. Extended neuropsychological assessments are done on the basis of referral by experts, which is sometimes difficult to validate [17]. In current study, the mean age was 45.47 ± 13.28 years (95% CI: 43.77 to 47.18). Out of 235 cases, 146 (62.13%) were male and 89 (37.87%) female. The male-to-female ratio was 1.64:1. In present study, most patients (53.6%) successfully performed four and five PHES tests, while 52 (22.13%) patients successfully performed three tests, and 36 (15.32%) and 21 (8.94%) successfully performed two and one PHES test, respectively. Frequency of minimal HE (MHE) was observed in 24.68% (58/235). Maldonado-Garza *et al.* reported in their study that, prevalence of MHE was 55.8% ($n=58$) [18]. In another study, Li *et al.*, in 409 cirrhotic patients using TMT and SDT, the prevalence of MHE was 29% [19]. By various validation studies, the cutoff of PHES for diagnosis MHE was ≤ -4 points [20-22]. However, validation studies in other countries reported a cutoff of PHES for diagnosis MHE at ≤ -5 points [23]. In another investigation, 48% of patients with cirrhosis were found to be afflicted with MHE. In a study, however, a reduced MHE

incidence (25.6%) had been reported [24]. It may be because the liver function of the patients involved in the research was not the same. In another research, age and education impacted all 5 neuropsychological PHES tests. However, they were not discriminated against by gender at any age bracket. PHES did not correlate with age, education and gender in the healthy volunteer group [25]. This study was limited by the use of a single diagnostic tool (PHES), which may not capture all aspects of cognitive impairment, and the lack of consideration of confounding factors such as liver disease severity and educational status. Future studies should incorporate multiple neuropsychological tools and stratify patients by disease severity to improve the accuracy of MHE diagnosis.

CONCLUSIONS

It was concluded that this research brings to the fore the usefulness of the DOTS-psychometric hepatic encephalopathy score (PHES) tests in the identification of minimal hepatic encephalopathy of cirrhotic patients and the importance of screening patients routinely. Disease progression can be stopped by intervention, and early diagnosis can enhance the patient outcome and boost the standard of living.

Authors' Contribution

Conceptualization: HZ

Methodology: HZ, AM, HK

Formal analysis: HZ

Writing and Drafting: AK, WM, HA, MFW

Review and Editing: HZ, AK, WM, HA, MFW

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 Overuse in Paediatric Gastroenteritis: A descriptive cross-sectional study from Children's Hospital

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ABSTRACT

There is a major role of gastroenteritis in pediatric patients. Knowing about prescription trends is very useful in optimizing treatment and minimizing the use of unnecessary medication.

Objective: To assess the frequency of antibiotic prescriptions in children with gastroenteritis and evaluate the appropriateness of these prescriptions based on clinical criteria and the impact this line of management has on the duration of their hospital stay. **Methods:** A total number of participants was n= 200 children, diagnosed as gastroenteritis. Demographic, clinical and antibiotic data were collected. SPSS version 21.0 was used in performing statistical analysis with p < 0.001 as the level of significance. **Results:** In 200 children with gastroenteritis (mean age 4.5 ± 2.3 years; weight 14.2 ± 4.1 kg), 50% had severe dehydration, 60% had fever, and 75% had vomiting. IV rehydration was required in 65%, with a mean hospital stay of 24.2 ± 5.5 hours. Inappropriate antibiotic use occurred in 75% of cases. Dehydration (OR = 3.50), fever (OR = 1.87), and inappropriate antibiotic use (OR = 2.75) significantly predicted IV rehydration (all p < 0.001). Dehydration and inappropriate antibiotic use also significantly prolonged hospital stay.**Conclusion:** Antibiotic prescription rates for pediatric gastroenteritis are extremely high and alarmingly, the majority of them are inappropriate.

INTRODUCTION

Diarrhea, vomiting, fever and dehydration due to gastroenteritis is one of the most common illnesses of children in the world [1, 2]. Prevalence of invasive disease is high and it plays a major role in morbidity and hospitalization in pediatric patients and constitutes a major cause of morbidity and hospitalization in developing countries of the low- and middle-income categories characterized by poor sanitation and poor access to health services. The causes of the disease include viruses (such as rotavirus, norovirus), bacteria (such as Escherichia coli, Salmonella, Shigella, Campylobacter), and parasites (such as Giardia, Cryptosporidium) [3]. Supportive management of gastroenteritis is directed towards purely supportive

care, with the aid of lots of fluids and oral electrolyte replacement, tailored diet modifications and symptomatic treatments [4]. In children, most of the cases are caused by viral gastroenteritis; antibiotics are often prescribed even though indications are limited [5]. A much lesser proportion is due to bacterial gastroenteritis for which specific antibiotic treatment is necessary. Antimicrobial resistance (AMR), or the resistance bacteria build up due to indiscriminate antibiotic use, is associated with higher risk of treatment failure and complications in a patient [6]. According to The World Health Organization (WHO) and national guidelines, the use of antibiotics should be judicious, only done in cases of suspected bacterial



infection, e.g. severe dysentery, high fever especially with systemic signs, and only when the bacteria are confirmed with culture results [7]. Yet, common clinical prescribing practices are not appropriate, which results in too much drug use, development of resistance, and adverse drug reaction [8]. In Pakistan, the current management and therapeutic guidelines for acute gastroenteritis (GE) appear to be ineffective, leading to suboptimal cure rates and a rising number of hospital admissions.

Many patients experience recurrent GE episodes, indicating that the existing treatment protocols may not be adequately addressing the underlying causes or providing long-term relief. This highlights the need for further research to identify the key factors contributing to treatment failure, including potential gaps in adherence to guidelines, antimicrobial resistance, and socioeconomic constraints affecting access to care. Additionally, there is an urgent need to develop cost-effective treatment strategies that align with international guidelines while being specifically tailored to Pakistan's healthcare infrastructure, resource availability, and patient population. To assess the frequency of antibiotic prescriptions in children with gastroenteritis and evaluate the appropriateness of these prescriptions based on clinical criteria and the impact this line of management has on the duration of their hospital stay.

METHODS

It was a descriptive cross-sectional. The study was conducted for six months from August 2024 to January 2025 at the department of Pediatrics, Khairpur Medical college Khairpur Mir's. The age range of children was 1-8 years, diagnosed as having gastroenteritis. The sample size for this cross-sectional study was calculated using Cochran's formula: $n = (Z_{1-\alpha/2})^2 \times p \times (1-p) / d^2$, where $Z = 1.96$ for 95% confidence, $p = 0.5$ (assumed prevalence of antibiotic overuse), and $d = 0.07$ (margin of error). The final sample size was rounded up to 200. Patients with the diagnosis of acute gastroenteritis (GE) defined by symptoms such as diarrhea, vomiting, dehydration, abdominal pain, or fever, presenting for medical care within 48 hours of symptom onset were included in this study. Male patients of all ages eligible at hospitals, clinics, or primary healthcare centers in Pakistan provided they given informed consent. Patients who have chronic or recurrent GE lasting greater than 2 weeks, pre-existing gastrointestinal disorders or severe comorbid medical conditions such as uncontrolled diabetes mellitus, renal failure or immunodeficiency were excluded. Subjects were then be excluded if they had taken antibiotics or probiotics in the last seven days, have incomplete medical records, or did not enroll in the study. Information from both children and their parents, regarding the patient biodata, hospital admission history of the patient, previous surgical procedures of the patient, oral hygiene habits, for example,

tooth brushing and the medical tests which are performed in hospital during the stay of the patient, was gathered using a structured data collection form. Mostly commonly prescribed antibiotics were used for gastroenteritis. In taking a decision as to the prescribing of antibiotics, hospital indicators such as laboratory test results (especially culture sensitivity tests), past medication history, current symptoms and physical condition at time of admission were employed. An informed consent was obtained from the parent/guardian to collect additional data from the child by administering a structured questionnaire. The questionnaire covered the person's name, age, sex, and symptoms like diarrhea, vomiting, fever, and abdominal cramps. Data were analysed using SPSS version 21.0. Descriptive statistics were used to summarize the data. Categorical variables (e.g., gender, residence, antibiotic use, dehydration status, socioeconomic level) were presented as frequencies and percentages. Continuous variables (e.g., age, weight, fever duration, hospital stay length) were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on the distribution. To assess associations between categorical variables, the Chi-square test was used. For continuous variables, independent sample t-tests or ANOVA were applied where appropriate. A p-value ≤ 0.05 was considered statistically significant. This study was conducted following ethical principles from the Institutional Review Board (IRB: KMC/RERC/118), and informed consent obtained from all participants.

RESULTS

The study included 200 pediatric patients with gastroenteritis, with a mean age of 4.5 ± 2.3 years and weight of 14.2 kg. Dehydration was common, with 50% having severe dehydration, and 60% experienced fever, while 75% had vomiting. The average duration of diarrhea was 3.5 days. Antibiotic use was reported in 60% of cases, with 75% of those being inappropriate. Approximately 65% of the children required intravenous rehydration, and the average hospital stay was 24.2 hours. These findings highlight the prevalence of dehydration, inappropriate antibiotic use, and the need for IV rehydration in managing pediatric gastroenteritis see Table 1.

Table 1: Demographic Characteristics of Pediatric Gastroenteritis Patients

Variables	Frequency (%) / Mean $\pm$ SD
Age (Years)	4.5 $\pm$ 2.2
Gender	
Male	200 (100)
Weight (Kg)	14.2 $\pm$ 4.1
Dehydration Status	
Mild	30 (15)
Moderate	70 (35)

Severe	100 (50)
Fever (Present)	120 (60)
Vomiting (Present)	150 (75)
Abdominal Pain (Present)	140 (70)
Diarrhea Duration (Days)	3.5 ± 1.7
Antibiotic Use (Yes)	120 (60)
Inappropriate Antibiotic Use	150 (75)
IV Rehydration Required	130 (65)
Hospital Stay (Hours)	24.2 ± 5.5

The study showed that 60% of pediatric gastroenteritis cases were treated with antibiotics, even though 80% were viral in origin, which need not be treated by antibiotics. Thus, the high level of inappropriate antibiotic use (75%) indicates that treatment is probably prescribed in the face of diagnostic uncertainty, symptoms severity. Bacterial gastroenteritis was only found to be justified to use antibiotics in 20% of cases. This underlines the necessity to strictly follow guidelines and provide diagnostic examination before giving antibiotic see Table 2.

Table 2: Antibiotic Use and Clinically Presumed Etiology in Pediatric Gastroenteritis Cases

Variables	Frequency (%)
Prevalence of Antibiotic Use	120 (60)
Clinical Presentation	
Viral Gastroenteritis (presumed)	160 (80)
Bacterial Gastroenteritis (presumed)	40 (20)

Multivariate regression analysis identified moderate-to-severe dehydration, fever, poor oral intake, and inappropriate antibiotic use as significant predictors of longer hospital stays in children with acute watery diarrhea. Dehydration increased the stay by 3.8 hours, fever by 2.6 hours, poor oral intake by 3.1 hours, and inappropriate antibiotic use by 3.7 hours. A presumed viral etiology reduced the stay by 2.2 hours, while higher body weight was linked to a shorter stay. Gender, residence, and vomiting had no significant impact see Table 3.

Table 3: Unadjusted and Adjusted Analysis of Clinical Characteristics Associated with Length of Hospital Stay

Variables	Mean LOS (Hours)	Unadjusted β (SE)	p-value	Adjusted β (SE)	p-value
Age (Years)	38.2	1.2 (0.4)	0.001**	0.9 (0.3)	0.001**
Male Gender	39.5	2.1 (1.1)	0.06	1.4 (1.0)	0.150
Weight (Kg)	37.0	-0.8 (0.3)	0.001**	-0.6 (0.2)	0.020*
Urban Residence	35.6	-1.5 (1.2)	0.21	-0.9 (1.1)	0.400
Fever Present	41.3	3.0 (1.0)	0.001**	2.6 (0.9)	0.004**
Moderate-to-Severe Dehydration	45.8	4.5 (1.2)	0.001**	3.8 (1.1)	0.001**
Vomiting	36.4	1.1 (0.9)	0.23	0.8 (0.8)	0.310
Poor Oral Intake	44.2	3.9 (1.1)	0.001**	3.1 (1.0)	0.001**
Viral/bacterial	36.5	-2.6 (1.0)	0.008	-2.2 (0.9)	0.010*
Inappropriate Antibiotic Use	42.7	4.2 (1.2)	0.001**	3.7 (1.1)	0.001**

Unadjusted and adjusted analyses show that dehydration, fever, vomiting, and inappropriate antibiotic use are significant factors influencing the need for intravenous (IV) rehydration in children with gastroenteritis. Dehydration remained the strongest predictor (adjusted OR = 3.50, $p < 0.001$), followed by fever (adjusted OR = 1.87, $p < 0.001$) and inappropriate antibiotic use (adjusted OR = 2.75, $p < 0.001$). Vomiting was not statistically significant after adjustment (adjusted OR = 1.35, $p = 0.07$), and age, weight, and presumed viral etiology had no strong impact on IV rehydration need see Table 4.

Table 4: Unadjusted and Adjusted Analysis of Clinical Characteristics and Need for Intravenous Rehydration After 24 Hours in Children with Gastroenteritis

Clinical Characteristics	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value
Age (Years)	1.02 (0.98 - 1.06)	1.01 (0.98 - 1.05)	0.620
Gender (Male)	1.40 (1.05 - 1.86)	1.25 (0.92 - 1.70)	0.160
Weight (Kg)	1.05 (1.00 - 1.09)	1.02 (0.98 - 1.06)	0.350
Presence of Dehydration	4.10 (3.20 - 5.27)	3.50 (2.68 - 4.61)	0.001**
Fever ($\geq 38^\circ\text{C}$)	2.15 (1.65 - 2.82)	1.87 (1.38 - 2.54)	0.001**
Vomiting	1.60 (1.18 - 2.17)	1.35 (0.98 - 1.85)	0.070
Duration of Diarrhea (Days)	1.07 (1.02 - 1.12)	1.04 (1.00 - 1.09)	0.150
Viral/Bacterial	0.50 (0.37 - 0.67)	0.55 (0.39 - 0.77)	0.001**
Inappropriate Antibiotic Use	3.05 (2.15 - 4.29)	2.75 (1.88 - 4.07)	0.001**

DISCUSSION

A tertiary care hospital investigated the clinical characteristics and treatment methods along with factors that affect hospital outcomes in acute watery diarrhea patients among children. This study presents crucial information about dehydration-related impact and antibiotic misuse levels plus hospital resource management trends in resource-constrained settings. The patients who experienced moderate-to-severe dehydration needed the longest hospitalization periods and required intravenous (IV) rehydration treatment [9, 10]. The study showed that more than 85% of our child participants suffered from moderate or severe dehydration thus resulting in prolonged hospital stays by 3.8 hours ($p < 0.001$) and a 3.5-times greater likelihood ($p < 0.001$) for IV rehydration. The findings match earlier work from Posovszky et al., (2020) along with WHO recommendations which identify dehydration to be the main clinical factor that guides severe gastroenteritis treatment choices [11]. Early detection and appropriate correction of dehydration remains crucial for minimizing both patient health deterioration and hospital expenses [12]. The presence of fever resulted in patients needing two additional hours of hospitalization while increasing the odds of IV rehydration to 1.87 times above baseline. The

presence of fever in pediatric patients triggers closer clinical observation so healthcare providers decide to admit patients longer to hospital. Yeasmin *et al.*, (2022) developed comparable findings when they conducted research demonstrating febrile children received intensified hospital admission procedures [13]. A patient's inability to consume food from their mouth (+3.1 hours) prolongs hospitalization duration as reported by Vecchio *et al.*, (2021). This observation reaffirms their findings about problems encountering food intake requiring intravenous fluids as a consequence of nausea or fatigue [14]. The usage of inappropriate antibiotics reached 75% among patients because most diarrhea cases proved to be viral (80%). The researchers found antibiotic misuse trends similar to the results of previous studies who studied pediatric diarrhea utilization [15, 16]. The administration of inappropriate antibiotics increased hospitalization duration by +3.7 hours while simultaneously increase the need for intravenous rehydration treatment by 2.75 times in our study. The research demonstrates the necessity to follow strict national and WHO guidelines while developing better diagnostic methods (such as stool cultures) and providing education to healthcare providers [17]. According to results the attribution of cases to viral causes led to reduced hospital stay duration by 2.2 hours because viral gastroenteritis has self-limiting characteristics similar to studies conducted by previous literature. Lighter patients remained at the hospital for shorter periods when compared to heavier patients but the association was slight. Strong nutrition may reduce recovery time in children by helping their immune responses and storing extra energy [18, 19]. The adjusted analysis did not link IV rehydration to vomiting occurrence although this symptom was found in three out of four patients. Possibly because vomiting symptomatically overlaps with dehydration effects and providers managed nausea effectively with antiemetics. The independent influences of age, gender and residence location failed to produce significant effects on the study outcomes. The research findings from other South Asian studies confirm that demographic variables lose their significance after healthcare severity reaches certain clinical levels [20].

This study has several limitations. First, it was conducted at a single center, which may limit the generalizability of the findings to other settings. Second, the study design was observational, and causality between antibiotic use and clinical outcomes cannot be established. Third, diagnostic confirmation of etiologies was limited due to resource constraints, which may have led to misclassification. Lastly, data on long-term outcomes were not collected, which restricts the ability to assess the prolonged impact of antibiotic usage. Future studies should include multi-

center designs with improved diagnostic tools and longitudinal follow-up to better evaluate antibiotic use and long-term outcomes in pediatric diarrhea.

CONCLUSIONS

Antibiotic prescription rates for pediatric gastroenteritis are extremely high and alarmingly, the majority of them are inappropriate. Understanding on the part of healthcare providers helps reduce antibiotic use that is without clinical indication.

Authors' Contribution

Conceptualization: MAB

Methodology: UB, PK, AAK

Formal analysis: UB, MZ

Writing and Drafting: HIS, MZ

Review and Editing: MAB, UB, PK, AAK, HIS, MZ

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



Effect of Sample Storage at 2-8°C for 24 Hours on Reticulocyte Count Determined by Manual Method

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ABSTRACT

Reticulocytes are immature red blood cells that contain residual RNA and ribosomes but no nucleus. Reticulocytes count is a haematological test that assists in assessing bone marrow activity. It can be determined by manual and flow cytometric method. Reticulocytes mature in vitro within six hours of sample collection; hence the sample should be processed within this time frame for accurate results. **Objective:** To determine the difference in reticulocyte count between a fresh sample and a sample stored for 24 hours at 2-8°C by manual method. **Methods:** This quasi-experimental study included a total of 220 EDTA-anticoagulated blood samples submitted to the Hematology Department of Allama Iqbal Medical College/Jinnah Hospital, Lahore, from June 12, 2024, to December 18, 2024, for reticulocyte count analysis using non-probability consecutive sampling technique. Each sample was processed using brilliant cresyl blue stain, within one hour of collection and reported two times: within 6 hours of sample collection and after a period of 24 hours of storage. **Results:** The manual reticulocyte count showed a significant difference between freshly prepared slides and those stored for 24 hours. Mean reticulocyte count at 6 hours was 2.99 ± 0.09 , while after 24 hours, it decreased to 2.41 ± 0.10 , resulting in a mean difference of 0.58 ± 0.16 . **Conclusions:** In regions where automated methods are not available, performing a reticulocyte count manually on a fresh sample can significantly contribute to improving healthcare quality. This simple yet essential test is crucial for diagnosing and managing various clinical conditions effectively.

INTRODUCTION

Reticulocytes are newly formed erythrocytes that originate in the bone marrow, enter the bloodstream and develop into mature red blood cells within 1-2 days. The reticulocyte count reflects the bone marrow's ability of red blood cell production and is an essential metric for diagnosing anemia, evaluating treatment effectiveness, and determining prognosis. Reticulocyte count can be measured using two primary methods: the manual method, which involves light microscopy, and the automated flow cytometric method. Although flow cytometric method is more precise but it can give spurious counts in some situations, so manual counting by light microscopy, although tedious, remains an accepted reference method

especially in resource limited countries like Pakistan [1]. The manual method for reticulocyte counting is a routine hematology test that is simple to perform and widely used in laboratories [2]. Since 1940, it has been considered a traditional and standard technique due to its simplicity and cost-effectiveness [3]. A local study conducted at Aga Khan University, Karachi, confirmed that manual reticulocyte counting is both reliable and economical, making it particularly beneficial for resource-limited settings [4]. A study conducted nearly four decades ago investigated the effects of storing samples at room temperature on reticulocyte count and concluded that the results remain reliable for up to 24 hours without



significant changes compared to baseline values [5]. Reticulocyte count is determined by microscopic examination of peripheral blood smears that are stained using supravital stains, such as brilliant cresyl blue or new methylene blue. Reticulocytes mature in vitro within six hours of sample collection, making it essential to process samples ideally within this time window. A comparison of reticulocyte count at different time intervals by George L et al., using a manual technique indicated a notable difference between freshly prepared and stored slides at 6 hours (2.92 ± 3.56) and 24 hours (2.36 ± 3.18) with a difference of 0.56 ± 0.38 [6]. For precise estimation of reticulocyte count, it must be reported in six hours if stored at room temperature, or within 72 hours if stored at $2-6^{\circ}\text{C}$, as the maturation process is dependent on both time and temperature [7]. Tsuda I and Tatsumi N observed an approximate 60% decrease in relative proportion of reticulocytes from its original value after 03 weeks of storage at 4°C with a strong negative correlation ($r = -0.9972$) [8]. Furthermore, a study conducted in Oslo, Norway, examining the stability of reticulocyte and erythrocyte parameters over six days in three diagnostic groups (iron-deficient, thalassemia and healthy subjects) revealed an unexpected increase in reticulocyte count in all groups after 03 days of room temperature storage [9]. Reticulocyte count is a fundamental haematological test that is routinely requested in the facility. Since it is affected by both temperature and time, therefore, the goal of my study is to track any change in its count that may result from sample storage at $2-8^{\circ}\text{C}$.

Although the Reticulocyte Count is a routinely used and essential indicator of bone marrow function, existing literature on the effects of sample storage—particularly under controlled temperatures—is limited, outdated, and shows inconsistent findings, especially in local settings. This creates uncertainty in clinical interpretation and highlights a significant research gap. Therefore, the present study aims to evaluate the changes in reticulocyte count associated with sample storage at $2-8^{\circ}\text{C}$, in order to provide clearer evidence for accurate laboratory practices and improve reliability of results in resource-limited contexts.

METHODS

This quasi-experimental study was carried out in the Hematology Department of Allama Iqbal Medical College/Jinnah Hospital, Lahore, from June 12, 2024, to December 18, 2024 after approval by institutional ethical review board (Ref No: ERB166/4/11-06-2024/S1 ERB). Non-probability consecutive sampling technique was used. Sample size was calculated using OpenEpi software which came out to be 220 keeping 95% confidence interval, power 80% with absolute precision 0.05 and anticipated

mean difference in reticulocyte count as 0.56 ± 0.38 . Samples older than 06 hours or without mention of time of collection, insufficient sample quantity (less than 3cc) and clotted samples were excluded. Each blood sample was processed using brilliant cresyl blue stain within an hour and reported at two time points: within six hours of collection and following 24 hours of storage. The brilliant cresyl blue stain highlights the RNA as blue color against an otherwise pink cell. Light microscopic examination of stained peripheral blood films was done to determine the number of reticulocytes among 1000 RBCs and expressed as a percentage. Prior consent was taken from all patients, authorizing use of their personal information for research purpose. Data were entered and analyzed using SPSS version 27.0. Qualitative variables were shown as frequency and percentage while quantitative variables were reported as mean $\pm$ standard deviation. To assess the significant difference in reticulocyte count between the baseline (6 hours) and 24 hours post-storage, a paired t-test was applied, with a p-value of < 0.05 regarded statistically significant. Following stratification, a t-test was conducted as well. This was based on findings by George L et al., who reported a difference of 0.56 ± 0.38 in a similar setting [6]. Prior to this, normality of data was assessed using the Shapiro-Wilk test.

RESULTS

The subjects in this study ranged in age from 15 to 60 years, with mean age of 38.05 ± 10.09 years (Table 1). The study comprised 116 males (52.73%) and 104 females (47.27%), yielding a male-to-female ratio of 1.1:1.

Table 1: Patient Distribution Based on Age (n=220)

Age (Years)	Number of Patients Frequency (%)
15-40	141 (64.09)
41-60	79 (35.91)
Total	220 (100)
Mean $\pm$ SD	38.05 ± 10.09 Years

A comparison of reticulocyte counts at various time intervals using the manual method showed a significant difference between freshly prepared and stored sample slides (Table 2).

Table 2: Reticulocyte Count: Fresh Versus 24-Hour Stored Sample (Manual Method)

Reticulocyte Count	Mean $\pm$ SD
Reticulocyte Count within 6 Hours	2.99 ± 0.09
Reticulocyte Count at 24 Hours	2.41 ± 0.10
Difference	0.58 ± 0.16

Table 3 stratification of the mean difference in reticulocyte count based on age groups and gender respectively.

Table 3: Stratification of Mean Difference in Reticulocyte Count with Respect to Age Groups

Age Groups	Difference in Reticulocyte Count Mean $\pm$ SD	p-Value
15-40	0.57 $\pm$ 0.16	0.111
41-60	0.60 $\pm$ 0.15	

Table 4: Stratification of Mean Difference in Reticulocyte Count with Respect to Gender

Gender	Difference in Reticulocyte Count Mean $\pm$ SD	p-Value
Male	0.61 $\pm$ 0.15	0.011
Female	0.55 $\pm$ 0.17	

DISCUSSION

Reticulocytes are developing red blood cells that contain residual RNA and ribosomes but lack a nucleus. Upon entering circulation, they shed their RNA within a day while continuing hemoglobin production despite the absence of a nucleus [10]. Reticulocytes take about 1 to 3 days to develop in the bone marrow, and once they are released into the bloodstream, they become mature red blood cells in 1 to 2 days. The Reticulocyte Count (RC) is a simple hematological test used to assess the bone marrow activity [11]. It serves as a useful diagnostic tool for identifying anemia and provides critical information for monitoring and managing anemic patients. An elevated reticulocyte count, or reticulocytosis, is often seen after blood loss, in hemolytic anemia, recovery from nutritional anemia, and hemoglobin disorders [12]. In contrast, a low reticulocyte count, or reticulocytopenia, can result from conditions such as aplastic anemia, pure red cell aplasia, bone marrow failure, chronic kidney disease, anemia of chronic disease, blood transfusion and alcoholism. Reticulocyte counting in clinical laboratories is performed using two primary methods: the conventional manual technique and the automated approach [3, 4]. The introduction of automation has significantly enhanced the accuracy and reliability of reticulocyte measurement [6]. A study conducted in Sri Lanka found that automated analyzers are increasingly being used in urban and high-volume laboratories, gradually replacing the traditional manual or visual method for reticulocyte counting. However, resource-limited laboratories, particularly in rural areas, continue to rely on the manual approach [13]. I have conducted this study to determine the mean difference in reticulocyte count between a fresh sample slide and a slide prepared after 24 hours of sample storage at 2-8°C by manual method. In my study, reticulocyte count comparison at various times using manual approach showed that there was a substantial difference between the fresh sample and stored sample slides at 06 and 24 hours with a mean of 2.99 ± 0.09 and 2.41 ± 0.10 with difference of 0.58 ± 0.16 . George L et al., conducted a study in Southern India and observed a

similar finding between the fresh and stored slides at 06 and 24 hours with a mean of 2.92 ± 3.56 and 2.36 ± 3.18 with difference of 0.56 ± 0.38 [6]. Schapkaitz et al., examined the impact of sample storage at room temperature and found that reticulocytes remained stable for up to 12 hours [14]. In contrast, Pintér E et al., reported that reticulocyte counts became unstable, showing a significant reduction over 24 hours [15]. Additionally, de Baca et al., observed that reticulocyte percentage and absolute values remained stable for four days when analyzed using an automated hematology analyzer [16]. Most studies in the literature indicate either no change in Reticulocyte Count (RC) or a reduction with sample storage. A study conducted in Oslo, Norway, examined erythrocyte and reticulocyte parameter stability over six days in three diagnostic groups i.e. iron-deficient, thalassemic and healthy subjects and found unexpected results. Reticulocyte counts increased in all groups after three days of storage at room temperature [9]. There was a statistically significant difference in the mean manual Reticulocyte Count (RC) between males and females ($P = 0.01$) observed in the study. The existing literature offers mixed findings when comparing RC between genders, but it does not specifically compare the methods used [17, 18]. This suggests that both manual and automated techniques are appropriate for determining mean RC; however, the manual method may be preferable as it is cost-effective. Various studies have reported differing results when comparing mean RC values obtained through manual and automated methods. For instance, Osgood et al., did not observe a remarkable variation in the mean RC %age among individuals between 4-13 years age, whereas Jain P et al., observed a notable decrease in RC in the elderly population. Bukhari and Zafar reported a notable difference in reticulocyte count ($P < 0.05$) [19-21]. Likewise, Tarallo P et al., found no statistically significant difference in RC among girls and boys aged 4-19 years, but observed higher values in males compared to females over the age of 20 [17]. Lacombe et al., studied the stability of reticulocyte percentage after sample storage at room temperature and at 4°C for different time intervals. Their study found a marked decrease in the percentage of reticulocytes after 48 hours of storage at room temperature, whereas no reportable change was observed after storage at 4°C for same duration. Additionally, they reported that the Immature Reticulocyte Fraction (IRF) parameter significantly decreased after sample storage for 08 hours at both room temperature and 4°C [22]. Similarly, Cavill et al., examined the in vitro stability of reticulocytes and found that there was no notable decrease in reticulocyte count at either temperatures i.e. room temperature and 4°C. However, a reduction was noted in samples that had reticulocytosis within the first 24

hours at room temperature, with no such decline observed at 4°C [23]. Brugnara *et al.*, compared three types of automated methods with the manual technique and assessed their agreement using intraclass correlation coefficients. Their findings showed intraclass correlation coefficients between Manual/Flow Cytometry, Manual/SYSMEX R-2000 and Manual/H*3 Analyzer of 0.755, 0.538 and 0.610, respectively. Based on the findings, they concluded that manual reticulocyte counting technique cannot be regarded as comparable to the three types of automated methods [24]. The manual method, however, has certain limitations, including low reproducibility, the evaluation of a smaller number of cells, and the need for significant time and effort. It also requires skilled personnel for accurate reporting and depends on the observer's visual acuity and patience. Despite these challenges, it remains a cost-effective option for smaller laboratories and is more affordable for patients. On the other hand, automated reticulocyte counting can be affected by various interferences, such as platelet clumps, giant platelets, fragmented or abnormal WBCs, nRBCs, and RBC inclusions like basophilic stippling, Howell-Jolly bodies and Heinz bodies [25]. These interferences can be identified and addressed through manual examination, making the visual method valuable in assessing ineffective erythropoiesis.

This study was limited using the manual reticulocyte counting method, which is observer-dependent and may affect reproducibility and accuracy. Additionally, the study did not compare findings with automated analyzers or assess long-term sample stability beyond 24 hours. Future studies should incorporate automated methods and larger sample sizes to validate findings and evaluate reticulocyte stability over extended storage durations.

CONCLUSIONS

This study found that reticulocyte counts varied significantly over time when using the manual method. A notable difference was observed between freshly prepared slides and slides stored for 6 and 24 hours, with mean results of 2.99 ± 0.09 and 2.41 ± 0.10 , respectively, resulting in a difference of 0.58 ± 0.16 . Based on these findings, it was suggested that the manual reticulocyte counting method was utilized in areas where automated systems are unavailable. As a fundamental diagnostic tool, it can play a crucial role in enhancing healthcare quality by aiding in the diagnosis and treatment of various medical conditions.

Authors' Contribution

Conceptualization: MG

Methodology: AK, HA

Formal analysis: AK, MG, AM, RB, HA

Writing and Drafting: AK, MG, AM, RB, HA

Review and Editing: AK, MG, AM, RB, HA

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

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Original Article



Comparative Analysis of Surgical Outcomes in Chronic Otitis Media with Cholesteatoma: A Study of Canal Wall Up and Canal Wall Down Mastoidectomy

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ABSTRACT

Chronic otitis media with cholesteatoma (COMC) is a serious, potentially life-threatening middle ear condition characterized by keratinizing squamous epithelium growth, chronic inflammation, and progressive bone erosion. Surgical intervention remains the mainstay of treatment, with canal wall up (CWU) and canal wall down (CWD) mastoidectomies being the primary approaches. **Objectives:** To evaluate the prevalence, clinical presentation, and surgical outcomes of COMC, comparing the efficacy and complications of CWU and CWD mastoidectomy. **Methods:** A prospective study was conducted across multiple healthcare centers in Karachi. The study included 136 COMC patients, divided by surgical technique (CWU vs. CWD). Demographics, symptoms, audiometry, recurrence, and complications were assessed over six months. Data were analyzed using SPSS. **Results:** The mean age of patients was 32.6 ± 12.5 years, with a slight male predominance (60%). Otorrhea (80%) and hearing loss (73%) were the most common presenting symptoms. Recurrence was significantly higher in the CWU group (71.4%) compared to none in the CWD group ($p=0.003$). However, CWU surgery yielded better hearing outcomes postoperatively (mean gain: 15 dB) compared to CWD (mean gain: 8.9 dB), with a significant difference in final hearing thresholds ($p=0.04$). Complications were more frequent in the CWD group but were not statistically significant ($p=0.19$). **Conclusions:** It was concluded that canal wall down (CWD) offers better disease control with low recurrence, while canal wall up (CWU) preserves hearing. Surgical choice should balance disease clearance and function, with regular follow-up.

INTRODUCTION

Chronic otitis media with cholesteatoma (COMC) is a serious and progressive disease of the middle ear characterized by abnormal growth of keratinizing squamous epithelium inside the middle ear and mastoid cavity. This causes chronic inflammation, keratin debris

build up and enzymatic bone destruction [1]. Cholesteatoma is usually divided into congenital and acquired forms but the acquired type is more common. Acquired cholesteatoma develops mostly because of chronic eustachian tube dysfunction, repeat infections of



the middle ear, and formation of retraction pockets in the tympanic membrane [2]. The cause of acquired cholesteatoma is negative pressure in the middle ear that makes the tympanic membrane retract inward. Over time these retraction pockets trap epithelial debris which keeps shedding and forms a sac that contains chronic infection and bone-degrading enzymes like collagenases and osteoclast activating factors [3]. If untreated, COMC can cause serious problems like erosion of ossicles, facial nerve palsy, labyrinthine fistula, meningitis, brain abscess, and even death [4]. In developing countries, late presentation and a lack of awareness cause more severe disease at the time of diagnosis. The symptoms of COMC are usually persistent or bad-smelling ear discharge, conductive hearing loss, ear fullness, and sometimes vertigo or facial weakness. An otoscopic exam may show marginal perforation of the tympanic membrane or visible cholesteatoma debris. Diagnosis is mostly confirmed by ear exam and imaging. High resolution CT scan of the temporal bone is important to see how much disease and bone erosion and help surgical planning [5]. Surgery is the main treatment for cholesteatoma. The main aims of surgery are total removal of the disease, making the ear safe and dry, and improving or improving hearing [6]. The two main surgeries are canal wall up (CWU) and canal wall down (CWD) mastoidectomy. CWU is mostly preferred because it preserves ear canal anatomy and better hearing results, but has a higher chance of leftover or return disease and needs second-look surgery [7]. CWD is more aggressive but better to see and remove all disease. But it makes an open cavity which needs regular cleaning and hearing results are not good like CWU [8]. Even with progress in diagnosis and surgery, cholesteatoma is still difficult because of the chance of recurrence and complications. So, understanding how common it is, how it presents, and the results of treatment are important to improve care.

Despite advances in surgical techniques for chronic otitis media with cholesteatoma (COMC), there is limited local evidence comparing the outcomes of canal wall up (CWU) and canal wall down (CWD) mastoidectomy, particularly in settings where late presentation and disease severity are common. This lack of context-specific data limits optimal surgical decision-making and outcome prediction. This study aimed to find the prevalence of COMC in a tertiary hospital and evaluate the outcome of management, especially comparing CWU and CWD surgeries.

METHODS

This prospective study was conducted from June 2024 to April 2025. Data was collected from multiple healthcare centers in Karachi. Ethical approval was obtained from the Institutional Ethical Review Committee of Al-Tibri Medical College and Hospital, Isra University, Karachi Campus

under approval number IERC/ATMC/15(02-2024)/06. The study included 136 patients diagnosed with chronic otitis media with cholesteatoma. Patients were selected using a consecutive non-probability sampling technique. Based on clinical findings and high-resolution CT scans of the temporal bone, patients with localized disease and preserved canal anatomy were assigned to the canal wall up (CWU) group, while those with extensive disease, erosion of the canal wall, or poor eustachian tube function were assigned to the canal wall down (CWD) group, minimizing selection bias. Inclusion criteria comprised patients undergoing primary CWU or CWD mastoidectomy with complete data and at least six months of postoperative follow-up. Exclusion criteria included previous otologic surgery, bilateral disease, intracranial complications, facial nerve palsy, labyrinthine fistula, immunocompromised status, coexisting ear pathologies, or incomplete records. Sample size was calculated using OpenEpi software based on a 30% recurrence rate for CWU and 10% for CWD, with 95% confidence and 80% power, resulting in 68 patients per group [9, 10]. Hearing outcomes were measured using pure-tone audiometry, and improvement was defined as the difference between pre- and postoperative average hearing thresholds. Recurrence was defined as residual or re-developing cholesteatoma detected clinically or radiologically during follow-up. Postoperative complications, such as facial nerve weakness or cavity infections, were also documented. Follow-up evaluations were performed at 2 weeks, 1 month, 3 months, and 6 months after surgery. Statistical analysis was performed using SPSS version 22. Independent t-tests were used for continuous variables, while chi-square and Fisher's exact tests were applied to categorical data, with a $p < 0.05$ considered statistically significant. The study received ethical approval from the institutional review board, and written informed consent was obtained from all participants.

RESULTS

Out of 136 patients enrolled, 68 underwent canal wall up (CWU) mastoidectomy and 68 underwent canal wall down (CWD) mastoidectomy. The mean age was significantly lower in the CWU group (28.7 ± 9.0 years) compared to the CWD group (33.8 ± 12.7 years), with a t-value of 2.62 and degrees of freedom ($df=134$) ($p=0.010$). Otorrhea was more commonly reported in the CWU group (89.7%) than in the CWD group (60.3%), and the difference was statistically significant ($\chi^2=14.2$, $p<0.001$). The prevalence of hearing loss was similar between the two groups (66.2% vs. 67.6%, $\chi^2=0.02$, $p=0.880$) (Table 1).

Table 1: Demographic and Clinical Characteristics of Patients

Characteristic	CWU (n=68)	CWD (n=68)	Test statistics	df	p-value
Age (years), mean $\pm$ SD ^a	28.7 $\pm$ 9.0	33.8 $\pm$ 12.7	t=6.62	134	0.010*

Male (%) ^a	51.5%	57.4%	$\chi^2=36.8$	134	0.520
Otorrhea (%) ^b	89.7%	60.3%	$\chi^2=14.2$	134	0.001*
Hearing Loss (%) ^b	66.2%	67.6%	$\chi^2=00.2$	134	0.880

^aIndependent samples t-test, level of significance <0.050, b Chi-square test was applied, level of significance <0.050

Recurrence was significantly more frequent in the CWU group (17.6%) compared to no recurrence in the CWD group, with a Fisher's exact test value of 13.2 ($p<0.001$). Postoperative complications, including facial nerve weakness and cavity infection, were observed only in the CWD group (11.8%), with a Fisher's exact test value of 6.7 ($p=0.020$) (Table 2).

Table 2: Surgical Outcomes and Complications

Outcome	CWU (n=68)	CWD (n=68)	Fisher's exact test	p-value
Recurrence (%)	17.6%	0.0%	13.2	<0.001*
Complications (%)	0.0%	11.8%	6.7	0.020*
- Facial Nerve Weakness	0	4	-	-
- Cavity Infection	0	4	-	-

Fisher's exact test, level of significance <0.050

Audiological assessment showed better postoperative hearing in the CWU group (38.4 ± 11.5 dB) compared to the CWD group (49.4 ± 12.3 dB), and this difference was statistically significant ($t=-5.14$, $df=134$, $p=0.010$). Although the mean hearing improvement was higher in the CWU group (14.7 dB) than in the CWD group (9.9 dB), the difference did not reach statistical significance ($t=1.89$, $df=134$, $p=0.060$). Preoperative hearing thresholds were also significantly better in the CWU group (53.2 ± 12.0 dB vs. 59.3 ± 13.5 dB, $t=-2.07$, $df=134$, $p=0.040$) (Table 3).

Table 3: Audiological Outcomes

Hearing Parameter	CWU (n=68) mean $\pm$ SD	CWD (n=68) mean $\pm$ SD	t	df	p-value
Preoperative hearing loss (dB)	53.2 ± 12.0	59.3 ± 13.5	2.07	134	0.030*
Postoperative hearing loss (dB)	38.4 ± 11.5	49.4 ± 12.3	5.14	134	0.010*
Mean hearing improvement (dB)	14.7	9.9	1.89	134	0.060

Independent Samples t-test, level of significance <0.050

DISCUSSION

Chronic Otitis Media with Cholesteatoma (COMC) still causes many clinical problems because it is very aggressive and destroys tissues, if not treated it can cause serious complications. Current study aimed to investigate the prevalence of COMC and its treatment outcomes, with a primary focus on surgery and its impact on disease control and hearing preservation. The patients in this study have an average age of 32.6 years and a slight more of males, which matches other studies showing cholesteatoma mostly affects young adults and no big difference between males or females [11, 12]. Right ear affected more (60%) also similar to other reports, but the side of the ear can be

different in other populations [13]. For surgery, we found more recurrence in patients who had canal wall up (CWU) mastoidectomy (71.4%) but none in the canal wall down (CWD) group ($p=0.003$). This agrees with previous studies that reported CWU keep the canal wall behind the ear and this can leave some cholesteatoma causing it to come back more [14,15]. While CWD removes this wall completely so the disease is removed better but makes a big cavity in the mastoid and this can cause more problems after surgery [16]. In the hearing test, the CWU group had better hearing improvement after surgery, mean gain of 15 dB versus 8.9 dB in the CWD group. Hearing level after surgery was significantly better in CWU ($p=0.04$). This agrees with studies that show keeping the ear canal and ossicles in CWU leads to better hearing [17, 18]. But the problem is disease comes back more in CWU, so patients need close follow-up and sometimes a second surgery to remove leftover disease [19]. Complications like temporary facial nerve weakness and infection in the cavity were more common in the CWD group but the difference was not statistically significant. These problems happen because CWD surgery is bigger and creates an open cavity which can get infected and irritate the nerve [20]. No complications in the CWU group show it is less invasive but the risk of recurrence is higher.

This study was limited by a relatively small sample size and short follow-up period, which may have affected the accurate assessment of long-term recurrence and complications. Future studies should include larger samples with longer follow-up to better evaluate long-term surgical outcomes and recurrence rates.

CONCLUSIONS

The study concluded the hard balance between removing disease fully and maintaining hearing good in cholesteatoma surgery. CWD surgery removes the disease better and has less recurrence but causes more complications and worse hearing. CWU surgery keeps hearing better but the risk of disease return is high. Careful surgical planning and close monitoring after surgery are important to get the best results for patients with cholesteatoma.

Authors' Contribution

Conceptualization: AW, GSM

Methodology: MRD,

Formal analysis: GSM

Writing and Drafting: MAJ, AW, ZA, MIB

Review and Editing: MRD, MAJ, AW, ZA, MIB, GSM, HK

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

Conflicts of Interest

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Original Article



Efficacy between 3-Dimensional and Champy Plates in Anterior Mandibular Fracture

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ABSTRACT

Facial bone fractures or maxillofacial fractures are on the rise, specifically as a result of more road traffic accidents and sports incidents. The face is very sensitive both in terms of appearance and functionality; people who have been attacked in the face can have difficulty eating and speaking, or are extremely shy to socialize due to disfiguration. **Objective:** To compare the results of using the 3D mini plates in the treatment of the anterior mandibular fracture with Champy's mini plates. **Methods:** A Quasi-experimental study was conducted at the Department of Oral and Maxillofacial Surgery of LUMHS Jamshoro, Pakistan, in six months, and the sampling technique used was non-probability convenience sampling. Data analysis was done using statistical software SPSS version 26.0. **Results:** At the end of six weeks, the results showed that the average surgical time that was taken in the surgical procedure was shorter in Group B than in Group A, being (50.94 ± 6.89) and (55.43 ± 3.24) respectively; $F=16.44$, $p=0.001$. Just as in Group B, the incidence of infection was considerably lower (8.6%) than in Group A, where it reached 28.6%, with all the differences being statistically significant ($p=0.031$). **Conclusions:** 3D plates provide a biomechanically stable and versatile solution to Champy's mini plates. Because of the high strength of the material and corresponding flexibility, as well as ease of utilization, there is evidence that the 3D plates used in surgeries should be effectively employed in managing mandibular fractures.

INTRODUCTION

Facial trauma is one of the most challenging issues in maxillofacial surgery to manage. The mandible is regarded as one of the most commonly fractured bones since it is highly protruded and has a complex shape [1]. ORIF techniques are the most preferred to treat fractures that involve the mandible. In many of the past few decades, the occurrence of traffic mishaps, violent episodes, sports and other accidents has led to an increase in cases of maxillofacial trauma. This bone, located more in the lower region of the face, is vulnerable to fracture and is among the most commonly fractured bones of the face [2].

Though new fracture management techniques help minimize the gap and improve occlusion in definitive management, the major challenge remains in helping the patient regain and return to his activities as early as possible. Factors such as the degree of fractures, the patient's dentition, and any other injuries, such as soft tissue injuries, are the basis for the choice of the fixation technique and hardware [3, 4]. Two approaches to the treatment of mandibular fracture have been developed in the process: the rigid screw osteosynthesis developed by Spiessl and the semirigid screw osteosynthesis by Champy.



Every strategy has its downside; the absolute rigidity is unfavorable when applying stress on the bone, and it takes time during the surgery. Semirigid fixation can cause certain instability in a fracture site [5, 6]. According to Michelet in 1973 and Champion in 1975, mini plate osteosynthesis has been regarded as a gold standard in the management of mandibular fractures. The field has only in the recent past integrated the use of three-dimensional (3D) titanium plates and screws for improved fracture stabilization. The plates to be used are quadrangular-shaped in three dimensions, with two crossbars connecting the two mini plates. These plates help in increasing the stability and offer better resistance to torsional loads. The main advantages of 3D plates are ease of application, high stability to torque force, and small size so that they can be considered as perspectives for mandibular fracture fixation [7-9]. When compared to the conventional mini plates and screws, this technique has certain benefits because three-dimensional plates request an average amount of plates and screws, such as four plates and six screws, for stabilization. In contrast to the mini plates used commonly in treating the mandible symphysis and parasymphysis defects, accompanied by two plates, 3D plates need only one plate for fixation. The reduction of the incorporation of foreign material makes the process less complicated and reduces operative time and the overall costs of the treatment [10-13]. Facial trauma is still a complex area of OMS, along with various techniques applied to achieve the desired results [14, 15]. Champy's miniplate system is widely used for treating mandibular fractures and has certain disadvantages. 3D mini plates are particularly in demand for their strength and surgery time effectiveness, which has increased in popularity in recent years [16, 17].

Despite the widespread use of Champy's miniplate system for mandibular fracture fixation, limitations such as instability and longer operative time have led to the introduction of 3D miniplates; however, evidence comparing their long-term effectiveness and clinical advantages remains limited and inconsistent. This lack of clear comparative data creates uncertainty in selecting the most optimal fixation technique for anterior mandibular fractures. This study aims to investigate whether, where and when the 3D miniplate system is more favorable than Champy's miniplate in reconstructive maxillofacial surgery by comparing their efficiency for the long-term advantage of the patient. To compare the effect of 3D miniplates versus Champy's miniplates fixation of anterior mandibular fractures.

METHODS

A quasi-experimental study was organized at the Department of Oral and Maxillofacial Surgery, Liaquat University of Medical and Health Sciences (LUMHS),

Jamshoro by using a non-probability consecutive sampling technique over six months (01-01-2021 to 30-6-2021) by getting approval of the research ethics committee (NO.LUMHS/REC/-996) on December 16, 2020, after obtaining the patients' written consent. The following formula was used to compute the sample size for this research: $n = Z^2 \times p \times q / e^2$. Where $z=95\%$ confidence interval, $e=5\%$ margin of error, $p=5\%$ infection rate [7], $q=95\%$. $n=1.96 \times 1.96 \times 4.8 \times 95.2 / 25$. $n=70$. Hence, the study had a sample size of 70 (35 in each group). The total sample size counted was 70 (35 per group). Group A (mini-plates) = 35, Group B (3D plates). The following criteria were used to define the participants for this study: Patients with anterior mandibular fracture, patients between the ages of 14 and 45 years, both sexes and those who signed informed consent. Therefore, the rationale for study inclusion involved mandibular fractures that were non-comminuted and non-infected in the symphysis and para-symphysis areas and needed ORIF. Exclusion criteria for the study involved patients with comminuted or infected mandibular fractures, geriatric patients, especially those with complete edentulism and those who did not meet all the inclusion criteria. The intervention plan entailed the ORIF method for treating such anterior mandibular fractures. According to the medical history, physical and radiological examination, and the following comprehensive investigations were done. The patients' fitness level for Surgery was also maintained at an anesthetic level for all patients undergoing ORIF. It was done under general anesthesia, and during the surgery, an arch bar was placed to allow inter-maxillary fixation before open reduction and internal fixation were made. After administering local anesthesia lidocaine with epinephrine at the operating site, trans-buccal incision was given 5mm apical to the mucogingival junction, muco-periosteal flap was reflected with careful retraction of mental nerve and fracture site was exposed, monocortical screws were used in both type of hardware used. The patient was divided into two groups using the port chit method. Group A (Mini-plates) patients in which 4-hole mini-plates were used. Group B (3D plates) consists of patients in whom 4-hole straight mini plates were used for fixation. In group A, the position of the plates aligned the horizontal link so that they were perpendicular to the fracture line of the bone, and the vertical link was parallel to the fracture line. The upper horizontal crossbar was set in the subapical position in the symphysis and parasymphysis areas. Drilling was conducted using a local anesthetic agent, following a 1.5 mm drill bit and saline solution to minimize the heat generation and the consequent damage to the cochlea. It was then fixed by using 7 mm of titanium screws. In the second group, B, a 4-holed titanium mini-plate with a 2 mm gap was contoured according to the fracture site and then applied with 7 mm titanium screws. After the plates were applied, the surgical field was washed with saline solution, and the mucoperiosteal flap was sutured with 3.0 Vicryl or silk

sutures. In particular, patients were treated with antibiotics and painkillers for five days in total. Following the IMF removal, they were advised to take proper oral care, use 0.2% chlorhexidine solution to rinse the mouth, and take soft meals for six weeks. Post-operative OPG was carried out for adequacy of fracture reduction and location of plates. Follow-up intervals were carried out at 1st, 2nd, 3rd, 4th and 6th week, and outcomes between this two hardware's were assessed in terms of infection, operative time, and outcome was recorded in the Performa at 6th week postoperatively. Statistical data analysis was done using the Statistical Package for the Social Sciences (SPSS) software version 26.0. Regarding gender, education, occupation, place of residence, and postoperative infection rate, frequency and percentage distributions were computed. A chi-squared test was used to analyze the infection data after the operation, whereas the independent samples t-test was used to analyze the differences in the operative time and infection rate, and normality of data was checked by Shapiro-Wilk's test; the level of significance taken was 0.05.

RESULTS

Results indicate demographic information of patients where most of the patients belonged to the age group 14-25 years, followed by 26-35 and 36-45 years, respectively. The average age of 26.14 ± 8.11 years was in group A and 29.66 ± 10.03 years in group B. Among the gender distribution, there were 37 individuals, constituting 52.86% male, whereas 33 individuals, making up 47.14% as female. Most of the patients were urban residents (68.58%) and rural (31.42%), (Table 1).

Table 1: Demographic Information of Patients

Variables	Group A (%)	Group B (%)
Age		
Mean $\pm$ SD	26.14 ± 8.11	29.66 ± 10.03
14-25	18 (51.43%)	16 (45.71%)
26-35	13 (37.14%)	10 (28.57%)
36-45	4 (11.43%)	9 (25.72%)
Gender		
Male	18 (51.43%)	19 (54.29%)
Female	17 (48.57%)	16 (45.71%)
Residence		
Urban	25 (71.43%)	23 (65.71%)
Rural	10 (28.57%)	12 (34.29%)

Findings show average time taken from incision between groups 6th week postoperatively was significantly low in group B as compared to group A (50.94 ± 6.89 vs. 55.43 ± 3.24 ; $p=0.001$) (Figure 1).

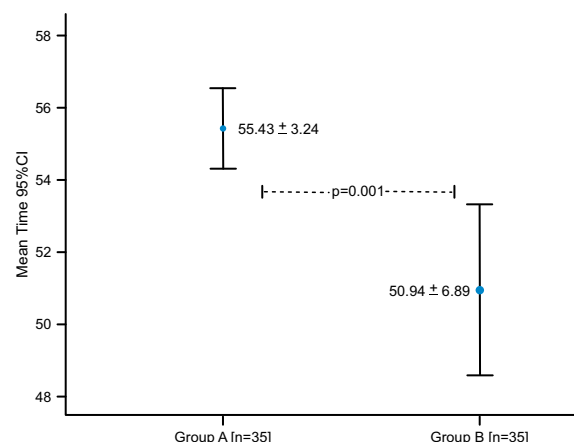


Figure 1: Comparison of Average Time Taken from Incision Between Groups 6th week Post

Similarly rate of infection was also significantly lower in group B than group A (11.42% vs. 28.6%; $p=0.031$) (Table 2).

Table 2: Comparison of Infection Rate (Final Outcome) Between Groups Within 30 Days of Post-Operatively

Infection	Group A	Group B	p-value
Yes	10 (28.6%)	4 (11.42%)	0.031
No	25 (71.4%)	31 (88.58%)	

ChiSquare=4.629

Findings demonstrate a comparison of infection between groups stratified by age groups, gender & residence 6th week post-operatively, where age group 14-25 years shows a p-value of 0.05 as indicates a significant association and 26-35 ($p=0.421$), followed by 36-45 ($p=0.522$). Whereas gender distribution shows in male ($p=0.056$) and female ($p=0.008$), and rural ($p=0.153$) and urban shows ($p=0.002$) respectively (Table 3).

Table 3: Comparison of Infection Between Groups Stratified by Age Groups, Gender and Residence 6th week Post Operatively

Variables	Infection	Group A	Group B	p-value
Age Group				
14-25	Yes	6 (33.3%)	1 (6.3%)	0.050
	No	12 (66.7%)	15 (93.8%)	
26-35	Yes	3 (23.1%)	1 (10%)	0.421
	No	10 (76.9%)	9 (90%)	
36-45	Yes	1 (25%)	1 (11.1%)	0.522
	No	3 (75%)	8 (88.9%)	
Gender				
Male	Time taken	54.89 ± 2.29	51.82 ± 6.12	0.056
Female	Time taken	56.00 ± 4.00	50.11 ± 7.64	0.008

Shapiro-Wilk test results are mentioned (Table 4).

Table 4: Test of Normality in Data Set

Variables	Shapiro-Wilk test		
	Statistic	df	Sig.
Patient's Age	0.9927	100	0.0086
Patient's Gender	N/A	N/A	N/A
Patient's Residence	N/A	N/A	N/A

DISCUSSION

The fractures of the mandibular angle constitute a technical problem. Moreover, different management strategies have been discussed in the literature. The study found that in managing unfavorable mandibular angle fractures, 3D plate osteosynthesis is as effective as the double mini-plate technique. He stated that both techniques provide adequate stability for correct fracture union, allow for functional occlusion, and enable early return to work. In large and severe displacement or fracture cases, mini-plate adjustment and placement require some time and are technically challenging. However, 3D applications of locking plates offer more efficiency and ease of deployment in operations compared with the current conventional plate systems. This type of plate is not only less time-consuming and easy to apply but also economical and shows better biomechanical properties. Sikora *et al.*, introduced mini plates with 3D dimensions, stating that any structurally stable construction has quadrilateral geometrical stability [18]. This structure enables a thinner plate thickness, which is normally about 1mm. There are four common specifications: the basic sizes are a 2X2-hole square flat plate, a 3X2 or a 4X2-hole rectangular flat plate. At the same time, these are described as "3D mini-plates," and most are not genuine 3D objects. They only ensure fracture stability by opposing forces in the fracture section in the form of shear force, bending moment and twisting moment. Nonetheless, while several writers have reported on the benefits of using 3D mini plates in the management of mandibular fractures, they are not as popular as expected. For instance, a mailed survey of 104 AO/ASIF surgeons established that only 6% use this plate in their practice. A single study comparing the differences in operative time to conventional mini-plates and 3D mini-plates was conducted, which showed that the former took an average of 1.88 ± 0.38 hours as opposed to 1.61 ± 0.27 hours for the 3D mini-plates. Another study of mandibular anterior fractures, single plate for fixation of recommended the use of a single plate for anterior mandibular fracture fixation using a 3D Titanium mini-plate as an effective method as that to Champy's two-mini-plate system. This technique also provides sufficient stability, needs relatively little working time, and is somehow related to the reduced rate of infections over the mini-plate systems [18, 19]. In this study, the average time taken from incision to the completion of the procedure at the sixth postoperative week, Group B 3D plates have recorded the least time as compared to Group A mini-plates $< \text{Chi}^2(p)=0.001$. Also, the level of infection rate was significantly lower in the second group as compared to the first one ($p=0.031$). Based on the findings of this experiment and literature findings made by Feledy *et al.*, Jain *et al.*, and

Zix *et al.*, it is clear that the use of 3D plates decreases average operating time [20-22]. These include greater ease of application, simplified incorporation of the bone, ability to stabilize the superior and inferior borders in one procedure, which makes the 3D plates associated with little morbidity and infection. The infection rates noted by various investigators on 3D plates have been as follows: Feledy *et al.*, 9% (2 out of 22 patients) [20] and Zix *et al.*, [22] (0 out of 20 patients). This protocol says that the mobility of the fractured segments contributes to postoperative infections, and this is contrary to the findings of the other two protocols. Because infection is one of the most frequent complications in mandibular fractures, improving the stability of the plates might reduce it. This study also concludes that there are advantages of employing 3D plates in the management of the anterior mandibular fractures, particularly concerning better three-dimensional stability, less morbidity, and infection rates. One of the threats of these plates could be the extra volume of the implant material due to the fact that supplementary vertical bars are intended to prevent torque forces from acting on the implant.

This study did not account for variability in fracture severity and surgeon expertise, which may have influenced operative time and complication rates. Additionally, short follow-up duration limited the assessment of long-term outcomes such as bone healing, implant stability, and late complications. Future studies should include standardized fracture classification, longer follow-up, and randomized multi-center trials to better evaluate long-term efficacy and safety of 3D plates in mandibular fractures.

CONCLUSIONS

This plate was 3D in shape with a strong mid-section but thin edges, thereby allowing easy reduction and stabilization at the superior and inferior aspects of the fracture site. It offers three-dimensional stability at the fracture site. It appears to be an easy solution to conventional mini plate champs.

Authors' Contribution

Conceptualization: BL

Methodology: BL, SK, SAM, BC

Formal analysis: BL

Writing and Drafting: ZK, HR

Review and Editing: BL, SK, ZK, HR, SAM, BC

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



Correlation of Depression and Nightmares in Young Medical Students

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ABSTRACT

Consistent dream sequences that appear genuine and become more upsetting as they progress are known as nightmares. A prevalent condition that significantly impairs psychosocial performance and lowers quality of life is major depression. Insomnia and nightmares independently but additionally have an impact on the exacerbation of depression. **Objectives:** To find the correlation between depression and nightmares in young medical students. **Methods:** A cross-sectional study was carried out from September 2021 to June 2022, involving 350 medical students aged 18 to 30, distributed across all academic years. The symptoms of depression were measured and assessed using the CES-D scale, while nightmares were evaluated by using a validated sleep 50 questionnaire. Data were analyzed in SPSS version 27.0. **Results:** A total of 350 medical students (49.1% male and 50.9% female), with most aged 19 to 23 years, 91.4%, and single, 97.7%. The mean CES-D score was 23.0 ± 12.42 , higher in females 24.8% than in males 21.0. Severe depression was more common in females 44.9% and first-year students 58.6%. Frequency of nightmares was reported by 23.9%, and the depressed feelings and the frequency of nightmares are significantly correlated ($P=0.019$). Pearson correlation analysis shows a substantial correlation between the frequency of nightmares and depressive moods. ($P \leq 0.01$). **Conclusion:** The study concluded a significant association between depression symptoms and nightmares, particularly in females and younger medical students. Academic and social factors significantly influence depression symptoms.

INTRODUCTION

Depression is a prevalent mental illness marked by persistent melancholy and an indifference to previously enjoyable events. It is often accompanied by difficulty performing daily activities for at least two weeks [1]. Depression symptoms begin at an early age and may either persist or increase over time, depending on an individual's environmental exposure and coping capacity throughout their life [2]. In 2015, over 300 million individuals were estimated to be living with depression, with a global prevalence rate of 4.4%. In Vietnam, depression affects approximately 4.0% of the population, and it occurs in every age group all over the world [3, 4]. It has been noted that medical students experience depression significantly higher compared to their non-medical peers. According to Rorenstein et al.'s systematic review, the pervasiveness of depressive symptoms in medical students ranges from

27% to 55%, influenced by factors such as academic pressure, lack of sleep, and exposure to traumatic clinical experiences. Depression not only affects their academic performance but also has long-term consequences on their professional competencies and patient care [5]. Sleep and issues related to insomnia have received more attention in recent years. Nightmares are disturbing dreams that often involve scenarios of danger, harm, or threats to personal safety, frequently waking the individual from sleep [6]. They may have no known cause, be brought on by post-traumatic stress disorder, or be a side effect of some drugs. Repeated nightmares have been linked to general psychological challenges and certain psychological disorders, such as serious depression and post-traumatic stress disorder, schizophrenia, and borderline personality disorder [7, 8]. One study reported



that frequent nightmares are predictive of depression severity, suggesting that disturbed dreaming may serve as a biomarker for mental health disorders [9]. Recent studies have highlighted a significant correlation between depression and nightmares among healthcare students. According to a 2023 meta-analysis, over 23.5% of medical students in Germany had clinically significant depression symptoms, a rate 2.4 times higher than the general population. This elevated prevalence is attributed to academic pressures, sleep disturbances, and exposure to traumatic clinical experiences. Notably, the study found a close relationship between depression and nightmares, with 16.2% of students experiencing nightmares alongside depressive symptoms [10]. Nightmares disorders have been related to conditions such as insomnia, excessive daytime sleepiness, and persistent fatigue.

Although depression and sleep disturbances, including nightmares, are common among medical students, limited evidence exists on their interrelationship, particularly regarding gender differences in specific populations. This lack of focused research restricts a deeper understanding of how nightmares may reflect or influence mental health outcomes in this group. Thus, this study's main goal is to look into the frequency of nightmares among medical students and explore their potential correlation with gender differences.

METHODS

An analytical cross-sectional study was carried out from September 2021 to June 2022. The sample size was calculated using the WHO calculator $n = z^2 \cdot qp/d^2$ (n: The required sample size. z: the z-score corresponding to the desired confidence level. p: the estimated proportion of the attribute of interest in the population. q: the complement of p, i.e., $q = 1 - p$. d: The desired margin of error or precision. The calculated sample size was 350 medical students, with a 1% margin of error and a 95% confidence level, taking an expected percentage of nightmares in young adults of 16.3% [11]. Upon acceptance by Shalamar Medical and Dental College Institutional Review Board (Ref: SMDC-IRB/AL/158/2021, IRB No: 0325). Data were collected using a non-probability sampling technique. Both male and female MBBS students of all years were included in the study. Students diagnosed with neurological or psychiatric disorders and taking any medication that significantly affects sleep patterns were excluded from the study. After obtaining consent, the questionnaire was shared via Google Forms. It consisted of three sections: demographic information (age, gender, and year of study), questions for assessing depression, and questions for assessing nightmares. The 20-item self-reported CES-D is a validated tool for evaluating depression symptoms. Likert scales with four points, from 0.0 (rarely or never) to 3.0

(most or always), are associated with each item. Scores >16 suggest the presence of significant depression symptoms [12]. The validated SLEEP-50 questionnaire was used to evaluate nightmares. A scale of 1 to 4 was used to rate each item. The questionnaire was scored by summing the responses to items. The scores of items 32 (>3) and items 33- 35 (>9) were the cut-off value to identify nightmares [13]. The questionnaire was shared with the students during their mid-semester. Data were analyzed in SPSS version 27.0. Age and CES-D score were presented as mean and SD. Gender, year of study, social status, and nightmare score were presented as frequencies and percentages. The data distribution was evaluated using the Shapiro-Wilk Test. Chi-square was used to analyze the relationship of severity of symptoms with gender, age, social status, and academic year, while a one-way ANOVA was employed for comparison of the mean scores of depression to nightmares. Pearson's correlation analysis was applied to check the significance of depression scores and nightmares. A P-value of less than 0.05 was considered significant.

RESULTS

In the study, 350.0 medical students participated, comprising 172 (49.1%) males and 178 (50.9%) females. Among these students, most were 19 to 23 years old (91.4%), and were single 342, 97.7%). According to the academic year, 116 (33.1%) from the first year, 63 (18.0%) from the second year, 127 (36.3%) from the third year, and 44 (12.6%) from the fourth year students (Table 1).

Table 1: Descriptive Statistics of Medical Students (n=350)

Variables	Category	N (%)
Gender	Male	172 (49.1)
	Female	178 (50.9)
Age Group (years)	19-23	320 (91.4)
	Others	30 (8.6)
Marital Status	Single	342 (97.7)
	Married/Other	8 (2.3)
Academic Year	First Year	116 (33.1)
	Second Year	63 (18.0)
	Third Year	127 (36.3)
	Fourth Year	44 (12.6)

The mean score for the CES-D was 23.0 ± 12.4 (average=21.0 for males and 24.8 for females). There was a significant difference in the average score between gender and age group. The prevalence of mild depressive symptoms was 32.3%, moderate level was 28.0%, and severe depression was 39.7% (Figure 1).

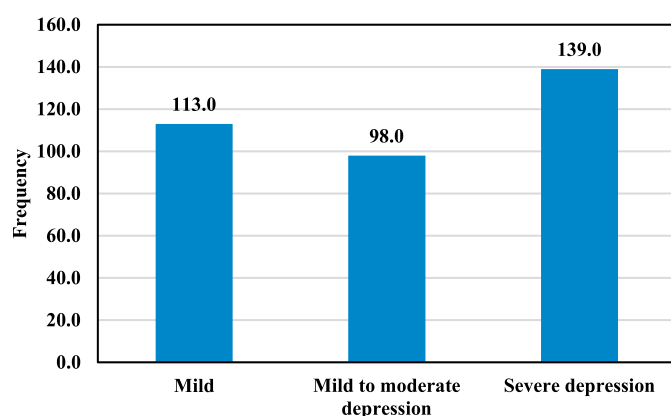


Figure 1: The Percentage of Depressive Symptoms among Students

Most individuals, 93 (26.6%), reported never experiencing nightmares, and 173 (49.4%) experienced them less than once a week. However, 60 (17.1%) experienced nightmares one to three times a week, and only 24 (6.9%) experienced them three or more times weekly, highlighting a smaller group with significant sleep disturbances potentially linked to underlying psychological factors (Figure 2).

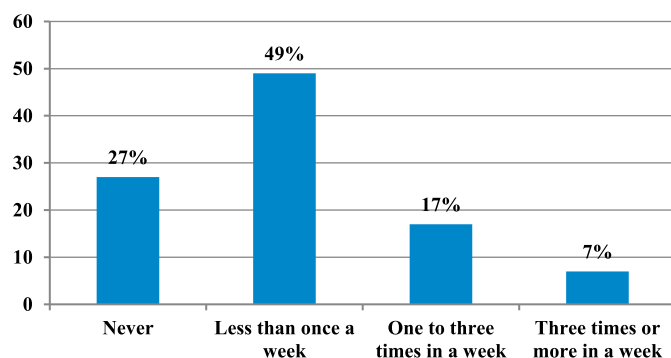


Figure 2: The Percentage of Nightmares among Students

Female participants reported higher rates of severe depression (44.9%) compared to males (34.3%), with males having a higher proportion of mild depression. Participants aged 17 to 21 reported the highest prevalence of severe depression (48.7%), compared to those aged above 21 (23.8%). The upper middle-class group had the highest prevalence of severe depression (44.3%), followed by the lower middle class (30.7%). Participants from the "elite" category exhibited the lowest rates of severe depression (17.6%). However, mild depression symptoms were more prevalent among those from the lower middle class (33.3%). These differences in depression symptoms based on social status were statistically significant ($P=0.025$). Severe depression was most common among first-year students (58.6%) and second-year students (46.0%), while third-year students showed the lowest prevalence of severe depression (23.6%). In contrast, mild depression symptoms were more common among third-year students (45.7%) and fourth-year students (43.2%). This distribution

shows a significant association between academic year and depression symptoms ($P=0.001$) (Table 2).

Table 2: The Relationship of Severity of Symptoms with Gender, Age, Social Status, and Academic Year (Chi-Square Test)

Depression Symptoms n (%)					
Variables	Category	Mild	Moderate	Severe	p-Value
Gender	Male	66 (38.4)	47 (27.3)	59 (34.3)	0.015*
	Female	47 (26.4)	51 (28.7)	80 (44.9)	
Age (year)	17 to 21	62 (27.7)	53 (23.7)	109 (48.7)	0.040*
	>21	51 (40.5)	45 (35.7)	30 (23.8)	
Social Status	Poor	2 (6.7)	1 (3.3)	0	0.025*
	Lower middle class	25 (33.3)	27 (36.0)	23 (30.7)	
	Upper middle class	81 (31.8)	61 (23.9)	113 (44.3)	
	Elite	5 (29.4)	9 (52.9)	3 (17.6)	
Academic year	First year	22 (19.0)	26 (22.4)	68 (58.6)	0.001*
	Second year	14 (22.2)	20 (31.7)	29 (46.0)	
	Third year	58 (45.7)	39 (30.7)	30 (23.6)	
	Fourth year	19 (43.2)	13 (29.5)	12 (27.3)	

* $P \leq 0.05$ significant

Depression scores are almost similar across groups, ranging from 21.4 to 24.0, with the highest mean score observed in individuals experiencing nightmares one to three times a week. Group differences are statistically significant, as indicated by the P value of 0.019 (Table 3).

Table 3: Relationship between Nightmare Experience with Depression Score (One-Way ANOVA)

Nightmare Experience	Depression Score			
	N	Mean $\pm$ SD	CI	p-Value
Never	96	21.7 $\pm$ 12.0	(19.3 to 24.2)	0.019*
Less than once a week	182	22.2 $\pm$ 11.6	(20.5 to 23.9)	
One to three times a week	51	24.2 $\pm$ 12.5	(20.6 to 27.7)	
Three times or more in a week	21	22.4 $\pm$ 13.2	(16.3 to 28.4)	

Values are presented as mean $\pm$ SD, * $P \leq 0.050$ significant

A Pearson correlation analysis was conducted to examine the relationship between nightmare frequency and depressive symptoms. The results indicated a weak but statistically significant positive correlation ($r=0.157$, $p=0.003$), suggesting that students who experienced nightmares more frequently tended to have higher depression scores. While the strength of the association was modest, given the significant p-value, it is improbable that the association happened by chance (Table 4).

Table 4: Correlation between Nightmare Distress and Depression Symptoms Among Medical Students (Pearson Correlation)

Variables		Nightmare Experience	Depression Scores
Nightmare Experience	Pearson Correlation	1	-
	Sig. (2-tailed)	0.003	-
Depression Scores	Pearson Correlation	0.157**	1
	Sig. (2-tailed)	0.003	350.0

**Correlation is significant at the 0.01 level (2-tailed)

DISCUSSION

Many tools were used to assess depression levels in the research population, often with differing cut-off points across studies [14, 15]. In current study, CES-D scale was used, a widely recognized self-report metric with proven reliability in different cultures. Study findings showed a mean CES-D score of 23.1, indicating depressive symptoms (CES-D scores of 16 or higher) among the students of medicine. This score was greater than the mean of 14.58 reported in a study of a diverse sample, including Asian society. These results highlight the need for education managers to address mental health issues among university students through screening and early intervention programs [16]. In this study, severe depression was more common in females 44.9% than males 34.3%, and in younger participants (48.7% for ages 17-21) compared to older ones (23.8%). In comparison, the weekly frequency of nightmares showed that male and female students differed significantly. Among females, 31.9% reported experiencing nightmares once a week compared to 4.1% of males. There were 9.8% versus 5.7% reported twice a week, 5.7% versus 0.8% three times weekly, and 3.2% versus 1.6% more than three times weekly. Overall, female students experienced nightmares more frequently than their male counterparts [17]. In the present study, female students reported higher rates of severe depression (47.8%) compared to males (34.3%), with males having a high frequency of normal depression. Previous study reported that 50.9% of males, mean age was 14.9 ± 1.45 , adolescents with frequent nightmares reported significantly higher nightmare distress and depressive symptoms ($P < 0.001$) compared to those without nightmares [18]. Another study found that the mean age was 15.31 ± 1.88 years, with 37.3% being boys. Frequent nightmares were reported by 49.3% of patients with psychosis. Females experience more depressive symptoms with nightmares and distress compared to males, and a significant association between them. Pearson correlation analysis revealed a slight positive correlation between nightmare experience and depression, with a significant relationship observed ($P < 0.01$). In comparison, in a 2023 study conducted in emergency department nurses, there was a positive correlation between nightmare distress levels and depressive symptom scores ($r = 0.732$). To lessen the incidence of depressed symptoms, early management is advised for professionals with this kind of sleep disturbance [19]. According to a study in European Psychiatry, 16.2% of depressed medical students reported having dreams, indicating a strong correlation between the frequency of nightmares and depressive symptoms [12]. Similarly, a meta-analysis in JAMA reported that approximately 27.2% of medical students exhibited

depressive symptoms, a prevalence higher than that of the population [20]. These findings suggest that the demanding nature of medical education may contribute to increased psychological distress, manifesting as both depression and sleep disturbances like nightmares.

This study relied on self-reported measures (CES-D and nightmare frequency), which may be subject to recall and reporting bias. Additionally, the cross-sectional design limits the ability to determine the direction of association between depression and nightmares. Future studies should use longitudinal designs with objective sleep assessments and psychological evaluations to better understand the causal relationship between nightmares and depression among medical students.

CONCLUSIONS

This study found an association between depression and nightmares among young medical students. Students experiencing frequent nightmares reported higher depression scores, with the strongest symptoms observed among females and first-year students. These findings highlight the potential of nightmares as clinical indicators of underlying depressive symptoms. Longitudinal and experimental studies are needed to clarify the directionality between nightmares and depression.

Authors' Contribution

Conceptualization: KY

Methodology: KY, HHP

Formal analysis: KY

Writing and Drafting: KY, HHP

Review and Editing: KY, HHP

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



YouTube, Med-Cram, Online Med-Ed, and Traditional Lectures: A Comparative Study of Healthcare Students' Preferences

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ABSTRACT

The computer technology revolution drove the widespread adoption of online learning resources in higher education, met the preferences of tech-savvy students, and was accelerated by the pandemic. **Objective:** To evaluate learning style preference among health care students. **Methods:** This comparative cross-sectional study was conducted between two groups: the first one attended conventional live lectures, and the second one used other online learning resources for undergraduate students at Combined Military Hospital (CMH) Lahore Medical College (LMC) and Institute of Dentistry (IOD) Lahore from May to July 2024. The study involved 296 undergraduate students from various healthcare disciplines. First-year students were excluded from the study. Data collection employed a validated questionnaire assessing dimensions such as social presence, interaction, and satisfaction. **Results:** The results revealed a strong preference for in-person learning, citing enhanced engagement, interaction, and immediate feedback as key advantages. Despite the convenience and flexibility of online learning, it fell short in replicating the depth of interpersonal communication and satisfaction achieved in traditional settings. **Conclusions:** It was concluded that a hybrid learning model, combining the strengths of both approaches, could better address diverse student needs. Future research should explore the effectiveness of such models in improving educational outcomes across healthcare fields.

INTRODUCTION

The computer technology revolution drove the widespread adoption of online learning resources in higher education, met the preferences of tech-savvy students, and was accelerated by the pandemic. This prompted rapid adaptation to remote teaching, fostered innovation in teaching methods and digital skills, and emphasized the

need for inclusive technology to address diverse student needs and ensure equitable access to education [1]. Emerging technologies like internet streaming videos on platforms like YouTube, Med-Cram, Online Med-Ed, Google, and Zoom have made higher education more accessible and affordable for many students [2]. In e-learning,



learners access instructional content and activities at any time, independent of classroom schedules, benefiting from various resources like course notes, e-books, and videos, and engaging in online activities tailored to enhance learning experiences [3]. In Pakistan, most higher education institutes used face-to-face modes of education, and online education was not as extensively used in the bygone days [4]. Online learning involves utilizing the internet for studying, communication, and support to enhance knowledge and growth. This necessitated the enhancement of e-learning in medical education through resource provision and training while ensuring safe on-site clinical teaching [5]. In contrast, a study highlighted that face-to-face dialogue resulted in more effective communication due to enhanced neural synchronization. Face-to-face lectures offered direct engagement, fostering interactive learning, immediate clarification, and personalized feedback for students. These in-person discussions allowed students to think more deeply and reflect on others' ideas, promoting richer intellectual exchange [6]. Each new generation of students had traits, concerns, and learning preferences that set them apart from previous generations. Understanding these differences was essential for educators to design learning environments that were engaging, motivating, and effective. As we moved into the modern era, significant advancements were made in face-to-face learning to accommodate these evolving needs and preferences [7]. A previous study indicates that students prefer face-to-face learning due to real-time social interaction, while online learning faces challenges like technology issues. Advantages of face-to-face include clarity and engagement, whereas online offers convenience but lacks effective interaction and support [8].

Previously, research focused on e-learning and conventional live lectures during the pandemic, specifically targeting medical students. Our study focused on face-to-face learning and online resources conducted outside the pandemic. This study aims to appraise the perception of medical students about conventional live lectures and online resources.

METHODS

It was a comparative cross-sectional study, conducted at CMH LMC and IOD Lahore (May to July 2024) after obtaining approval from the ethical review committee, letter no. 22/ERC/CMH/LMC. This study was conducted on students, currently enrolled in CMH LMC and IOD, belonging to five medical professions (MBBS, BDS, DPT, MIT, and Nursing) at various academic levels. Students belonging to the 2nd year to the final year were included in the study. First-year students were excluded from the study as they had limited exposure to both methods of teaching and learning in a professional set-up. The students were routinely exposed

to face-to-face learning due to a compulsory attendance requirement by the university (at least 75% in a given year). Online sessions, if required, were conducted via Zoom, wherein attendance was marked only if the student joined the session within the first 20 minutes and remained in the session for the entire duration of the class. A total of 296 undergraduate students participated in the study. The sample size was calculated by using Taro Yamane's formula with 95% confidence level and 5% margin of error as given below: $n = \frac{N}{1 + N(e)^2}$. In formula: n = sample size, N = Total number of populations, e = Margin of error (%), $n = \frac{1139}{1 + 1139(0.05)^2}$ and $n = 296$. A simple randomization technique was used to select subjects from the selected population. This study employed a pretested questionnaire [9] having three instruments (25 items and three dimensions) to gather the data from the target population. The questionnaire was used to measure learning preferences across healthcare disciplines towards online learning or conventional live lectures. The reliability of each variable used in this study was analyzed by Cronbach's alpha. The Social Presence Scale was developed by Spears [10]. The Social Interaction Scale was developed by Picciano [11] and the Students' Satisfaction Scale [13]. The reliability of the full survey (composed of three components) was 0.973 for the online study and 0.977 for the face-to-face learning. Different codes were allotted to different demographic items. To evaluate students' perceptions of social presence, a set of questions (Q1 to Q9) related to this topic was included in the student satisfaction survey. The section on Social Interaction comprised six questions (Q9 to Q14), designed to assess scholars' satisfaction and engagement during face-to-face literacy. The questions concentrated on colourful aspects of the literacy experience, such as clarity of instruction, commerce, and course applicability. Satisfaction section included ten questions (Q15 to Q25) that explored scholars' favoured literacy styles and their situations of their situations. Responses were collected to gauge overall satisfaction and engagement in face-to-face vs. online learning environments. Data were entered into SPSS version 25.0. Descriptive statistics were used to analyze data, and frequencies and percentages were determined.

RESULTS

The majority of participants were female (79.4%), and male were 20.6% of the total sample size. MBBS and BDS students formed about 48% of the total respondents, while the rest of the students (52%) belonged to allied health sciences (DPT, MIT & nursing). Of these students, the majority belonged to the 2nd (95, 32.1%) and 4th year (91, 31%), while the rest belonged to the 3rd and final year. Face-to-face learning was rated significantly higher than online learning, with students favouring in-person instruction across all dimensions (Table 1).

Table 1: Comparison of Responses to Face-to-Face Learning and Online Learning in Response to Social Presence Scale

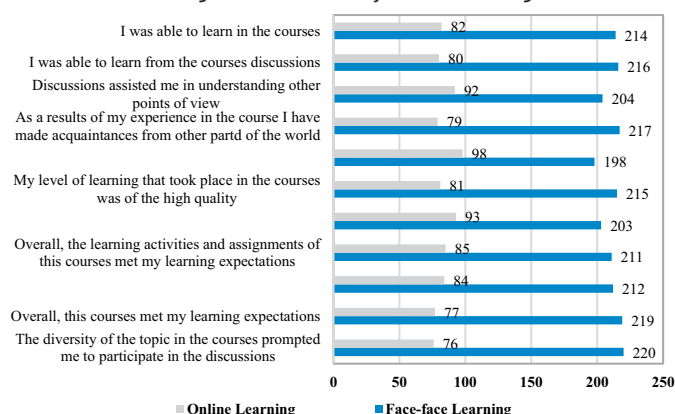
Questions	Face-to-face Learning	Online Learning
	n (%)	n (%)
Communication in the course was impersonal.	210 (70.9%)	86 (29.1%)
I felt comfortable conversing in the course.	228 (77%)	68 (23%)
I felt comfortable introducing myself in the course.	220 (74.3%)	76 (25.7%)
The course introduction enabled me to form a sense of community.	227 (76%)	69 (23.3%)
I felt comfortable participating in the course discussion.	228 (77%)	68 (23%)
The instructor created a feeling of community.	238 (80%)	58 (19%)
The instructor facilitated discussion in the course.	235 (79.4%)	61 (20.6%)
I felt that my point of view was acknowledged by other students in the course.	233 (78.7%)	63 (21.3%)

The results showed a strong inclination towards face-to-face literacy, with a maturity of students indicating an advanced level of satisfaction with this system (Table 2).

Table 2: Comparison of Responses to Face-Face Learning and Online Learning in Response to Social Interaction scale

Questions	Face-to-face Learning	Online Learning
	No. of responses (%)	No. of responses (%)
Courses are an excellent means for social interaction.	219 (74%)	77 (26%)
I felt comfortable interacting and participating with other students in courses.	221 (74.7%)	75 (25.3%)
The amount of interaction with other students in the course was appropriate.	228 (77%)	68 (23%)
The quality of interaction with other students in the courses was appropriate.	240 (81.1%)	56 (18.9%)
The amount of interaction with the instructor in the course was appropriate.	234 (79.1%)	62 (20.9%)
The quality of interaction with the instructor in the course was appropriate.	239 (80.7%)	57 (19.3%)

This preference was significantly more common compared to online or amalgamated literacy druthers (Figure 1).

**Figure 1:** Comparison of responses to face-face learning and online learning in response to Social Presence scale

Overall, the findings suggested that scholars feel more engaged and satisfied in traditional, in-person literacy surroundings.

DISCUSSION

Our research sought to investigate and compare the learning preferences of medical students regarding traditional in-person lectures versus online resources. It involved evaluating how these different modes affected student satisfaction, interaction, and engagement, as well as their perceived effectiveness in meeting learning objectives. A significant majority of participants expressed a strong preference for traditional in-person learning over online alternatives. Students rated in-person learning more favorably in terms of social presence, interaction, and overall satisfaction. These results indicated that direct engagement with instructors and peers is a vital component of effective learning. Similar to our study, various other researches indicate that many students favor traditional classroom settings due to the perceived benefits of direct interaction and engagement. A study found that 83% of students favored in-person classes, citing enhanced interaction and learning experiences as primary reasons for their preference [13]. Similarly, students reported higher levels of engagement and participation in face-to-face settings, which fosters better communication and collaboration [14, 15]. Another survey reported that 53.1% of students preferred face-to-face learning due to its effectiveness in achieving learning outcomes compared to online formats [16]. This supports theories that highlight the importance of interpersonal engagement in improving both cognitive and emotional dimensions of learning. Likewise, previous studies pointed to a preference for in-person learning, emphasizing its capacity to facilitate better interaction and engagement—also, they noted that while online learning provided flexibility, it often fell short in aspects such as student interaction, satisfaction, and perceived effectiveness [17,

18]. Face-to-face learning offers real-time interaction and social skill development but has drawbacks like limited material processing and discipline issues-conversely, online learning provides flexibility and better academic progress, indicating a complex preference landscape among students [19]. Face-to-face learning often requires adherence to strict schedules, which can be challenging for students with other commitments [20]. Online learning offers accommodating diverse lifestyles; not all students can easily attend in-person classes due to health-related constraints [21]. However, many students feel isolated in online environments, which can hinder their motivation and engagement [14, 20]. Issues with technology and digital literacy can impede the effectiveness of online learning, leading to frustration among students [21]. Current study suggested investigating hybrid learning models to combine the advantages of online flexibility with the engagement offered by in-person methods. Even though a minor number of participants but they nevertheless supported online mode of teaching and learning. An earlier research recommended blended learning as an effective strategy to balance flexibility with meaningful interaction [22]. Conducted in a post-pandemic context, our research focused on preferences beyond the limitations of emergency remote teaching. Many earlier studies such as [23] examined learning preferences during the pandemic, concentrating on the rapid shifts to online education driven by necessity, which emphasized short-term adaptability rather than long-term preferences. Our study involved undergraduate students representing various healthcare fields. Other studies often targeted more specific subgroups, such as orthodontic students or broader student populations across different academic disciplines, providing less emphasis on healthcare education [24]. Our research took place in Pakistan, focusing on localized educational systems and cultural learning contexts while previous studies were conducted in Western settings, often reflecting different technological infrastructures, teaching methodologies, and student expectations. The preference of students for in-person learning likely indicates the importance they attribute to these contextual experiences, which are crucial for acquiring practical skills in their respective fields. This observation supports the hypothesis of "Constructivism learning theories," which assert that learning is most effective when it takes place in genuine, context-rich settings. It posits that education is most beneficial when it is integrated into authentic contexts, enabling students to relate theoretical knowledge to real-world applications. In healthcare education, in-person learning promotes activities like clinical training and laboratory work, which are consistent with constructivist principles of situated cognition [25]. Our research indicated that in face-to-face learning environments, students received immediate feedback from both

instructors and peers, facilitating real-time reflection and adjustments. This iterative process fostered deeper learning and was in line with constructivist principles. Vygotsky's concept of the Zone of Proximal Development (ZPD) highlights the significance of instructors in providing support that enables students to accomplish tasks they could not manage alone. The immediate assistance and feedback available in face-to-face learning settings correspond with this principle, making it more effective for students compared to online formats [26]. In addition, our research indicated that in-person environments facilitate more effective communication through both verbal and non-verbal signals, including body language, tone, and facial expressions. These signals improve comprehension, lessen uncertainty, and contribute to a more engaging and personal educational experience, which students appreciate. Non-verbal communication, such as facial expressions and body movements, plays a crucial role in enhancing understanding and building connections during face-to-face learning [6]. The key findings of our research carry important implications for educators, educational institutions, and policymakers. Institutions ought to focus on developing interactive, engaging, and socially enriching classroom settings that promote student interaction and involvement. Educators might consider integrating more active learning methods, such as problem-based learning (PBL) and flipped classrooms, where students participate in hands-on activities and real-time discussions instead of merely attending passive lectures. Teacher training programs could offer workshops aimed at enhancing engagement through active learning strategies, improving communication in face-to-face settings, and delivering timely feedback to students. Although students showed a preference for in-person learning, the adaptability of online education also holds significant value. The inclination towards direct interaction implies that a hybrid or blended learning model could be the most effective. Educational institutions can create blended learning frameworks that merge the advantages of both in-person engagement and online resources, providing flexibility. This strategy can accommodate a broader spectrum of learning preferences, resulting in a more balanced educational experience.

This study relied on self-reported student perceptions, which may not accurately reflect actual learning outcomes or academic performance. Additionally, the study did not assess objective measures of effectiveness (e.g., exam scores) or account for variations in teaching quality and digital accessibility, which may influence learning preferences. Future studies should incorporate objective academic performance indicators and evaluate hybrid learning models across diverse educational settings to better determine the effectiveness of different teaching modalities.

CONCLUSIONS

This research examined the learning preferences of students in medical, dental, nursing, and allied health sciences at CMH LMC and IOD Lahore, comparing online resources like YouTube Med-Cram and Online Med-Ed with traditional in-person lectures. The results indicated a strong preference for face-to-face instruction, especially regarding social interaction, engagement, and overall satisfaction. Students appreciated the direct interaction and prompt feedback that traditional lectures provided, which were less common in online settings. Although online learning offered flexibility and ease of access, it fell short of replicating the personal interactions found in live lectures, resulting in lower satisfaction levels among students. These findings imply that future educational approaches should explore hybrid models that integrate the advantages of both online and in-person learning to cater to the varied needs of students.

Authors' Contribution

Conceptualization: AB, FI¹, FJ, TM, KHC

Methodology: AB, FI¹, FJ, TM, KHC, FI², RKA

Formal analysis: AB

Writing and Drafting: AB, FI¹, FJ, TM, KHC

Review and Editing: AB, FI¹, FJ, TM, KHC, FI², RKA

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

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Original Article

Association of Oxytocin-Augmented Labor with Neonatal Jaundice Requiring Phototherapy: A Comparative Study

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ABSTRACT

Neonatal jaundice is a dangerous illness that, if left untreated, can lead to deadly consequences. Oxytocin seems to have a dose-dependent influence on elevated plasma bilirubin levels in cord blood, which are likely exacerbated by the breakdown of fetal red blood cells. **Objectives:** To determine the frequency of patients who undergo labour augmentation with the use of oxytocin and to compare the frequency of neonatal jaundice among the gravid female who labor with and without oxytocin augmentation. **Methods:** This analytical cohort study was conducted in the Department of Obstetrics and Gynaecology, Sughra Shafi Medical Complex, Narowal from 01-07-2021 to 31-12-2021. A total of 186 gravid females were included in this study. These patients were divided into two groups: Group A (augmentation with oxytocin, n=30) and Group B (spontaneous labour without oxytocin augmentation, n=156). Neonatal jaundice was assessed based on serum bilirubin levels and whether phototherapy was required. Data were analyzed using SPSS-25, with descriptive statistics and relevant comparisons between the groups. **Results:** The mean age of the participants was 26.9 ± 4.3 years. There were 56 primigravida (30.1%) and 130 multigravida (69.9%). Neonatal jaundice requiring phototherapy occurred in 40% of neonates in Group A and in 19.2% in Group B. **Conclusions:** It was concluded that when maternal oxytocin is used to induce labor, newborn jaundice is more likely to occur and phototherapy is more frequently required. It is advisable to consider careful oxytocin dosing to avoid the risk of hyperbilirubinemia.

INTRODUCTION

Numerous factors have influenced the experience of childbirth, including medical interventions, the degree of labor pain, the quality of care and services, and awareness of the labor process. One of the most common complications observed in both term and preterm neonates is neonatal jaundice. Among the possible contributors to the increasing prevalence of neonatal jaundice is the use of oxytocin in labor management [1, 2]. Strong and synchronized uterine contractions are essential for cervical dilation and fetal delivery during

parturition. However, the first stage of labor can sometimes be prolonged; evidence suggests that approximately 14% of women entering labor for the first time experience a delay or arrest in cervical dilation. In such cases, after amniotomy (artificial rupture of membranes), labor augmentation achieved by increasing the frequency and intensity of contractions is often performed using intravenous oxytocin [3]. Although oxytocin is widely utilized for labor induction and augmentation, it may lead to adverse outcomes such as uterine hyper stimulation and



fetal distress. Prostaglandins are also commonly administered systemically or locally to ripen the cervix and induce or augment labor. Oxytocin, a naturally occurring peptide hormone, facilitates uterine and epididymal muscle contraction and is involved in milk ejection during lactation [4]. Several studies have confirmed the association between oxytocin administration and the development of neonatal jaundice. Findings suggest that oxytocin's vasopressin-like effects induce osmotic swelling in erythrocytes, making them more fragile and susceptible to hemolysis, ultimately leading to hyperbilirubinemia in neonates [5]. Erythrocyte deformability plays a critical role in cell survival, and a reduction in deformability has been associated with increased hemolysis in various contexts [6]. According to studies neonatal jaundice requiring phototherapy was more frequently observed (38%) among neonates born to mothers who underwent labor augmentation either with or without oxytocin during term spontaneous vaginal delivery. To the best of the candidate's knowledge, limited published data, both locally and internationally, are available on this specific association [7, 8]. This study is, therefore, significant in evaluating whether oxytocin, a drug frequently employed to augment labor increases the incidence of neonatal jaundice. If this relationship is confirmed in the local population, the identification of alternative therapeutic options could help in preventing this potentially serious neonatal complication, ultimately reducing associated neonatal morbidity and mortality [9]. In addition to its use in promoting labor progression, oxytocin is also routinely administered intramuscularly during the third stage of labor to prevent postpartum hemorrhage. According to the Listening to Mothers II study, approximately 50% of women giving birth in U.S. hospitals received oxytocin for labor induction or augmentation [10]. Oxytocin exerts its effects by binding to G-protein-coupled oxytocin receptors (OTRs) located on myoepithelial cells, resulting in increased intracellular calcium levels and smooth muscle contraction [11].

Given the widespread use of oxytocin in obstetric care and the growing concern over its potential side effects, it is crucial to further investigate its relationship with neonatal outcomes, particularly jaundice. If a significant association is confirmed between oxytocin use and increased rates of neonatal jaundice requiring phototherapy, this may have important clinical implications for labor management practices. Such findings could support the consideration of alternative methods or modified dosing protocols to reduce the risk of hyperbilirubinemia and its complications in neonates. This study aims to determine the frequency of labor augmentation with oxytocin and to compare the frequency of neonatal jaundice among gravid females who

undergo labor with and without oxytocin augmentation in a local population setting.

METHODS

This analytical cohort study was conducted at the Department of Obstetrics and Gynaecology, Sughra Shafi Medical Complex, Narowal, from 01-07-2021 to 31-12-2021, after obtaining ethical approval from Green International University (IRC-GIU-158-12-2024). Gravid female aged between 18 and 35 years, carrying a single live fetus in cephalic presentation and undergoing labor as per operational definition, were included in the study after signing written informed consent. Patients were excluded if they were primary gravida with a history of uterine surgery such as myomectomy, or if they had Rh incompatibility, neonates with WBC count $>15000/\text{mm}^3$, birth weight <2500 grams, gross congenital anomalies, or APGAR score <7 at five minutes. Mothers with comorbid conditions such as diabetes mellitus (random blood sugar >200 mg/dL) or hypertension (systolic blood pressure >140 mmHg on two separate occasions, 12 hours apart) were also excluded, based on clinical history, examination, and investigations. After approval, a total of 186 gravid females fulfilling the criteria and presenting to the Obstetrics Department were counselled, explained the study objectives, and enrolled after written consent. A detailed history was taken, and patients were clinically assessed and divided into two groups based on labor progression and need for augmentation. Group A consisted of those requiring augmentation with oxytocin, and Group B included those undergoing spontaneous labor without oxytocin. After the active stage of labor was established on clinical examination, patients were monitored in the labor room using cardiotocography (CTG), and labor progression was checked every 30 minutes. Labor arrest was defined as per operational criteria, and patients requiring augmentation were assigned to Group A. Oxytocin was administered at 6-8 drops per minute in 500 ml of normal saline, starting at 5 mIU/min and increased by 6 mIU/min every 30 minutes until effective uterine contractions were achieved or the baby was delivered. In Group B, labor was allowed to progress spontaneously with continuous CTG monitoring until delivery. After birth, neonates were handed over to the Pediatrics Department and monitored for hyperbilirubinemia requiring phototherapy for three days, as per operational definition. To minimize bias, all deliveries were conducted by the same obstetrics team, including the candidate, and all lab tests were performed in the hospital's laboratory to maintain uniformity. Neonatal jaundice was defined as serum bilirubin >15 mg/dL requiring phototherapy within the first three days of life. Data were entered and analyzed using SPSS version 25.0. Numerical variables such as maternal age, BMI, and

neonatal birth weight were presented as mean $\pm$ standard deviation. Categorical variables like oxytocin use and neonatal jaundice requiring phototherapy were presented as frequencies and percentages. The chi-square test was applied to compare the frequency of neonatal jaundice requiring phototherapy between the two groups, considering a p-value ≤ 0.05 as statistically significant. Parity was also recorded as frequency. Data were stratified for age, parity, BMI, and neonatal weight, and a post-stratification chi-square test was applied again, with a p-value ≤ 0.05 considered statistically significant.

RESULTS

Results present a summary of the demographic, clinical, and outcome characteristics of the total study population (n=186). The majority of participants were aged between 26 and 35 years, comprising 62.9% of the sample, with a mean age of 26.9 ± 4.3 years. Regarding parity, 30.1% of the women were primigravida, while 69.9% were multigravida, indicating a higher representation of women with previous deliveries. In terms of body mass index (BMI), 59.7% of the participants had a BMI below 30 kg/m^2 , whereas 40.3% had a BMI of 30 kg/m^2 or above. The mean BMI was calculated to be $29.8 \pm 5.0 \text{ kg/m}^2$. Neonatal weight distribution showed that 87.1% of the newborns weighed more than 2.5 kg, and the mean birth weight was $3.2 \pm 0.5 \text{ kg}$. The distribution of labor augmentation methods showed that 16.1% of the participants received oxytocin for augmentation (Group A), while 83.9% underwent spontaneous or non-augmented labor (Group B). Among those in Group A, 40.0% of the neonates developed jaundice that required phototherapy, compared to 19.2% in Group B. This difference was statistically significant ($p = 0.013$), indicating a potential association between oxytocin use during labor and the increased risk of neonatal hyperbilirubinemia necessitating phototherapy (Table 1).

Table 1: Demographic, Clinical, and Outcome Characteristics of the Study Population (n=186)

Variables	Category	n (%)	Mean $\pm$ SD
Age	18-25	69 (37.1%)	26.9 $\pm$ 4.3
	26-35	117 (62.9%)	
Parity	Primigravida	56 (30.1%)	—
	Multigravida	130 (69.9%)	
BMI (kg/m ²)	<30	111 (59.7%)	29.8 $\pm$ 5.0
	>30	75 (40.3%)	
Neonatal Weight (kg)	<2.5	24 (12.9%)	3.2 $\pm$ 0.5
	>2.5	162 (87.1%)	
Augmented Labour	Augmentation with Oxytocin	30 (16.1%)	—
	Augmentation without Oxytocin	156 (83.9%)	

Findings show that neonatal jaundice requiring phototherapy occurred significantly more often in newborns delivered with oxytocin-augmented labor (40%)

compared to those without oxytocin (19.2%). This difference was statistically significant ($p=0.013$), suggesting a potential link between oxytocin use and increased risk of jaundice (Table 2).

Table 2: Comparison of labor with and without Oxytocin Augmentation

Neonatal Jaundice Requiring Phototherapy	LABOUR		Total	p-Value
	Group A with Oxytocin Augmentation	Group B without Oxytocin Augmentation		
Yes	12 (40%)	30 (19.2%)	42 (22.6%)	0.013
No	18 (60%)	126 (80.8%)	144 (77.4%)	
Total	30	156	186	

Note. Neonatal jaundice was significantly more frequent in oxytocin-augmented labor ($p=0.013$).

The study illustrates that neonatal jaundice requiring phototherapy was significantly more common in the oxytocin group among mothers aged 26–35, multigravida women, and neonates weighing over 2.5 kg. No significant differences were observed for younger mothers (18–25 years), primigravida women, low birth weight neonates, or BMI categories. These findings suggest that specific maternal and neonatal factors may influence the risk of jaundice when labor is augmented with oxytocin (Table 3).

Table 3: Stratification of Neonatal Jaundice Requiring Phototherapy by Maternal and Neonatal Characteristics (n=186)

Variables	Category	Neonatal Jaundice	Group A	Group B	Total	p-Value
Age	18-25	Yes	2 (15.4%)	11 (84.6%)	13 (100%)	0.781
		No	7 (12.5%)	49 (87.5%)	56 (100%)	
	26-35	Yes	10 (34.5%)	19 (65.5%)	29 (100%)	0.007
		No	11 (12.5%)	77 (87.5%)	88 (100%)	
Parity	Primi-gravida	Yes	4 (36.4%)	7 (63.6%)	11 (100%)	0.119
		No	7 (15.6%)	38 (84.4%)	45 (100%)	
	Multi-gravida	Yes	8 (25.8%)	23 (74.2%)	31 (100%)	0.043
		No	11 (11.2%)	88 (88.9%)	99 (100%)	
Neonatal Weight	<2.5	Yes	1 (9.1%)	10 (90.9%)	11 (100%)	0.902
		No	1 (7.7%)	12 (92.3%)	13 (100%)	
	>2.5	Yes	11 (35.5%)	20 (64.5%)	31 (100%)	0.003
		No	17 (13%)	114 (87%)	131 (100%)	
BMI	<30	Yes	4 (14.8%)	23 (85.2%)	27 (100%)	0.692
		No	10 (11.9%)	74 (88.1%)	84 (100%)	

Note. A p-value <0.050 indicates a statistically significant association between oxytocin use and neonatal jaundice within specific subgroups.

DISCUSSION

Both term and preterm babies may be affected by hyperbilirubinemia, a benign illness that often affects newborns [12]. The extensive use of oxytocic medications to treat labor may be one of the causes of the higher frequency of neonatal hyperbilirubinemia (NNH) in healthy-term newborns. It is widely known that maternal oxytocin

usage is linked to NNH [6]. In contrast to spontaneous labor, oxytocin-induced labor results in less deformable fetal erythrocytes. According to in vitro research, oxytocin treatment reduced erythrocyte deformability in a time- and dose-related manner [12]. Despite recent improvements in the treatment of newborns with jaundice, bilirubin poisoning is still a major issue. Although rare, kernicterus accounts for at least 70% of long-term morbidities and 10% of deaths in these neonates [13]. Deformability was impacted by oxytocin crossing the placenta, as demonstrated by in vitro studies. The range of oxytocin concentrations in maternal blood during oxytocin-induced labor revealed both a time-related and a dose-related effect of oxytocin on erythrocyte deformability [14]. The clinical observations that NNH during labor induction is correlated with the dosage and duration of oxytocin administration are similarly explained by these in vitro findings. Our research confirmed that oxytocin-induced labor was associated with an increase in erythrocyte breakdown. Oxytocin's vasopressin-like activity triggers the passage of water and electrolytes across the erythrocyte membrane, resulting in osmotic swelling. This is a known factor that reduces erythrocyte deformability and speeds up erythrocyte breakdown. Clinical hyperbilirubinemia develops in the newborn because their hepatic enzymes cannot handle the increased bilirubin production. Since oxytocin is a crucial obstetrical medication and its usage is most likely unavoidable, it is also impossible to halt its effects on erythrocytes. Nonetheless, it makes sense to lower the oxytocin dosage to avoid hyperbilirubinemia [16]. In the current study, 16.1% of the patients underwent augmentation with oxytocin, and 83.9% of patients did not receive oxytocin. Our results are comparable with a study carried out by Kellie, who demonstrated that 14% of women underwent augmentation with oxytocin [17]. In the group with oxytocin augmentation, the frequency of neonatal jaundice requiring phototherapy was 40%, while in the group without oxytocin augmentation, 19.2% of neonates required phototherapy [18]. The difference between the two groups was statistically significant ($p=0.013$). The findings of our study are consistent with a study conducted by Balasubramanian et al., [19], who reported that neonatal jaundice requiring phototherapy occurred in 38% of neonates whose mothers received oxytocin, compared to 18% in the group without oxytocin augmentation [20]. This study did not quantify the exact dosage and duration of oxytocin administration, which could have influenced the severity of neonatal hyperbilirubinemia. Additionally, other contributing factors such as neonatal feeding patterns, gestational age variations, and genetic

predisposition to jaundice were not evaluated. Future studies should assess dose-response relationships of oxytocin and include comprehensive neonatal risk factors to better understand its role in hyperbilirubinemia.

CONCLUSIONS

It was concluded that inducing labor with maternal oxytocin raises the risk of newborn jaundice requiring phototherapy; therefore, it makes sense to lower the oxytocin dosage to avoid hyperbilirubinemia.

Authors' Contribution

Conceptualization: NAB, FS

Methodology: NAB, FS, SW, SA

Formal analysis: NAB, SW

Writing and Drafting: NAB, FS, SW, SA, ZA, AI

Review and Editing: NAB, FS, SW, SA, ZA, AI

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

Conflicts of Interest

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Original Article



Prevalence and Characteristics of Early vs. Late-Onset Preeclampsia: A Cross-Sectional Descriptive Study

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ABSTRACT

Preeclampsia is the most frequent medical complication of pregnancy and a leading contributor to maternal morbidity and mortality. However, there is a lack of data on the outcomes of pre-eclamptic women, making the current study necessary. **Objectives:** To determine the prevalence and compare the clinical characteristics of early-onset and late-onset preeclampsia among pregnant women. **Methods:** It was a descriptive cross-sectional study conducted for 6 months at the Department of Obstetrics and Gynecology, Sughra Shafi Medical Complex, Narowal. It involved 95 pregnant women. Patients were selected using non-probability and consecutive sampling. Women at ≥ 20 weeks of gestation and diagnosed with preeclampsia were categorized as early onset (≤ 34 weeks) and late onset (> 34 weeks) of preeclampsia, and their outcomes were compared based on age, parity, BMI and history of GDM and pre-existing hypertension. Data were analyzed using SPSS version 25.0. **Results:** The mean age of the patients was 26.2 ± 5.3 years, the mean gestational age was 34.4 ± 2.4 weeks, and the mean BMI was 26.9 ± 3.5 kg/m². There were 29 (30.5%) primiparas and 66 (69.5%) multiparas. Obesity was observed in 24 (25.3%) women, while 16 (16.8%) had pre-existing hypertension, and 23 (24.2%) had GDM. Early-onset preeclampsia was found in 27 (28.4%) women, while 68 (71.6%) had late-onset preeclampsia. **Conclusions:** It was concluded that a considerable proportion of women had early-onset preeclampsia. Both early and late onset preeclampsia warrant routine screening in pregnant women to allow timely identification and management, which may improve fetomaternal outcomes.

INTRODUCTION

Over 60,000 fatalities globally are attributed to preeclampsia, making it one of the primary causes of maternal death. It is among the most common complications of pregnancy, affecting an estimated 4–5% of pregnancies worldwide [1]. Preeclampsia is typically classified based on the timing of onset, with early-onset occurring before 34 weeks of gestation and late-onset after 34 weeks. The condition is characterized by new-onset hypertension, proteinuria, or signs of end-organ dysfunction, most commonly presenting after 20 weeks of gestation [2]. Pregnancy-induced hypertension is a heterogeneous syndrome responsible for more than 10% of all maternal deaths in the subcontinent, with nearly half of

these deaths being preventable. In Pakistan, hypertensive disorders during pregnancy rank among the top three contributing factors to maternal mortality [3]. Each year, between 5.8% and 18.8% of pregnancies are complicated by hypertensive disorders [4, 5]. A woman's risk of developing preeclampsia is influenced by various factors including family history, genetic predisposition, duration of sexual cohabitation, smoking, parity and maternal age, use of in vitro fertilization (IVF), and pre-existing medical conditions such as hypertension, diabetes, chronic kidney disease (CKD), and obesity [6]. Despite extensive research, the pathophysiology of preeclampsia remains unclear, and early diagnosis continues to be a clinical challenge. Known



contributors to its pathogenesis include late first pregnancy, hypertension, obesity, family history of preeclampsia, long inter-pregnancy intervals, multiple pregnancies, urinary tract infections, diabetes, and autoimmune disorders [7]. Hallmark features of preeclampsia include increased uterine artery resistance index, intrauterine fetal growth restriction, immune activation, elevated cytokine levels, maternal endothelial dysfunction, and reduced vasodilator production. Delivery of the placenta remains the only definitive cure, making preeclampsia a leading cause of preterm birth [8]. Early and late-onset preeclampsia are considered distinct in their pathophysiology, yet both contribute to the clinical syndrome of preeclampsia. According to the International Society for the Study of Hypertension in Pregnancy (ISSHP), early-onset preeclampsia is defined as occurring before 34 weeks of gestation, while late-onset preeclampsia occurs after 34 weeks. Outcomes tend to vary significantly, with early-onset cases typically presenting more severe clinical manifestations and higher risks[9].

The rationale for this study stems from the existing scarcity of data regarding the prevalence and characteristics of early versus late-onset preeclampsia. Preeclampsia continues to pose a serious challenge for obstetricians due to its contribution to maternal morbidity and mortality. This study aims to quantify the risk and prevalence of early and late-onset preeclampsia but also to serve as a foundation for improving evidence-based management practices. Furthermore, the findings of this study are expected to contribute to future research and ultimately lead to enhanced clinical outcomes for affected patients.

METHODS

This study was designed as a descriptive cross-sectional. The research was conducted at Department of Obstetrics and Gynecology, Sughra Shafi Medical Complex, Narowal. The study duration was six months, from September 4th, 2023, to March 11th, 2024, following the ethical approval of the study from Green International University IRC-GIU-157-02-2025. A sample size of 95 cases was determined using a 95% confidence interval and a 9.0% margin of error. Patients were selected using non-probability and consecutive sampling. The study included pregnant women aged 18 to 40 years with a BMI of 20–35 kg/m², booked singleton pregnancies, and diagnosed cases of pre-eclampsia. Exclusion criteria included twin or molar pregnancies, un-booked cases, congenital malformations on ultrasound, and a history of eclampsia in a previous pregnancy. After taking written informed consent, data were recorded on a pre-designed proforma. A thorough history and detailed examination were conducted,

including demographic details such as maternal age, gestational age, parity, and BMI. The history of pre-existing hypertension and gestational diabetes mellitus (GDM) was also recorded. Blood pressure was checked twice, six hours apart, and a 24-hour urine sample was tested for proteinuria in hypertensive patients. Data were analyzed using SPSS version 25.0.

RESULTS

Patients ranged from 28–37 weeks with a mean of 34.4 ± 2.4 weeks. The parity of the patients ranged from 1–4 with a mean of 2.2 ± 1.1 . There were 29 (30.5%) primiparas and 66 (69.5%) multiparas. 16 (16.8%) women had pre-existing hypertension, while 23 (24.2%) women had GDM. BMI ranged from 21.2–34.6 Kg/m² with a mean of 26.9 ± 3.5 Kg/m². 24 (25.3%) women were obese (Table 1).

Table 1: Baseline Characteristics (n=95)

Characteristics	n (%)
Age	
Years	26.2 ± 5.3
18–26	50 (52.6%)
27–35	45 (47.4%)
Weeks	
Gestational Age	34.4 ± 2.4
28–34	27 (28.4%)
35–37	68 (71.6%)
Parity (2.2 ± 1.1)	
Primiparas	29 (30.5%)
Multiparas	66 (69.5%)
BMI	
(Kg/m ²)	26.9 ± 3.5
20–25	25 (26.3%)
25–30	46 (48.4%)
30–35	24 (25.3%)
Pre-Existing Hypertension	
Yes	16 (16.8%)
No	79 (83.2%)
Gestational Diabetes Mellitus	
Yes	23 (24.2%)
No	72 (75.8%)

27 (28.4%) women had early onset pre-eclampsia, while 68 (71.6%) women had late onset preeclampsia (Table 2).

Table 2: Frequency of Early and Late Onset Pre-eclampsia (n=95)

Pre-eclampsia	n (%)
Early Onset	27 (28.4%)
Late Onset	68 (71.6%)
Total	95 (100.0%)

No statistically significant difference in the distribution of early and late onset preeclampsia across various subgroups of women based on age, parity, BMI and history of GDM and pre-existing hypertension (Table 3).

Table 3: Comparison of Frequency of Early and Late Onset Preeclampsia across Various Subgroups (n=95)

Subgroups	n	Early-Onset (n=27)	Late-Onset (n=68)	p-Value
Age				
18-26 years	50	14 (28.0%)	36 (72.0%)	0.924
27-35 years	45	13 (28.9%)	32 (71.1%)	
Parity				
Primiparas	29	8 (27.6%)	21 (72.4%)	0.905
Multiparas	66	19 (28.8%)	47 (71.2%)	
BMI				
20-25 Kg/m ²	25	6 (24.0%)	19 (76.0%)	0.513
25-30 Kg/m ²	46	12 (26.1%)	34 (73.9%)	
30-35 Kg/m ²	24	9 (37.5%)	15 (62.5%)	
Pre-Existing Hypertension				
Yes	16	5 (31.3%)	11 (68.8%)	0.783
No	79	22 (27.8%)	57 (72.2%)	
Gestational Diabetes Mellitus				
Yes	23	7 (30.4%)	16 (69.6%)	0.806
No	72	20 (27.8%)	52 (72.2%)	

Note: No statistically significant differences were observed between early and late onset preeclampsia across subgroups of age, parity, BMI, pre-existing hypertension, and gestational diabetes ($p > 0.005$ for all comparisons).

DISCUSSION

Preeclampsia is a pregnancy-related condition that affects approximately 4.6% of pregnancies and remains a significant global contributor to maternal and neonatal morbidity and mortality. A notable rise in perinatal complications is observed in severe forms of preeclampsia, which often present during mid-pregnancy [1, 2]. The pathophysiology of preeclampsia is complex and not yet fully understood, involving genetic, immunological, and environmental factors. The primary underlying factor is believed to be placental insufficiency, resulting from disrupted trophoblastic remodeling of uterine spiral arterioles. This leads to the release of circulating factors into the maternal bloodstream, triggering the clinical manifestations of preeclampsia [1]. Preeclampsia commonly emerges in the third trimester, characterized by new-onset hypertension and proteinuria, and may progress rapidly to life-threatening maternal and fetal complications [3]. The present study addresses a significant gap in the limited body of literature comparing early and late onset preeclampsia, which is vital for guiding timely clinical management and improving maternal-fetal outcomes. In this study, the mean age of patients was 26.2 ± 5.3 years, consistent with findings from Khan et al., who reported a mean age of 26.87 ± 5.22 years among women [10]. Tesfa et al., noted a slightly higher mean age of 28 ± 4.49 years, whereas Radon et al., reported a comparatively lower mean age of 23.25 ± 1.25 years [11, 12]. Siddiqui et al., reported a slightly higher obesity rate of 31.3 ± 5.1 kg/m² and

a comparable GDM frequency of 23.1% [13]. Emanuel M and Butt S observed a mean BMI of 26.9 ± 3.5 kg/m² among preeclamptic women, with 24 (25.3%) women categorized as obese. Additionally, 16 (16.8%) women had pre-existing hypertension, and 23 (24.2%) had gestational diabetes mellitus (GDM) [14]. Similarly, Soomro et al., reported a GDM rate of 25.9% and a higher prevalence of chronic hypertension (28.7%) among preeclamptic women in Sukkur, Pakistan [15]. Comparable rates of chronic hypertension have also been observed in Poland and Russia, with frequencies of 15.8% and 15.0%, respectively, as reported by Wojtowicz et al., [16]. In our study, 27 (28.4%) women had early-onset preeclampsia, while 68 (71.6%) had late-onset disease. These findings align closely with those of Gomathy et al., who observed 27.4% early and 72.6% late onset cases in India [17]. Similarly, Damayanti et al., reported 29.6% early and 70.4% late onset preeclampsia in Indonesia [18], while Hegazy et al., found 31.2% early and 68.8% late onset cases in Iraq. Li et al., also reported 35.5% early and 64.5% late onset preeclampsia in China [19, 20]. The strengths of the present study include a reasonably large sample size of 95 patients and the stratification of results to examine potential effect modifiers such as age, parity, BMI, GDM, and pre-existing hypertension.

Despite a reasonable sample size, the study was limited by its single-center design and lack of longitudinal follow-up, which may restrict generalizability and outcome assessment. Additionally, potential confounding factors may not have been fully controlled. Future studies are warranted to evaluate the fetomaternal outcomes associated with early and late onset preeclampsia and to explore potential interventions that could improve prognoses in these patients. This further contributed to the clinical understanding and management of preeclampsia in diverse populations.

CONCLUSIONS

It was concluded that a considerable proportion of women had early-onset pre-eclampsia, which warrants routine screening of pregnant women for preeclampsia so that timely identification and management may improve the fetomaternal outcome of such cases.

Authors' Contribution

Conceptualization: FB, RS

Methodology: FB, RS, KA

Formal analysis: FB, MA

Writing and Drafting: FB, RS, MA, KA, AK, AH

Review and Editing: FB, RS, MA, KA, AK, AH

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 Low Birthweight in Pregnant Women with Rheumatic Heart Disease

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ABSTRACT

Rheumatic heart disease (RHD), a complication of rheumatic fever, can cause serious valve damage and is a significant risk during pregnancy. It increases the chances of maternal and fetal complications, including low birth weight and maternal morbidity. **Objectives:** To determine the prevalence of low birth weight in full-term pregnancies among women diagnosed with rheumatic heart disease. **Methods:** A cross-sectional study was conducted in the Department of Obstetrics and Gynaecology at Services Hospital in Lahore. A sample of 96 pregnant women aged 18-40 years with rheumatic heart disease and full-term gestation (37-41 weeks) was selected by using non-probability consecutive sampling. Relevant laboratory and radiological investigations, including ECG and echocardiography, were done. The diagnosis of RHD was established, and women were followed until delivery, and fetal birthweight was measured and assessed for LBW. The data were recorded on specially designed Proforma and analyzed using SPSS version 25.0. **Results:** The average age of the women was 26.78 ± 6.22 years. The mean gestational age, BMI and birth weight were 38.68 ± 1.20 weeks, 24.93 ± 2.06 kg/m and 2550.13 ± 403.1 g. The fetal male gender was dominant, as 59 (61.5%). The frequency of LBW was 57 (59.4%). The analysis revealed no significant differences in the frequency of low birth weight (LBW) with age, gestational age and BMI groups ($p > 0.05$). **Conclusions:** Pregnant women with rheumatic heart disease were found to have a high rate of low birth weight among their infants. However, no significant links were established between low birth weight and factors such as maternal age, gestational age, or BMI.

INTRODUCTION

Rheumatic fever can lead to a serious heart condition known as rheumatic heart disease (RHD). Although it is believed to be autoimmune, the exact mechanism through which acute rheumatic fever progresses to RHD is not fully understood. The disease occurs when rheumatic fever damages the heart valves, leading to inflammation of the valves (valvulitis), heart muscle (myocarditis), or the heart's outer lining (pericarditis) [1]. Over time, chronic RHD often results in narrowing of the mitral valve, causing atrial enlargement, weakening of the ventricles, valve leakage, and irregular heart rhythms. Although the mitral valve is most commonly affected, the damage may also involve the aortic and tricuspid valves [2]. The World Health Organization (WHO) provides guidelines for the diagnosis

and treatment of both rheumatic fever and RHD. While rheumatic fever has become rare among children in the United States, it remains prevalent in developing countries, where both rheumatic fever and RHD continue to pose significant public health challenges [3, 4]. The major diagnostic criteria for RHD include chorea (involuntary movements), carditis (inflammation of the heart), polyarthritis (joint inflammation), erythema marginatum (a distinctive rash), and subcutaneous nodules. Minor criteria may include polyarthralgia (joint pain), fever, a prolonged PR interval on ECG, and elevated levels of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [5]. In acute RHD, pancarditis may occur, indicated by new or changing heart murmurs or



echocardiographic findings. Low birth weight (LBW), defined as a birth weight below 2,500 grams (5.5 pounds), is a key indicator of neonatal health, with significant implications for both immediate and long-term outcomes [6]. LBW is influenced by a range of maternal, fetal, and environmental factors and is a major concern among healthcare professionals, researchers, and policymakers globally. Maternal nutrition plays a vital role in determining birth weight, and deficiencies in nutrients such as folic acid, iron, and protein can contribute to LBW. Maternal health conditions like hypertension, diabetes, and substance abuse also negatively impact fetal growth, increasing the risk of LBW [7]. Maternal heart disease complicates approximately 1% to 4% of pregnancies worldwide and accounts for up to 15% of maternal deaths. In the United States, it is the leading cause of maternal mortality [8]. In Pakistan, about 1.2% of pregnant women have some form of heart disease, with RHD constituting 32% of these cases. The most commonly observed cardiac conditions during pregnancy include peripartum cardiomyopathy (PPCM), congenital heart disease (CHD), and RHD [9, 10]. Current trends suggest that maternal heart disease is likely to increase due to improved survival among women with congenital heart disease and delayed childbearing, which is associated with higher rates of comorbidities such as metabolic syndrome. As a result, cardiac disease may become an even more significant contributor to feto-maternal morbidity worldwide, affecting both developed and developing countries [11]. Fetal birth weight is one of the most commonly used indicators for evaluating pregnancy outcomes. LBW is linked to adverse outcomes, including increased risk of comorbid conditions and fetal mortality [12, 13]. Maternal cardiac disease, including RHD, is a known risk factor for LBW and other complications such as intrauterine death and poor Apgar scores [4]. The present study aims to determine the frequency of low birth weight in term pregnancies complicated by RHD. Despite being one of the most common cardiac conditions during pregnancy, RHD remains under-researched in Pakistan, particularly with its impact on birth weight. Furthermore, the reported frequency of LBW in RHD-affected pregnancies varies widely in international literature, ranging from 12.98% to 39.7% [4]. This study will help identify the frequency of LBW in women with RHD in our population, enabling better recognition of high-risk cases and contributing to improved feto-maternal outcomes through targeted antenatal care and management.

Despite rheumatic heart disease (RHD) being a significant cause of maternal morbidity and adverse fetal outcomes, limited local evidence exists on its specific impact on birth weight, particularly in term pregnancies, with reported

frequencies of low birth weight (LBW) varying widely in international literature. This lack of context-specific data in Pakistan hinders accurate risk identification and optimal antenatal management for affected women. This study aims to assess the prevalence of low birth weight among full-term pregnancies in women diagnosed with rheumatic heart disease.

METHODS

The cross-sectional study was conducted in the Obstetrics and Gynaecology Department, Services Hospital, Lahore, over six months, from 1st January 2024 to 30th June 2024, after the approval of the ethics review committee (Ref no. IRB/2023/1257/SIMS). A sample size of 96 cases was determined based on a 53.7% frequency of low birth weight (LBW) among women with RHD. The confidence level was 95% and the margin of error was 10%. Rheumatic heart disease (RHD) was defined as a confirmed diagnosis during pregnancy based on clinical assessment and echocardiographic findings. Low birth weight (LBW) was defined as a neonatal weight of less than 2,500 grams (5.5 pounds), measured within one hour of birth using a calibrated digital scale. The study included pregnant women aged 18–40 years diagnosed with RHD and carrying full-term pregnancies (37–41 weeks), as determined by the last menstrual period (LMP). Exclusion criteria included pregnancies complicated by diabetes, presence of fetal anomalies on anomaly scan, and refusal to provide written informed consent. After obtaining approval from the hospital's ethics committee and relevant authorities, a total of 96 patients who fulfilled the inclusion and exclusion criteria were chosen from the antenatal clinic at Services Hospital in Lahore. All patients were informed about the study, and informed written consent was obtained. The demographic details were noted down, and clinical evaluation by detailed history and examination was done. Relevant laboratory and radiological investigations, including ECG and echocardiography, were done. The diagnosis of RHD was established as per operational definitions. The women were monitored until delivery, and the fetal birth weight was measured and evaluated for low birth weight (LBW) according to the operational definitions. All patients were managed following the hospital's standard care protocols, maintaining close collaboration with the cardiology department. The data was entered into a specially designed Performa. The data were analyzed using SPSS version 20.0. Quantitative variables such as age, gestational age, maternal BMI, and fetal birth weight were reported as mean $\pm$ standard deviation (SD). Qualitative variables, including low birth weight (LBW) and fetal gender, were expressed in terms of frequency and percentage. To control for effect modifiers such as age, gestational age, BMI, and neonatal gender,

stratification was performed. The Chi-square test was applied after stratification, and a p-value of less than 0.05 was regarded as statistically significant.

RESULTS

The study summarizes the baseline characteristics of the 96 women included in the study. The mean maternal age was 26.78 ± 6.223 years, with a slightly higher proportion of participants under 27 years of age (56.3%). The average gestational age at delivery was 38.68 ± 1.201 weeks, and the mean BMI was 24.93 ± 2.063 kg/m². Male neonates were more common, accounting for 61.5% of the births. The mean birth weight was 2550.13 ± 403.1 grams, and low birth weight (LBW) was observed in 59.4% of the neonates (Table 1).

Table 1: Baseline Maternal and Neonatal Characteristics of the Study Population (n=96)

Variables	n (%) / Mean $\pm$ SD
Maternal Age (Years)	26.78 ± 6.223
Age < 27 Years	54 (56.3%)
Age $\geq$ 27 Years	42 (43.8%)
Gestational Age (Weeks)	38.68 ± 1.201
BMI (kg/m ²)	24.93 ± 2.063
Fetal (Male)	59 (61.5%)
Fetal (Female)	37 (38.5%)
Birth Weight (BW) (g)	2550.13 ± 403.1
Low Birth Weight (LBW)	57 (59.4%)

Association between various maternal and fetal characteristics and the occurrence of low birth weight in newborns. Among mothers younger than 27 years, 61.4% of LBW cases were observed, compared to 38.6% in mothers aged 27 years or older, though this difference was not statistically significant ($p=0.210$). Similarly, gestational age below 38 weeks was associated with 47.4% of LBW cases, while 52.6% were observed in those delivered >38 weeks, also showing no significant association ($p=0.530$). For maternal BMI, 54.4% of LBW cases were associated with BMI <25 , versus 45.6% for BMI >35 ($p=0.340$). Male fetuses accounted for 57.9% of LBW cases compared to 42.1% in females, with no significant gender-based difference ($p=0.380$). Overall, none of the factors showed significant associations with low birth weight (Table 2).

Table 2: Comparison of Low Birth Weight by Maternal Age, Gestational Age, BMI, and Fetal Gender

Variables		Low Birth Weight		Total	p-Value
		Yes	No		
Age	<27 Years	35 (61.4%)	19 (48.70%)	54 (56.30%)	0.218
	≥ 27 Years	22 (38.60%)	20 (51.30%)	42 (43.80%)	
Gestational Age (Week)	<38	27 (47.40%)	16 (41.0%)	43 (44.080%)	0.530
	>38	30 (52.60%)	23 (59.0%)	53 (55.20%)	
BMI (kg/m ²)	<25	31 (54.40%)	25 (64.10%)	56 (58.30%)	0.340
	>25	26 (45.60%)	14 (35.30%)	40 (41.70%)	

Fetal Gender	Male	33 (57.90%)	26 (66.70%)	59 (61.50%)	0.380
	Female	24 (42.10%)	13 (33.30%)	37 (38.50%)	

DISCUSSION

Rheumatic heart disease (RHD) is a chronic, immune-mediated condition that arises following a group A beta-hemolytic streptococcal infection of the pharynx. It remains a significant public health concern, particularly in low- and middle-income countries, affecting over 15 million people globally [14, 15]. In the context of pregnancy, RHD poses unique challenges, contributing to elevated risks of maternal and fetal complications due to the increased hemodynamic demands of gestation. Our study explored the frequency of low birth weight (LBW) among full-term pregnancies complicated by RHD. The mean maternal age was 26.78 ± 6.22 years, with an average gestational age of 38.68 ± 1.20 weeks and a mean BMI of 24.93 ± 2.06 kg/m². Male fetuses accounted for 61.5% of births. The mean birth weight was 2550.13 ± 403.1 grams, and the overall frequency of LBW was 59.4%. This finding aligns closely with Khanna et al., who reported a similar LBW rate of 53.7% in women with RHD [16]. Despite stratified analysis, no statistically significant associations were observed between LBW and maternal age, gestational age, BMI, or fetal gender. This suggests that these common maternal characteristics may not serve as reliable predictors of LBW in this population. The absence of significant associations may also reflect the complex interplay of other unmeasured factors, such as severity of valvular involvement, functional cardiac status (e.g., NYHA class), medication use, and access to antenatal care. Several large-scale studies have similarly highlighted the burden of fetal complications in women with RHD. A meta-analysis of 3928 pregnancies found high rates of preterm delivery (43%), LBW (39.7%), and intrauterine growth restriction (22.4%), reinforcing the importance of maternal cardiac health in determining neonatal outcomes [17]. Rivera et al., also reported a substantial burden of LBW (33%) and NICU admissions in a cohort of women with cardiovascular disease, 37.2% of whom had RHD [18]. Likewise, Hu et al., noted increased perinatal risk in pregnancies complicated by heart disease, including RHD, arrhythmias, and cardiomyopathies [19]. A study from a rural cohort reported a 1.72% prevalence of maternal heart disease with LBW in 30% of term neonates. The study emphasized the role of early diagnosis and optimal functional status in improving outcomes [20]. These findings, along with ours, underscore the importance of pre-pregnancy counselling, multidisciplinary antenatal care, and individualized delivery planning in women with RHD.

This study was limited by its single-center design and relatively small sample size, which may limit the generalizability of the findings. Additionally, important

clinical variables such as severity of valvular disease, NYHA functional class, and antenatal management details were not included, which may have influenced neonatal outcomes. Future studies should incorporate multi-center, larger cohorts with detailed cardiac severity assessment and longitudinal follow-up to better understand predictors of adverse neonatal outcomes in pregnancies complicated by rheumatic heart disease.

CONCLUSIONS

It was concluded that pregnant women with rheumatic heart disease were found to have a high rate of low birth weight among their infants. However, no significant links were established between low birth weight and factors such as maternal age, gestational age, or body mass index. These results indicate that additional factors beyond basic maternal characteristics may play a role in negative fetal outcomes in RHD pregnancies. This underscores the importance of specialized antenatal care and the need for further investigation.

Authors' Contribution

Conceptualization: RA

Methodology: RA, ZN, FF

Formal analysis: RA, ZN, FF

Writing and Drafting: RA, SK, TR, HS

Review and Editing: RA, SK, TR, HS, ZN, FF

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



Correlation between Vitamin D Deficiency and Osteopenia in Women Residing in Karachi, Pakistan

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ABSTRACT

Osteopenia is one of the primary health concerns among Pakistani women. **Objective:** To assess the Correlation Between Vitamin D Deficiency and Osteopenia in Women in Karachi, Pakistan. **Methods:** A cross-sectional survey was conducted among 200 women in Karachi, Pakistan. A self-reported questionnaire was given to all participants so that they could fill in the demographic data. Only participants who were willing to participate in the study were included, and those who failed to provide any data regarding the status of menopause were excluded. SPSS version 23.0 was used to analyze the data. **Results:** The 200 women in the study had a high reproductive burden (mean pregnancies = 12), with a mean age of 65.2 years and a BMI of 25.6 kg/m². Age-related decreases in bone mineral density were significant ($p=0.0002$), and osteoporosis was most prevalent in older age groups. The distribution of vitamin D deficiency across age groups was not statistically significant ($p=0.22$), but it was associated with ageing ($p=0.011$). **Conclusions:** It was concluded that although vitamin D deficiency is common among women, age is a better indicator of deteriorating bone mineral density. Age-focused bone health interventions are needed, as osteoporosis and osteopenia were significantly correlated with advancing age.

INTRODUCTION

The long-term health of the ageing population is being negatively impacted by osteoporosis and osteopenia, which raises the risk of death, reduces autonomy, increases hospitalization rates, and places a significant financial and social load on the healthcare system. The longer life expectancy is linked to a higher prevalence of age-related illnesses, including osteopenia [1]. Osteopenia is one of the biggest health issues faced by Pakistani women currently [2]. The World Health Organization (WHO) defines osteopenia as having a T-score between -1.0 and -

2.5, which indicates that bone density is lower than usual but not low enough to be categorized as osteoporosis [3]. A T-score of -2.5 or less indicates osteoporosis, which is characterized by a more severe loss of bone mass [4]. A degenerative disease that affects all of the bones in the body is called osteoporosis [5]. When the levels of bone mass density are below normal, it is called osteopenia [6]. Osteopenia is 40.40% and osteoporosis is 19.75% prevalent worldwide [7]. Hence, the burden of these conditions has been rising for almost three decades [8]. It



has a complex etiology since numerous factors affect bone health, such as exercise and diet [9, 10]. Pakistani women's osteopenia rates are high due to sedentary lifestyles, a deficiency in foods high in calcium, and the popularity of fast food. Osteopenia is primarily linked to inadequate vitamin D intake or lack of availability of sufficient sunlight [11]. Serum levels of 25-hydroxyvitamin D (25 (OH)D) are commonly used to determine vitamin D status, and classifications have become more uniform in recent years. Gupta et al., 2022 define vitamin D deficiency as serum 25 (OH)D levels below 12 ng/mL (30 nmol/L), insufficiency as levels between 12 and 20 ng/mL (30 and 50 nmol/L), and sufficiency as levels above 20 ng/mL (50 nmol/L). These cutoff points are used for screening and treatment decisions in both adult and pediatric populations, and they are based on correlations with outcomes related to bone health [12]. The main causes of vitamin D deficiency are nutritional deficiencies, limited sun exposure among women, and other chronic conditions. Appropriate amounts of vitamin D are available in the subcontinent with adequate sun exposure. The body uses vitamin D as a hormone, and it is crucial for the mineralization of bones. It also supports immunological function, muscular integrity, and cell proliferation. It contributes to healthy skin development, reproduction, and other metabolic processes. Given its increasing significance, scientists advise taking it at a dosage of at least 1000 IU. Worldwide, the prevalence of vitamin D deficiency is estimated to be 50%. Obesity and malnutrition can be detrimental to one's health and can cause bone problems such as osteoporosis, osteoarthritis, sarcoidosis-related osteoporosis, and osteopenia. Food, medication, and nutritional supplements are used to treat metabolic bone disease [13]. Pakistan is underfunded to address this disease's burden because of its slow progression and high cost of care. A population-based study found that osteopenia and osteoporosis affect millions of people in Pakistan [14]. The Osteoporosis Risk Assessment Instrument now includes current estrogen therapy in addition to the Osteoporosis Self-Assessment Tool and OST for people residing on the Asia continent. Hence, the prognostic instruments (OST, OSTA, and Osteoporosis Index) of Risk, as well as straightforward computed osteoporosis risk estimation. Concentrate on postmenopausal women's osteoporosis risk. Certain biomarkers, such as blood or urine indicators, are readily available during normal medical examinations and have been shown to enhance the sensitivity of osteoporosis prediction at the preclinical stage [15]. Despite the high prevalence of osteopenia and vitamin D deficiency among women in Pakistan, there is limited local evidence exploring their direct correlation, particularly using standardized biomarkers in specific populations. This lack of context-specific data restricts early

identification, risk assessment, and targeted prevention strategies for bone health in women. Therefore, this study aims to assess the correlation between vitamin D deficiency and osteopenia among women residing in Karachi, Pakistan.

METHODS

In Karachi, Pakistan, 200 participants with an average age of 65.2 years were recruited for this cross-sectional study between June and September 2024. With $Z=1.96$ at a 95% confidence level, p =expected prevalence, and d =margin of error (0.05), the sample size was calculated using open epi based on past research conducted by Khan et al., [16] showing high rates among Karachi women (an expected prevalence of 75% for vitamin D deficiency). We recruited 200 participants to account for the estimated sample size of 196 with an 80% power and a 5% margin of error. A non-probability purposive sampling strategy was used to find participants from outreach clinics and community health centers located throughout Karachi. Women who were at least 45 years old, Karachi residents, and willing to give informed consent were among the requirements for inclusion. Women who reported not being menopausal or who were receiving treatment for any bone-related conditions or recent fractures were not included in the study. To further reduce confounding, people taking vitamin D supplements or having comorbid conditions like liver or kidney disease were not included. The Sir Syed Medical and Dental College for Girls' Ethical Review Committee granted ethical approval for the study (Ref. No: 032 SSCMS-Ethics/2024). After being made aware of the goals and methods of the study, each participant gave their written informed consent. A structured, self-reported questionnaire that was pilot-tested and approved by public health specialists for relevance and clarity was used to gather data. Age, weight, height, number of pregnancies, lifestyle factors, history of vitamin D supplementation, sun exposure, and known comorbidities were all included in the questionnaire. Where possible, laboratory studies were used to supplement clinical data. Dual-Energy X-ray Absorptiometry (DEXA) scans were used to measure bone mineral density (BMD). According to WHO guidelines, osteoporosis was defined as a T-score ≤ -2.5 , and osteopenia as a T-score between -1.0 and -2.5 . According to Gupta et al., vitamin D status is classified as deficient (<12 ng/mL), insufficient (12–20 ng/mL), and sufficient (>20 ng/mL) based on serum 25-hydroxyvitamin D ([25(OH)D] levels [12]. SPSS version 23.0 was used for statistical analysis. Standard deviations and means were used to summarize continuous variables. For non-parametric data, independent samples were compared using the Mann-Whitney U test. Since vitamin D status and BMD were both ordinal/non-parametric variables, the relationship

between them was evaluated using Spearman's rank correlation coefficient. Unless otherwise noted, all tests were two-tailed and performed at a 5% level of significance. Correlation analyses took into account confounding variables like age and BMI.

RESULTS

The results of the study revealed that the demographic characteristics of the participants, showing an average age of 65.2 years, mean BMI of 25.6 kg/m² (overweight range), and a high average number of pregnancies (12), reflecting a population at elevated risk for bone health issues (Table 1).

Table 1: Participants' Demographic Details

Variables	Mean
Age (Years)	65.2
Weight (kg)	59
Height (m)	1.51
BMI (kg/m ²)	25.6
No. of Pregnancies	12

The mean age of participants is categorized by vitamin D classification and bone mineral density (BMD) status. The mean age of the 200 participants was 67.3 ± 9.3 years for those with normal BMD (n=28), whereas the mean ages of those with osteopenia (n=117) and osteoporosis (n=55) were higher at 68.5 ± 8.6 years and 74.2 ± 9.9 years, respectively. Growing older is linked to a higher risk of having less bone mineral density, as evidenced by the statistically significant difference in mean age between the BMD categories (p=0.002). Similarly, participants with vitamin D deficiency (n=74) had the highest mean age of 71.5 ± 9.4 years, followed by those with sufficient levels (n=16; 69.3 ± 9.1 years) and those with insufficient levels (n=110; 68.6 ± 8.5 years). Additionally, this difference was statistically significant (p=0.011), pointing to a possible connection between deteriorating vitamin D levels and ageing. These results highlight the link between vitamin D deficiency, ageing, and deteriorating bone health in the population under study (Table 2).

Table 2: The Average Patient Age (in Years) for Osteopenia and Vitamin D3

Variables	n	Age Mean ± SD	p-Value
Classification of Bone Mineral Density			
Normal	28	67.3 ± 9.3	0.002
Osteopenia	117	68.5 ± 8.6	
Osteoporosis	55	74.2 ± 9.9	
Classification of Vitamin D			
Deficiency	74	71.5 ± 9.4	0.011
Insufficient	110	68.6 ± 8.5	
Sufficient	16	69.3 ± 9.1	

Age and BMD status were found to be significantly

correlated (p=0.005). Osteoporosis prevalence rose steadily with age, rising from 1% in the 45–59 age group to 14% in the 80–99 age group. Osteopenia also became more common as people aged, reaching a peak of 15% in those aged 60 to 79. On the other hand, the percentage of women with normal bone mineral density was highest in the 60–79 age range and decreased in the oldest group, indicating a definite age-related decrease in bone mineral density. Hence, there was no statistically significant variation in the distribution of vitamin D status among age groups (p=0.220). While vitamin D insufficiency was consistently seen in all age groups, ranging from 7% to 13%, vitamin D deficiency was most common in the 70–79 age group (13%). While vitamin D deficiency was consistently found in all age groups, ranging from 7% to 15%, vitamin D deficiency was most common in the 70–79 age group (13%). It's interesting to note that the percentage of participants with adequate vitamin D levels was essentially constant across age groups, with the oldest group experiencing a minor increase (5%) (Table 3).

Table 3: Correlation of Women's Age with Each Variable

Variables	45-59 Years	60-69 Years	70-79 Years	80-99 Years	p- Value
Bone Mineral Density					
Normal	6(3%)	15(7%)	15(7%)	12(6%)	0.005
Osteopenia	9(4%)	30(15%)	31(15%)	19(9%)	
Osteoporosis	3(1%)	13(6%)	19(9%)	28(14%)	
Vitamin D Status					
Deficiency	10(5%)	21(10%)	27(13%)	15(7%)	0.220
Insufficient	16(8%)	30(15%)	30(15%)	14(7%)	
Sufficient	6(3%)	11(5%)	9(4%)	11(5%)	

DISCUSSION

Osteopenia is a symptom of osteoporosis and a major indicator of bone health among women in Asia [18]. Deficits in vitamin D, which is essential for calcium absorption, are uncommon in young, healthy people but common in elderly persons, particularly in areas with little sunshine [19]. The results of our investigation showed that while vitamin D deficiency is widespread, its association with osteopenia is complicated and is probably impacted by confounding variables such as age, body mass index, and reproductive history. Interestingly, the results indicated that there was no correlation between vitamin D levels and BMD status across age groups (p=0.220), even though 74 out of 200 people had vitamin D deficiency. The lack of a statistically significant correlation between vitamin D levels and BMD status (p=0.110) implies that while vitamin D may affect bone health, age may be a more relevant predictor of BMD. Women with osteoporosis had a considerably higher mean age (74.2 ± 9.9 years) than those with osteopenia (68.5 ± 8.6 years) and normal bone mineral density (67.3 ± 9.3 years), which supports the notion that ageing-related

physiological changes have a major impact on bone density ($p=0.002$). Deteriorating bone health may also result from the cumulative demands on calcium stores during pregnancy and lactation [20]. This problem is especially important in South Asia, where there are several lifestyle variables, limited sun exposure, and low consumption of foods high in vitamin D [21]. According to this study, women with osteopenia and osteoporosis frequently have vitamin D deficiency, and age seems to have a bigger influence on their BMD status in this group.

This study was limited by its cross-sectional design, which restricts the ability to establish causal relationships between vitamin D levels and bone mineral density. Additionally, potential confounding factors such as dietary intake, physical activity, sun exposure, and socio-economic status were not fully accounted for. Future studies should consider longitudinal methods, looking at additional important elements including exercise, dietary patterns, and socio-economic status.

CONCLUSIONS

It was concluded that bone mineral density (BMD) significantly decreases with age, and osteopenia and vitamin D deficiency are highly prevalent among older women in Karachi. Despite being widespread, vitamin D deficiency did not statistically significantly correlate with BMD status, indicating that ageing is a more reliable indicator of declining bone health. To prevent bone-related complications in postmenopausal women, these findings emphasize the necessity of early screening and age-targeted interventions.

Authors' Contribution

Conceptualization: YB, SM

Methodology: YB, KP, NA, SM

Formal analysis: BZ, SM

Writing and Drafting: AH, KP, NA, PR

Review and Editing: YB, AH, BZ, KP, NA, PR, 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



The Role of Focused Assessment with Sonography for Trauma (FAST) in Identifying Intra-Abdominal Injuries in Blunt Abdominal Trauma

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ABSTRACT

Blunt Abdominal Trauma (BAT) remains a diagnostic challenge, even for experienced trauma surgeons. **Objective:** To evaluate the diagnostic accuracy of Focused Assessment with Sonography for Trauma (FAST) in detecting intra-abdominal injuries among patients presenting with blunt abdominal trauma in a tertiary care emergency setting. **Methods:** This cross-sectional analytical study was conducted at the Emergency Department of Lady Reading Hospital, Peshawar, from May 2024 to February 2025. A total of 106 patients were enrolled, calculated using OpenEpi based on an expected FAST sensitivity of 78%, 20% IAI prevalence, 80% confidence level, and 5% margin of error. Patients with penetrating abdominal trauma or contraindications to FAST were excluded. Positive FAST was defined by free fluid in standard regions (perihepatic, perisplenic, pelvic, or pericardial). CT scan, interpreted by a radiologist, served as the reference standard for IAI—defined as evidence of organ laceration, hematoma, or active bleeding. FAST scans were performed by trained emergency physicians during initial assessment, with CT scans conducted within one hour in stable patients. Operator qualifications included certification in trauma ultrasonography. **Results:** Of the 106 patients, FAST demonstrated a sensitivity of 78.9%, specificity of 91.8%, and overall diagnostic accuracy of 84.9% in detecting IAI. There were no significant demographic or clinical differences between FAST-positive and FAST-negative groups. Data were analyzed using SPSS v23.0, with $p < 0.05$ considered significant. **Conclusion:** FAST is a valuable, rapid bedside screening tool for initial evaluation of BAT, offering high specificity and acceptable sensitivity.

INTRODUCTION

Even highly trained and experienced trauma surgeons find diagnosing Blunt Abdominal Trauma (BAT) a challenging task [1]. Major reason for this is because clinical findings are usually unreliable. Examination of the abdomen tends to be complicated by various factors such as abrasions, contusions of abdominal wall and lower chest ribs fractures, reduced consciousness levels and fracture of lumbar vertebrae with hematoma (retroperitoneal) [2]. Intra-abdominal Injuries (IAI) are highly challenging, initially remaining unrecognized can be fatal, in as high as 8.5 % of patients. Although both adults and children are susceptible to IAI, children remain more susceptible to IAI due to less

fat, rib and muscle protection, in addition to receiving blunt force on small surface area of body [3]. The most common form of abdominal trauma is BAT, which is followed up by less commonly reported penetrating injury like stab wounds. In majority (95 %) of BAT patients, conservative management is carried out without any intervention [4]. Nonetheless, overlooking injuries can be possible fatal. Computed Tomography (CT) scan is regarded as the gold standard technique for diagnosing IAI, be it for adults or in children [5]. However the technique is linked to certain limitations, most important factor being exposure to radiation that raises risk of malignancy in the future [6].



Another modality that is increasingly gaining popularity in evaluating IAI among adults is the Focused Assessment with Sonography for Trauma (FAST) [7]. Primarily, the goal of FAST is to select patients which might benefit from surgical intervention. Even though FAST is not used for identifying anatomical injuries, rather mainly used for detecting presence of supra-pubic or intra-abdominal hemorrhage or fluid [8]. Multiple researchers have evaluated FAST that it might not be effective tool for screening IAI especially among children due to poor characteristics of the test [9]. Nonetheless, the choice of using particular technique for trauma assessment depends upon hemodynamic stability of patient, physical examination reliability, availability of particular technique and severity of associated injuries [10]. Main aim of FAST is to detect intra-peritoneal fluid. It is regarded as a rapid, safe and non-invasive diagnostic tool [11]. It has value in patients that are unstable hemodynamically and those that cannot be transferred to CT scan room [12]. Another advantage of FAST is that it can be performed at bedside even during resuscitation without need for moving patient from resuscitation room [13]. Value of FAST is increased due to high sensitivity for detection of intra-peritoneal fluid that tends to accumulate in dependent abdominal areas such as spleen, liver and in females, pouch of Douglas. In some studies, a sensitivity of 100 has also been reported [14, 15]. BAT is a common presentation in emergency departments and can lead to life-threatening intra-abdominal injuries. Traditional imaging modalities such as Computed Tomography (CT) scans, although highly sensitive, may not be immediately accessible in all settings, especially in resource-limited environments [16]. FAST is a rapid, non-invasive, bedside ultrasound technique widely used to detect intra-abdominal free fluid, which may indicate organ injury? Despite its widespread use, the diagnostic accuracy of FAST in identifying clinically significant intra-abdominal injuries in blunt trauma patients remains a subject of ongoing investigation [17]. Assessing the reliability and diagnostic value of FAST in comparison to standard imaging and surgical findings can help optimize trauma protocols and resource utilization [18].

Despite the widespread use of Focused Assessment with Sonography for Trauma (FAST) in the initial evaluation of blunt abdominal trauma, its diagnostic accuracy in detecting clinically significant intra-abdominal injuries remains variable and controversial, particularly in resource-limited settings where reliance on CT imaging may be restricted. This uncertainty limits its optimal use in trauma protocols and decision-making. The objective of this research was to evaluate the diagnostic accuracy of the Focused Assessment with Sonography for Trauma

(FAST) in detecting intra-abdominal injuries among patients presenting with blunt abdominal trauma, using Computed Tomography (CT) scan as the reference standard.

METHODS

This was a cross-sectional analytical research conducted at the emergency department of Lady Reading Hospital Peshawar from May 2024 to Feb 2025. The ethical review was taken from IRB with Ref No: 388/LRH/MTI. The trauma registry of the hospital was checked for patients who came with blunt abdominal trauma, and suitable patients were included in the study. Informed consent was taken from each patient/ guardian before including their data in the study. The sample for the study was calculated using Openepi online software for sample size calculation. Keeping the hypothesized frequency of BAT in IAI at 20% as reported in a recent study, the sample size came out to be 106 at 80% confidence level and 5% margin of error. Therefore, a total of 106 patients were included in this research [1]. Patients of either gender irrespective of age diagnosed with BAT on clinical findings that suggested possible intra-abdominal injury (such as abdominal tenderness, distention, hypotension or any other signs of peritonitis and given consent (either from patients or guardian/relative) were included in the study. Patients with penetrable abdominal trauma, contraindication to FAST like previous upper abdominal surgery that would have impaired ultrasonography and presence of co-morbidities which would have interfered with evaluating and managing injuries were also excluded from the research. The data were collected on a pre-designed questionnaire, FAST examination findings were taken as independent variable in terms of positive or negative for intra-abdominal free fluid. Dependent variables included presence of intra-abdominal injury which was confirmed through CT scan, metrics of diagnostic accuracy such as sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) and accuracy were also reported. Other demographics include hemodynamic stability, time from injury to presentation age and BMI of patient. For analyzing the data, SPSS version 23.0 was used. Continuous data were presented in the form of mean and standard deviation while categorical data were reported in terms of frequency and percentage. Diagnostic accuracy was reported in terms of presence and absence of IAI. The association of FAST positivity was tested by using chi-square test keeping $p < 0.050$ statistically significant.

RESULTS

In table 1, the description of the demographic and clinical characteristics of the 106 patients included in the study is presented. The mean age of participants was 37.2 ± 14.5

years overall, with those in the FAST-positive group having a mean age of 35.34 ± 11.2 years and those in the FAST-negative group having a mean age of 39.21 ± 12.9 years ($p = 0.27$). There were 67 (63.21%) males and 39 (36.8%) females in total. Among males, 29 (27.36%) were FAST-positive and 38 (35.85%) were FAST-negative; among females, 20 (18.87%) were FAST-positive and 19 (17.92%) were FAST-negative ($p = 0.80$). A total of 84 (79.2%) patients were hemodynamically stable, with 38 (77.6%) in the FAST-positive group and 46 (80.7%) in the FAST-negative group. Hemodynamic instability was noted in 22 (20.8%) patients: 11 (22.4%) FAST-positive and 11 (19.3%) FAST-negative ($p = 0.70$). The mean time from injury to presentation was 3.6 ± 1.4 hours overall, 3.4 ± 1.3 hours in the FAST-positive group, and 3.8 ± 1.5 hours in the FAST-negative group ($p = 0.12$). The mean BMI was 23.1 ± 3.5 kg/m² overall, with FAST-positive patients having a mean BMI of 22.8 ± 3.4 kg/m² and FAST-negative patients having a mean BMI of 23.4 ± 3.6 kg/m² ($p = 0.38$).

Table 1: Demographical and Clinical Characteristics of Patients Included in the Study (n=266)

Variables		Total Mean $\pm$ SD / Frequency (%)	FAST Positive Mean $\pm$ SD / Frequency (%)	FAST Negative Mean $\pm$ SD / Frequency (%)	P-Value
Age (Years)		37.2 ± 14.5	35.34 ± 11.2	39.21 ± 12.9	0.27
Gender	Male	67 (63.21)	29 (27.36)	38 (35.85)	0.80
	Female	39 (36.8)	20 (18.87)	19 (17.92)	
Hemodynamically Stability	Stable	84 (79.2)	38 (77.6)	46 (80.7)	0.70
	Unstable	22 (20.8)	11 (22.4)	11 (19.3)	
Time from injury to presentation (Hours)		3.6 ± 1.4	3.4 ± 1.3	3.8 ± 1.5	0.12
BMI (Kg/m ²)		23.1 ± 3.5	22.8 ± 3.4	23.4 ± 3.6	0.38

In table 2, the contingency table demonstrates the diagnostic accuracy of FAST in detecting intra-abdominal injury confirmed by reference standard methods. Among the 49 FAST-positive cases, 45 (true positives) had intra-abdominal injury, while 4 (false positives) did not. Of the 57 FAST-negative cases, 12 (false negatives) had intra-abdominal injury, and 45 (true negatives) did not. The total number of confirmed intra-abdominal injuries was 57, while 49 patients did not have any injury, making a total sample of 106 patients.

Table 2: Diagnostic accuracy of FAST versus Intra-abdominal Injury (n=106)

Variables	Presence of Intra-Abdominal Injury	Absence of Intra-Abdominal Injury	Total
FAST Positive	45 (TP)	4 (FP)	49
FAST Negative	12 (FN)	45 (TN)	57
Total	57	49	106

Table 3 summarizes the diagnostic performance of FAST. The sensitivity of FAST for detecting intra-abdominal injury

was 78.9%, while specificity was 91.8%. The positive predictive value (PPV) was 91.8%, and the negative predictive value (NPV) was 78.9%. The overall diagnostic accuracy of the FAST examination in this study was 84.9%.

Table 3: Diagnostic Performance of FAST (n=106)

Diagnostic Metric	Percentage (%)
Sensitivity	78.9
Specificity	91.8
Positive Predictive Value	91.8
Negative Predictive Value	78.9
Accuracy	84.9

DISCUSSION

The study included 106 patients with blunt abdominal trauma, with a mean age of 37.2 ± 14.5 years and a male predominance (63.21%). No statistically significant differences were found between FAST-positive and FAST-negative groups in terms of age, gender, hemodynamic stability, time to presentation, or BMI. FAST demonstrated a sensitivity of 78.9%, specificity of 91.8%, PPV of 91.8%, NPV of 78.9%, and an overall diagnostic accuracy of 84.9% in detecting intra-abdominal injuries compared to CT and surgical findings. In our study, 57 (53.77 %) patients demonstrated IAI while 49 (46.23 %) had absent IAI on FAST. Similar findings have been reported in other studies as well where 68 % of FAST were found to have IAI. A meta-analysis reported the sensitivity, specificity, PPV and NPV of FAST ranging from 28 to 76 %, 83 to 97 %, 87 to 96 % and 37 to 94 % respectively [19]. A study observed that FAST showed false-negative results, thereby reducing sensitivity and false-negative results on FAST were associated with insignificant findings [20]. A study by Kim et al., FAST demonstrated a sensitivity of 33.3 %, while specificity of 98.8 %, PPV of 82.8 % and NPV of 89.6 % with 135 true positive and 270 false negative cases with 85.3 % of patients showing no or minor injury to the abdomen [21]. Other studies have reported the sensitivity of FAST lower than our study, i.e. between 43 to 76 % [22]. This is in line to current study, where sensitivity of FAST was observed to be 78.9 %. Likewise, Kumar et al., in their study on accuracy of FAST in BAT reported 77.3 % sensitivity, with 100 % specificity [23]. In other research by Fleming et al., sensitivity of FAST was observed to be 46.2 %, with specificity of 94.7 %, PPV of 96 % and NPV of 39 % [24]. The role of FAST in trauma remains a matter of debate. Majority of studies on the role of FAST in BAT, were carried out by radiologists, however need for a emergency physician is also pivotal. The Australian Injury Society recommends critical ultrasonography should be accessible within critical division with radiologist and emergency physician present [25]. In current study, FAST was found to be valuable in terms of high sensitivity and specificity and was

carried out at bedside with ease.

However, our study was not free from limitations. A single centered study along with limited sample size and observer bias was some of the limitations that were noted in the research. Further, multi-centered studies with greater sample size and stratification of confounder would be enlightening to the findings reported in this research.

CONCLUSIONS

FAST is a valuable bedside screening tool for the initial assessment of patients with blunt abdominal trauma. With high specificity and acceptable sensitivity, it can reliably identify most cases of intra-abdominal injury, especially in resource-limited or emergency settings. While it should not replace definitive imaging when available, its rapid application can guide timely decision-making and improve patient outcomes.

Authors' Contribution

Conceptualization: MA

Methodology: SH, AZ

Formal analysis: HZ

Writing and Drafting: MA, HA, MAS, AZ

Review and Editing: MA, SH, HA, MAS, AZ

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 Demographic Correlates of Post-Stroke Dementia in A Tertiary Care Hospital

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ABSTRACT

Post-stroke dementia (PSD) is a significant yet under-recognized complication following cerebrovascular events, contributing to long-term disability and reduced quality of life.

Objectives: To determine the frequency and demographic correlates of PSD among stroke survivors admitted at Liaquat University Hospital, Jamshoro. **Methods:** This prospective cohort study was conducted in the Department of Neurology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro. A total of 143 ischemic stroke patients aged 55–90 years were enrolled using non-probability consecutive sampling. Patients with confounding neurological or psychiatric conditions were excluded. Dementia was assessed six months after stroke onset using the Mini-Mental State Examination (MMSE), with a score <24 indicating post-stroke dementia (PSD). **Results:** The mean age was 69.25 ± 10.11 years. Of the participants, 51.7% were male, 67.8% were urban residents, and 55.9% were unemployed. PSD was observed in 22.4% of patients. Although slightly higher frequencies of PSD were noted among older, urban, and unemployed individuals, none of the demographic factors, including age, gender, employment, residence, education, or family history of dementia, were significantly associated with PSD ($p > 0.05$ for all). **Conclusions:** Post-stroke dementia affects a substantial proportion of stroke survivors. Despite the lack of statistically significant demographic correlates, the observed burden warrants routine cognitive assessment and post-stroke rehabilitation strategies, particularly in tertiary care centers in Pakistan.

INTRODUCTION

Post-stroke dementia (PSD) is a common and debilitating complication among stroke survivors, characterized by a decline in cognitive function that adversely affects quality of life, functional independence, and long-term outcomes. It encompasses a spectrum of cognitive impairments occurring after a clinically evident stroke and may present immediately or develop progressively over months [1]. Globally, PSD affects approximately 30% of stroke survivors within one-year post-event, with incidence varying depending on stroke type, location, and associated

risk factors [2]. The World Stroke Organization identifies PSD as a significant public health challenge, particularly in low- and middle-income countries where healthcare systems may lack the capacity for long-term neurocognitive monitoring and rehabilitation [3]. In Pakistan, stroke is among the leading causes of adult disability, with an estimated incidence of 250 per 100,000 individuals per year, amounting to nearly 350,000 new cases annually [4]. A majority of these patients are younger than 50 years, which contrasts with global trends and



suggests a potential for an extended cognitive and socioeconomic burden [5]. However, despite this growing concern, national data on PSD remain scarce, and there is limited integration of routine cognitive assessments in post-stroke care protocols in tertiary settings [6]. Multiple studies have identified demographic variables such as advanced age, low educational attainment, female gender, and unemployment as risk factors significantly associated with PSD [7, 8]. Clinical comorbidities, including hypertension, diabetes mellitus, atrial fibrillation, and recurrent strokes, further compound the risk of cognitive decline [9, 10]. A study from 2021 revealed that ischemic strokes are more frequently associated with cognitive impairment when compared to hemorrhagic strokes, though this relationship is complex and multifactorial.

The lack of trained personnel, limited access to neuropsychological services, and cultural stigma associated with mental decline pose additional challenges in timely diagnosis and management of dementia/PSD in Pakistani healthcare settings [11, 12]. This study aims to assess the frequency and demographic correlates of PSD at Liaquat University Hospital, Hyderabad/Jamshoro, to bridge the critical knowledge gap and contribute evidence-based insights into the burden and determinants of PSD in a resource-limited context.

METHODS

This prospective cohort study was conducted at the Department of Neurology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, from March 21, 2022, to September 20, 2022, following the approval of the research synopsis by CPSP (CPSP/REU/NEU-2019-164-581). The sample size was calculated using the WHO sample size calculator based on a previously reported prevalence of post-stroke dementia (PSD) at 20.8% [7], a 7% margin of error, and a 95% confidence level. The estimated sample size was 130; however, accounting for a potential 10% loss to follow-up, the final sample included 143 patients. A non-probability consecutive sampling technique was used for participant recruitment. Participants of either gender with an age of 55-90 years, who presented within one week of acute ischemic stroke, and had a diagnosis established through clinical and radiological findings. Exclusion criteria included patients with other brain lesions (e.g., tumors), those with hepatic or renal dysfunction, individuals with postictal symptoms or known psychiatric disorders, and those already diagnosed with mild cognitive impairment. Patients unable to communicate effectively due to conditions like sensory aphasia or those on cognition-affecting medications such as antipsychotics or antidepressants were also excluded. After obtaining informed consent from a close relative, each patient underwent a thorough clinical history, neuroimaging, and

neurological examination. Participants were followed up at intervals, and PSD was evaluated at the six-month mark using the Mini-Mental State Examination (MMSE). A score of less than 24 out of 30 was considered indicative of cognitive impairment. The MMSE is a widely used 30-point screening tool that evaluates five main cognitive domains: orientation, registration, attention and calculation, recall, and language, including visuospatial ability [13]. In the Pakistani context, particularly in Sindh, the MMSE requires cultural and linguistic adaptation to enhance validity. Administration in Urdu and interpretation adjustments based on education level are essential to minimize false positives. For illiterate individuals, a score of ≤ 21 may suggest impairment, while the traditional cutoff of < 24 remains suitable for those with primary or higher education [14]. The MMSE was administered at the six-month, by the first three authors, who were residents at the time of the study and had received adequate training in standardized administration and scoring procedures before data collection. This ensured consistency, cultural appropriateness, and reliability of cognitive assessment across all participants. The secondary variables included demographic factors like Age, Gender, Residential Status, and Family History of Stroke. Data analysis was performed using SPSS version 23.0. Descriptive statistics were computed for both continuous and categorical variables. The Shapiro-Wilk test was used to check data normality. Continuous variables, such as age, were labeled as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Data were stratified by key demographic and clinical variables to assess their effect on the primary outcome, post-stroke dementia. Post-stratification comparisons were made using Chi-square, where appropriate, with a p-value of < 0.050 considered statistically significant.

RESULTS

A total of 143 stroke patients were included in the study, with a mean age of 69.25 ± 10.11 years. Males constituted 51.7% ($n=74$) of the sample, while 48.3% ($n=69$) were females. Most participants resided in urban areas (67.8%), and a majority were unemployed (55.9%). In terms of education, 41.3% had completed secondary-level education, while only 10.5% had no formal education. A positive family history of dementia was reported in 13.3% of patients (Table 1).

Table 1: Demographic Statistics of Patients

Variables	n (%)
Mean Age Group (Years)	69.25 $\pm$ 10.11
Gender	
Male	74 (51.7%)
Female	69 (48.3%)

Residential Status	
Rural	46 (32.2%)
Urban	97 (67.8%)
Employment Status	
Unemployed	80 (55.9%)
Employed	63 (44.1%)
Educational Status	
No Formal Education	15 (10.5%)
Primary Level Education	25 (17.5%)
Secondary Level Education	59 (41.3%)
Graduate Level Education	27 (18.9%)
Professional Level	17 (11.9%)
Family History of Dementia	
Positive	19 (13.3%)
Negative	124 (86.7%)

Post-stroke dementia (PSD) was present in 32 (22.4%) patients (Figure 1).

Presence of Post Stroke Dementia

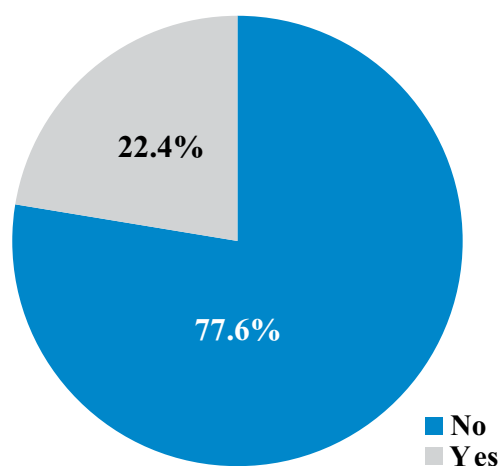


Figure 1: Presence of Post Stroke Dementia

When comparing demographic variables with PSD, no statistically significant associations were observed. Among patients aged 55–70 years, 15 (10.5%) had PSD, while 17 (11.9%) cases were reported in those older than 70 ($p=0.592$). PSD was found in 19 males (13.3%) and 13 females (9.1%) ($p=0.327$). Among employed individuals, 16 (11.2%) had PSD, compared to an equal number among the unemployed ($p=0.442$). Urban residents had a slightly higher frequency of PSD (14.7%) than rural residents (7.7%), though the difference was not significant ($p=0.762$). Educational status also showed no significant association with PSD ($p=0.910$), with cases distributed across all levels. Lastly, PSD was found in 5 patients (3.5%) with a positive family history and 27 (18.9%) with a negative family history ($p=0.658$) (Table 2).

Table 2: Demographic Correlates of Post Stroke Dementia among Stroke Survivors

Variables	Dementia		p-value
	Present	Absent	
Age Group (Years)			
55-70	15 (10.5%)	58 (40.6%)	0.592
>70	17 (11.9%)	53 (37.1%)	
Gender			
Male	19 (13.3%)	55 (38.5%)	0.327
Female	13 (9.1%)	56 (39.2%)	
Employment Status			
Employed	16 (11.2%)	47 (32.9%)	0.442
Unemployed	16 (11.2%)	64 (44.8%)	
Residential Status			
Urban	21 (14.7%)	76 (53.1%)	0.762
Rural	11 (7.7%)	35 (24.5%)	
Educational Status			
No Formal Education	4 (2.8%)	11 (7.7%)	0.910
Primary Level Education	7 (4.9%)	18 (12.6%)	
Secondary Level Education	12 (8.4%)	47 (32.9%)	
Graduate Level Education	5 (3.5%)	22 (15.4%)	
Professional Level	4 (2.8%)	13 (9.1%)	
Family History of Dementia			
Positive	5 (3.5%)	14 (9.8%)	0.658
Negative	27 (18.9%)	97 (67.8%)	

DISCUSSION

The findings of this study indicate that 22.4% of stroke survivors in a tertiary-care setting developed post-stroke dementia (PSD), and none of the demographic factors, age, gender, employment, residence, education, or family history, showed a statistically significant association with PSD. This prevalence is comparable to regional studies; for instance, Egyptian data report a PSD rate of 20.8%, with higher dementia risk among older, illiterate, and unemployed individuals [7]. Similarly, a recent Ugandan study found that 66.4% of stroke survivors experienced cognitive impairment, with low education and increasing age as independent predictors [15]. Although our prevalence is lower than Uganda's, it aligns with the expectation that milder cognitive decline is captured using the MMSE instrument. Contrary to international evidence linking female sex with worse cognitive outcomes post-stroke [16], our study did not identify a significant gender difference ($p=0.327$), resonating with recent meta-analyses that found no sex-based discrepancy in PSD incidence [17]. Educational attainment, another known predictor [16, 18], also did not demonstrate significance ($p=0.910$), though our sample skewed heavily toward secondary education (41.3%). This suggests that severe educational deprivation, rather than duration alone, may be more critical for predicting PSD. Our results concur with emerging evidence suggesting that in low- and middle-

income countries (LMICs), contextual factors like vascular health, stroke severity, and rehabilitation access might outweigh demographic variables [19]. Notably, Pakistan's neurological and geriatric service capacity remains constrained, with a limited number of trained clinicians and few standardized cognitive screening protocols [20]. Additionally, Pakistan's estimated 150,000–200,000 dementia patients represent a rapidly growing public health burden, exacerbated by systemic under diagnosis and stigma [21]. Globally, dementia affects more than 55 million individuals as of 2020, predominantly in LMICs, a number expected to nearly double by 2030 [22]. Stroke-related cognitive decline contributes significantly to this trajectory; cognitive impairment affects up to 64% of stroke survivors worldwide [15].

This study was limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings. Additionally, the use of MMSE alone may have underestimated milder forms of cognitive impairment. Future studies should use larger, multicenter samples with comprehensive cognitive assessment tools to better evaluate post-stroke dementia.

CONCLUSIONS

It was concluded that 22.4% of stroke survivors at a tertiary care hospital developed post-stroke dementia (PSD) within six months of an acute ischemic stroke. While PSD was more frequent among older, urban, and unemployed individuals, none of the demographic variables, including age, gender, residential status, education, or employment, showed a statistically significant association with PSD.

Authors' Contribution

Conceptualization: SK

Methodology: SK, WA, SAN, AHB

Formal analysis: WA, SAN, SHS, AK

Writing and Drafting: WA, SAN

Review and Editing: WA, SAN, AHB, SHS, 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



Stone Clearance and Duration of Surgery in Percutaneous Nephrolithotomy Using Laser versus Pneumatic Lithotripsy

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ABSTRACT

Nephrolithiasis is common ailment causing pain and renal impairment. Management strategies depend on stone size and location, with stones larger than 2 cm treated with Percutaneous Nephrolithotomy (PCNL). This study compares two energy sources pneumatic lithoclast and Holmium: YAG laser used in PCNL, focusing on stone-free rate and surgery duration. **Objective:** To know of any difference in Ho:YAG laser and pneumatic probe in terms of stone free rate and surgery duration during PCNL. **Methods:** This study was conducted retrospectively at the Department of Urology, Lahore General Hospital. The data of patients admitted from June 13, 2021, to June 12th, 2022, was taken. 120 patients were enrolled in this study (60 each for pneumatic lithoclast and Ho: YAG laser), using a non-purposive consecutive sampling technique. Data collection included demography, stone size, site, side, clearance status, and surgery duration. Analysis was conducted using SPSS version 21.0, with quantitative variables assessed via t-tests and qualitative variables via chi-square tests. A p-value ≤ 0.05 was considered statistically significant. **Results:** Mean age was 36.6 ± 12.68 years in the pneumatic group and 40.40 ± 8.29 years in the laser group. Stone clearance rates were 60% (n=36) for the pneumatic group and 70% (n=42) for the laser group. Mean surgery duration was shorter in pneumatic group (44.87 ± 22.85 minutes) compared to laser group (142 ± 29.41 minutes). **Conclusion:** Pneumatic lithoclast and Holmium: YAG laser provides comparable stone clearance rates for PCNL. However, the pneumatic probe reduces surgery duration.

INTRODUCTION

Urolithiasis, or nephrolithiasis, refers to the formation of stones within the urinary tract including the kidneys, ureters, bladder, or urethra and encompasses various management approaches, particularly for complex cases like staghorn stones [1]. Globally, nephrolithiasis affects approximately 12% of the population, with a higher incidence in men. Its development is influenced by hydration status, dietary patterns, and underlying metabolic abnormalities [2]. In Pakistan, the estimated prevalence is around 16%, particularly among middle-aged adults due to environmental and dietary factors [3]. The

introduction of Percutaneous Nephrolithotomy (PCNL) in 1976 marked a turning point in renal stone management, becoming the gold standard for stones larger than 2 cm or those located in the lower pole exceeding 1 cm [4]. Vitamin D metabolism and hypercalciuria have been linked to stone formation, and hypercalciuria is also considered a specific biomarker in systemic conditions like sarcoidosis [2, 3, 5]. It has largely supplanted open surgery, while smaller stones are typically treated with Extracorporeal Shockwave Lithotripsy (ESWL). PCNL involves percutaneous access to the collecting system, followed by



stone fragmentation using energy sources. Among these, the Holmium:YAG laser has gained widespread use, offering an alternative to traditional pneumatic lithoclast systems [6, 7]. Studies comparing these modalities report mixed outcomes. For instance, one study from Karachi noted higher stone clearance rates with pneumatic lithoclast (87%) than with the Holmium:YAG laser (83%), while another reported better results with the laser (81%) versus the pneumatic device (67%) [8, 9]. Further complexity arises from studies on high-grade cases, such as Guy's Stone Score Grade 4, where outcomes between methods showed no significant differences. These inconsistencies point to a knowledge gap and underscore the need for further comparative research [10, 11]. While Holmium:YAG lasers are increasingly used in Pakistan, local literature comparing their efficacy to pneumatic lithoclast in PCNL remains limited. As laser technology becomes more prevalent, a clearer understanding of its impact on stone-free rates and surgical efficiency is essential. Recent studies have examined the safety profile of laser modalities and compared the clinical outcomes of various lithotripsy techniques in PCNL, reinforcing the need for localized data to support evidence-based decision-making [12, 13].

Although percutaneous nephrolithotomy (PCNL) is the gold standard for managing large renal stones, there is inconsistent evidence regarding the comparative effectiveness of Holmium:YAG laser and pneumatic lithoclast systems, with studies reporting variable stone-free rates and outcomes. In Pakistan, where laser use is increasing, local comparative data remain limited, creating uncertainty in selecting the most effective lithotripsy modality. Therefore, this study aims to compare the efficacy of Holmium:YAG laser versus pneumatic lithoclast in terms of stone-free rates and surgical outcomes in patients undergoing PCNL.

METHODS

This was a retrospective descriptive study conducted at the Department of Urology, Lahore General Hospital (LGH) and Lahore, Pakistan. The study was approved by the Ethical Committee of this hospital via reference number 2025/ERC/24. The study included patients with renal calculi more than 2 cm in size located anywhere in the kidney, or above 1 cm in size in the lower pole. These patients were assessed using X-ray KUB. A total sample of 120 patients (60 in each group) was calculated using a 95% confidence level, 80% power of the test, and the expected frequency of stone clearance: 88.4% in the laser group versus 47.3% in the pneumatic group. Sampling was done by Non-probability consecutive method [14]. All the patients were included who had a stone of above 1cm in lower pole and 2cm anywhere else in kidney as seen by Xray

KUB. All patients with positive urine culture, bleeding disorders and active pregnancy were excluded from the study. A total data of 120 patients who fulfilled the inclusion criteria was included in the study, with 60 patients who underwent pneumatic (Group B) and 60 who underwent Ho:YAG laser (group A) PCNL. Medical charts were reviewed and data was recorded for patients who underwent treatment between 13th June 2021 and 12th June 2022. Patients were counseled about the use of their data in the study and consent was obtained for this telephonically. Stones were broken using Holmium: YAG laser for Group A and pneumatic lithoclast for Group B. Postoperatively, all patients underwent KUB radiograph (Villa Xray machine, model: MoviPlan with 500MA power) on the post-op day 1 to confirm stone clearance. Stone clearance rate was calculated as a percentage of people with stone clearance among the total number of patients in that group. The duration of surgery was recorded starting from the time of successful access to the time of taking out the nephroscope at the end, as it was mentioned in the patient notes. Data were collected through patient records. Patient demographic details, stone size, stone location, and other relevant clinical information were recorded. Stone clearance and duration of surgery were documented for analysis. Data analysis was done using SPSS version 21.0. Descriptive statistics were applied to present quantitative variables such as age and surgery duration as mean and standard deviation. The T-test was employed to compare these variables between the two groups. Qualitative variables, including gender and stone clearance, were expressed as frequency and percentage. The Chi-square test was employed to compare these variables between groups. Post-stratification, Chi-square was applied for stone clearance comparison, and T-test was used to compare surgery duration in stratified groups. A p-value of ≤ 0.050 was considered statistically significant.

RESULTS

The sample was divided into two groups with 60 patients each in the pneumatic lithotripsy group and Ho:YAG laser group. Variables analysed among these groups included stone clearance rate and surgery duration. In the pneumatic group, 30 patients (50%) were of age 35 years or younger, and 30 patients (50%) were older than 35 years. In the Holmium: YAG group, 16 patients (26.6%) were aged 35 years or younger, while 44 patients (73.2%) were older than 35 years. The mean age in the pneumatic group was 36.6 ± 12.68 years, and for the Holmium: YAG group was 40.40 ± 8.29 years. (A table is not made for this line for the purpose of brevity). The mean stone size in pneumatic group was 2.93 ± 1.25 cm, and in the Holmium: YAG group was 3.167 ± 0.59 cm. (table not made for the purpose of

brevity). Both groups demonstrated comparable stone sizes. In pneumatic group, 44 patients (73.4%) were male, and 16 patients (26.6%) were female. In Holmium: YAG group, 40 patients (66.6%) were male, and 20 patients (33.3%) were female. Both groups showed similar gender distributions (Table 1).

Table 1: Distribution According to Age and Gender

Group	Age		Total Frequency (%)
	Less than or Equal to 35 Years Frequency (%)	Greater than 35 Years Frequency (%)	
Pneumatic	30 (25.0)	30 (25.0)	60 (50.0)
Holmium Yag Laser	16 (13.3)	44 (36.7)	30 (50.0)
Total	46 (38.3)	74 (61.7)	120 (100.0)
Group	Gender		Total Frequency (%)
	Male Frequency (%)	Female Frequency (%)	
Pneumatic	44 (36.7)	16 (13.3)	60 (50.0)
Holmium Yag Laser	40 (33.3)	20 (16.7)	60 (50.0)
Total	84 (70.0)	36 (30.0)	120 (100.0)

In pneumatic group, 26 patients (43.3%) were operated on the right side and 34 patients (56.7%) on the left side. In Holmium: YAG group, 32 patients (53.3%) were operated on the right side, and 28 patients (46.7%) on the left side. The mean surgery duration in pneumatic lithotripsy group was 44.87 ± 22.85 minutes. Mean surgery duration in Holmium: YAG group was significantly longer at 142 ± 29.41 minutes. In pneumatic group, 60% of the patients had full stone clearance. In Holmium: YAG group, 70% of patients achieved complete stone clearance (Table 2).

Table 2: Comparison of Side Distribution and Stone Clearance in PCNL Using Pneumatic vs. Holmium:YAG Laser

Group	Anatomical Side		Total Frequency (%)
	Right Frequency (%)	Left Frequency (%)	
Pneumatic	26 (21.7)	34 (28.3)	60 (50.0)
Holmium Yag Laser	32 (26.3)	28 (23.3)	60 (50.0)
Total	58 (48.3)	62 (51.7)	120 (100.0)
Group	Stone Clearance		Total Frequency (%)
	Yes Frequency (%)	No Frequency (%)	
Pneumatic	36 (30.0)	24 (20.0)	60 (50.0)
Holmium Yag Laser	42 (35.0)	18 (15.0)	60 (50.0)
Total	78 (65.0)	42 (35.0)	120 (100.0)

The table compares stone clearance outcomes by anatomical side (right vs. left) in patients undergoing percutaneous nephrolithotomy (PCNL) using either pneumatic lithotripsy or Holmium:YAG laser (Table 3).

Table 3: Distribution of Anatomical Side Concerning Stone Clearance According to the Chi-Square Test

Anatomical Side	Group	Stone Clearance		Total Frequency (%)	p-Value (chi-Square Test)
		Yes Frequency (%)	No Frequency (%)		
Right	Pneumatic	20 (34.5)	6 (10.3)	26 (44.8)	0.400
	Holmium Yag Laser	20 (34.5)	12 (20.7)	32 (55.2)	
	Total	40 (69.0)	18 (31.0)	58 (100.0)	
Left	Pneumatic	16 (25.8)	18 (29.0)	34 (54.8)	0.073
	Holmium Yag Laser	22 (35.5)	6 (9.7)	28 (45.2)	
	Total	38 (61.3)	24 (38.7)	62 (100.0)	

Comparison of mean operative time (in minutes) between pneumatic and Holmium:YAG laser lithotripsy by anatomical side, showing significantly shorter durations with the pneumatic group across all categories ($p < 0.050$, t-test) (Table 4).

Table 4: Duration of Surgery According to T-Test

Operative Time (minutes)	Anatomical Side	Group	N	Mean $\pm$ SD	p-Value (t-test)
Overall	-	Pneumatic	60	44.87 ± 22.85	<0.001
		Holmium: YAG Laser	60	142.00 ± 29.41	
By Side	Right	Pneumatic	52	47.69 ± 15.97	<0.001
		Holmium: YAG Laser	64	146.25 ± 30.74	
	Left	Pneumatic	68	42.71 ± 27.27	<0.001
		Holmium: YAG Laser	56	137.14 ± 28.13	

Operative time was significantly lower with pneumatic lithotripsy compared to Holmium:YAG laser for both right and left kidney stones ($p < 0.050$, t-test) (Table 5).

Table 5: Comparison of Mean Operative Time Between Pneumatic and Holmium:YAG Laser Lithotripsy by Anatomical Side

Anatomical Side	Group	N	Mean $\pm$ SD (min)	p-Value (t-test)
Overall	Pneumatic	60	44.87 ± 22.85	<0.001
	Holmium: YAG Laser	60	142.00 ± 29.41	
Right Side	Pneumatic	52	47.69 ± 15.97	<0.001
	Holmium: YAG Laser	64	146.25 ± 30.74	
Left Side	Pneumatic	68	42.71 ± 27.27	<0.001
	Holmium: YAG Laser	56	137.14 ± 28.13	

Patients treated with Holmium:YAG laser had significantly longer mean operative times than those treated with pneumatic lithotripsy in both age groups ($p < 0.001$) (Table 6).

Table 6: Comparison of Mean Operative Time (in Minutes) Between Pneumatic and Holmium:YAG Laser Lithotripsy Across Age Groups

Variables	Group	N	Operative Time (Mean ± SD)	p-Value (t-test)
Age				
≤35 Years	Pneumatic	30	45.73 ± 26.52	<0.001
	Holmium: YAG Laser	16	142.50 ± 31.05	
>35 Years	Pneumatic	30	44.00 ± 19.40	<0.001
	Holmium: YAG Laser	44	141.82 ± 6.30	
Gender				
Male	Pneumatic	44	40.18 ± 18.85	<0.001
	Holmium: YAG Laser	40	138.00 ± 28.21	
Female	Pneumatic	16	57.75 ± 28.94	<0.001
	Holmium: YAG Laser	20	150.00 ± 31.62	

DISCUSSION

Renal stones are one of the most prevalent conditions encountered in urology, often requiring surgical intervention. Percutaneous Nephrolithotomy (PCNL) is the gold standard procedure for the renal stones, using many energy sources for stone fragmentation among these, pneumatic lithotripsy, and Ho: YAG laser are commonly used, though understanding the differences in their results particularly for stone clearance rates and surgery duration is crucial. This study compares these two energy sources to assess their efficacy [13-15]. In this study, and compared two key variables: stone clearance and duration of surgery. Stone clearance is a critical objective in PCNL, as the primary aim is to achieve complete removal of renal stones. The duration of surgery is another important factor, influencing both the feasibility of the procedure and its cost. Additionally, prolonged surgical duration can raise concerns regarding patient safety, especially concerning anesthesia. These findings indicate that the pneumatic and Ho: YAG laser groups demonstrated comparable stone clearance rates, with no statistically significant difference. This suggests that both energy sources are similarly effective in achieving stone clearance. These results align with studies by Malik *et al.*, at the Sindh Institute of Urology and Transplant (SIUT), which reported stone clearance rates of 87% with pneumatic lithotripsy and 83% with Ho: YAG laser [16]. Similarly, Liu *et al.*, and Hong *et al.*, found insignificant differences in stone clearance between the two energy modalities in their studies [17, 18]. However, contrasting findings have emerged in some studies. For example, Zyczkowsky *et al.*, from Poland observed a stone-free rate of 88.4% with the laser compared to 47.3% with pneumatic lithotripsy, highlighting the variability in stone clearance rates [19]. This discrepancy in the literature underscores the need for further studies to comprehensively evaluate the efficacy of different energy sources in PCNL. The duration of surgery is a crucial

parameter when evaluating energy sources. It impacts the feasibility, cost, and patient safety during the procedure. In this study, the mean duration of surgery for the Ho: YAG laser group was significantly longer (142 $\pm$ 29.41 minutes) compared to the pneumatic group (44.87 $\pm$ 22.85 minutes). This substantial time difference reflects the well-known limitation of the Ho: YAG laser regarding the time consumption during PCNL. However, variations in the literature regarding surgery duration are evident. Malik *et al.*, found minimal difference between the two modalities at SIUT, with pneumatic PCNL taking 37.2 $\pm$ 13 minutes and laser PCNL taking 39.6 $\pm$ 11.9 minutes [16]. Similarly, Liu *et al.*, observed a minor difference, with pneumatic lithotripsy taking 55.9 $\pm$ 16.5 minutes and laser lithotripsy taking 62.4 $\pm$ 17.6 minutes [17]. Conversely, Zyczkowsky *et al.*, reported a shorter mean duration of 34 minutes for laser lithotripsy and 56 minutes for pneumatic lithotripsy, which contradicts these findings [20]. These discrepancies in surgery duration across different studies highlight the complexity of comparing energy sources and indicate that further research is required to establish the true impact of each energy source on surgery time. This study primarily found a significant difference in the duration of surgery between pneumatic lithotripsy and Ho: YAG laser, with the latter taking substantially longer. However, both energy sources showed similar efficacy in achieving stone clearance, with no statistically significant difference. Given the variability in the literature regarding both stone clearance rates and surgery duration, there is a compelling need for further trials and research to better understand the practical differences between these energy sources and to guide clinical decisions. Studies that focus on the economic implications of prolonged surgery duration and the long-term outcomes of different energy sources in PCNL are essential. Additionally, randomized controlled trials with robust methodologies are necessary to establish concrete guidelines for the selection of energy sources in PCNL.

This study was limited by its single-center design and relatively small sample size, which may affect the generalizability of the findings. Additionally, important procedural factors such as stone size, location, density, and surgeon experience were not fully standardized, which may have influenced operative time and outcomes. Future studies should include multi-center randomized controlled trials with stratification of stone characteristics and standardized surgical protocols to better compare the efficacy and operative efficiency of different energy sources in PCNL.

CONCLUSIONS

This study compared the pneumatic probe and Ho: YAG laser probe in percutaneous nephrolithotomy (PCNL),

evaluating stone-free rate and duration of surgery for each method. Both sources demonstrated comparable effectiveness in stone clearance. However, the mean duration of surgery was significantly longer with the Ho: YAG laser as compared to pneumatic probe.

Authors' Contribution

Conceptualization: AA

Methodology: MA, UHK, ATA

Formal analysis: QAK

Writing and Drafting: UMK, AA, MFA, KHG

Review and Editing: UMK, AA, MA, UHK, QAK, ATA, MFA, KHG

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



Psycho-Social Quality of Life Among Children with Cerebral Palsy

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ABSTRACT

Cerebral Palsy (CP) is known to cause severe physical disability in children. Social, along with mental and physical wellness, constitute a subset of Quality Of Life (QOL) related to general health. **Objective:** To find out the psycho-social QOL among children with CP. **Methods:** This cross sectional study was conducted at the department of Pediatrics Medicine, Sir Sadiq Abbasi Hospital, Quaid-e-Azam Medical College, Bahawalpur, Pakistan from March 2023 to September 2023. Children of either gender between 4-12 years and diagnosed cases of CP were included. Study information like age, gender, weight, area of residence and type of CP were noted. Psycho-social quality of life was assessed as per CP QOL-Child questionnaire. **Results:** In a total of 86 children with CP, the mean age was 7.64 ± 2.63 years while 57 (66.3%) children were aged between 4 to 8 years. There were 64 (74.4%) male and 22 (25.6%) female children. The most common type of CP was spastic quadriplegia, noted in 29 (33.7%) children. The mean psychosocial QOL score was 4.93 ± 1.90 . High psychosocial QOL among children with CP was found in 25 (29.1%) patients, whereas there was low quality of life was in 61 (70.9%) children. Relatively younger age was associated with significantly low QOL ($p=0.001$). Urban place of live was also associated with low QOL ($p=0.001$). **Conclusions:** CP affects psycho-social QOL in high proportion of children. Younger age, urban residential affiliation were found to be significant association with low QOL scores.

INTRODUCTION

Cerebral Palsy (CP) is known to cause severe physical disability in children [1]. CP refers to a collection of movement and posture abnormalities caused by an injury or malfunction in the developing brain. A complicated disorder, CP causes a range of motor impairments in different degrees and types [2]. Movement and posture development are thought to be impacted by CP, which might occur during fetal development or in the brain resulting from non-progressive disruptions. An injury to the developing Central Nervous System (CNS), occurring in the uterus, during childbirth, or in the initial life span, are some of the potential factors behind development of CP

[3]. The estimated prevalence of CP in high income countries has declined to 1.6 per 1000 live births while among low income countries, it stands around 3.4 per 1000 live births [4]. The exact prevalence of CP in Pakistan is not known, while local data has identified CP as the most common disability among children [5]. A local study from district Swabi of Khayber Pakhtunkhwa found that among each 1000 live births, 1.22 had CP [6]. Literature shows that spastic CP is the most frequent presentation, followed by athetoid, ataxic, and mixed types [1, 7]. The cerebral injuries that result in the motor dysfunction of CP have no exact treatment, rather, the focus of treatment is on a



variety of interventions such as medication, surgery, and physical therapy, to improve the patient's overall Quality Of Life (QOL) by reducing pain and musculoskeletal limitations [8]. Social, along with mental and physical wellness, constitute a subset of QOL related to general health. Studies reveal that, when compared to their counterparts who do not have CP, children and adolescents with CP have lower functional and psychosocial QOL [9, 10].

The rationale behind the planning of this study was that, although standard CP treatments have been linked to increases in child's functional QOL, but their effects on psychosocial QOL are not fully understood. Moreover, not much local data exists regarding QOL of CP children in Pakistan. So, the psychosocial characteristics of CP children remain relatively unknown. Therefore, the objective was to assess the psychosocial quality of life among children with cerebral palsy. The study's findings can help guide better interventions to address psychosocial QOL concerns in these children.

METHODS

This cross-sectional study was performed at the department of pediatric medicine, Civil Hospital, Bahawalpur, Pakistan, from March 2023 to September 2023. A sample size of 86 was estimated considering high social quality of life in children with a CP frequency (p) of 33.8%, $z = 1.96$ for a confidence level ($1-\alpha$) of 95%, and margin of error (e) of 10%, using the formula: $n = z^2 p(1-p)/e^2$ [11]. The inclusion criteria were both male and female children aged 4–12 years and who were diagnosed with CP. The exclusion criteria were children with conditions like neurodegenerative disorders, myopathies, metabolic disorders, neuropathies, and the syndrome of early hypotonia, as such conditions are associated with progressive deterioration or distinct clinical features that can independently and substantially affect psychosocial QOL, thereby confounding the assessment specific to CP. CP was labeled on the basis of medical history and record as an inability to fully control motor skills [11]. A prior approval from the Institutional Ethical and Research Committee was obtained (letter number: 407/DME/QAMC Bahawalpur, dated: 24-09-2020). All of the parents/guardians were asked for informed and written consent after they were briefed about the objective of this research. Demographic information like age, gender, weight, residential status, level of education of caregivers, and type of CP were recorded. Urban area of residence was labeled if the child belonged to a district-level city, while a child who belonged to a below-district-level city was assigned rural area of residence. Types of CP were considered to be: i) Spastic cerebral palsy, as arm and hand on one side of the body are affected by spastic hemiplegia, also known as hemiparesis. Due to tight heel tendons, the child walks later and on tiptoe. Often, the afflicted side's

arm and leg are thinner and shorter. While intellectual ability is typically normal, speech tends to be delayed and may be competent at best. ii) Spastic diplegia or diparesis, characterized by muscle stiffness, mainly in the legs, with less severe effects on the arms and face; hands may also be imprecise. Leg tendon reflexes are overactive. When the foot's bottom is stimulated, toes point upward. Legs that move like scissor arms are caused by tightness in specific leg muscles. Leg braces or a walker may be necessary for children. Language and cognitive assessments were typically normal. iii) Spastic quadriplegia or quadripareisis: The children have a loose neck but excruciating limb stiffness and hardly ever walk. It's challenging to communicate and be understood. Frequent seizures are difficult to control. iv) Dyskinetic cerebral palsy: An abrupt, uncontrollably slow writhing of the hands, feet, arms, or legs. Some kids squirm or drool because of hyperactive facial and tongue muscles. v) Ataxic cerebral palsy: The children are having trouble coordinating and have a wide-based gait when walking. Inability to control voluntary actions, like reaching for a book, or difficulty with rapid or precise movements, like writing or buttoning a garment. vi) symptoms that are mixed up and don't fit into one specific form of CP. Psychosocial QOL was assessed as per CP QOL-Child questionnaire and labeled as low or high [12]. The questionnaire consists of 42 questions in 5 main categories. Caregivers were asked to describe the feelings of their children (according to their perception) about family, friends, participation, communication, health, and special equipment. Questions with rating scales from 1 to 9 (1 is the worst score and stands for very unhappy, while 9 is the best score and stands for very happy), scores of less than or equal to 6 were labeled as low QOL, while scores above 6 were taken as depicting high QOL. Patients were labeled as either having low QOL (scores < 6) or high QOL (scores > 6). All of the necessary information were recorded on a pre-designed proforma. IBM-SPSS Statistics version 26.0, was used to analyze data. The quantitative variable, like age, was represented by the Mean and Standard Deviation (SD). The qualitative variables like gender, area of residence, types of CP, and QOL (as low or high) were described by calculating frequencies and percentages. The analysis of CP QOL-Child was highlighted as scores in terms of mean and standard deviation. Stratification for age, weight, gender, and area of residence was done to address the effect modifiers. A post-stratification chi-square test was applied. Bi variate correlation analysis was performed employing Pearson's correlation test. A p -value < 0.05 was considered standard for significance.

RESULTS

In a total of 86 children with CP, the mean age was 7.64 ± 2.63 years (ranging 4 to 12 years) while 57 (66.3%) children were aged between 4 to 8 years. There were 64 (74.4%) male and

22 (25.6%) female children with male to female ratio of 2.9:1. The mean body weight was 17.74 ± 4.29 kg. Distribution of patients according to type of CP revealed spastic quadriplegia to be the most common type, noted in 29 (33.7%). Table 1 is showing demographic and clinical characteristics of children with CP.

Table 1: Characteristics of Children with CP (n=86)

Study Variables	Categories	Frequency (%)
Age (Years)	4-8	57 (66.3)
	9-12	29 (33.7)
Gender	Male	64 (74.4)
	Female	22 (25.6)
Weight (Kg)	≤ 20	46 (53.5)
	> 20	40 (46.5)
Place of Living	Urban	47 (54.7)
	Rural	39 (45.3)
Type of Cerebral Palsy	Spastic Quadriplegia	29 (33.7)
	Spastic Diplegia	24 (27.9)
	Spastic Hemiplegia	23 (26.7)
	Dyskinetic	3 (3.5)
	Hypotonia	7 (8.2)

The mean psycho-social QOL score was 4.93 ± 1.90 . High psycho-social QOL among children with CP was found in 25 (29.1%) patients, whereas there was low quality of life was in 61 (70.9%) children. Relatively younger age was associated with significantly low QOL ($p=0.001$). Urban place of living was also associated with low QOL ($p=0.001$). Details about the stratification of study variables with respect to psycho-social QOL are shown in table 2.

Table 2: Stratification of Psycho-social Quality of Life with Respect to Study Characteristics (n=86)

Study Variables	Categories	Psycho-social quality of life		p-Value
		High Frequency (%)	Low Frequency (%)	
Age (Years)	4-8	10 (17.5)	47 (82.5)	0.001
	9-12	15 (51.7)	14 (48.3)	
Gender	Male	18 (28.1)	46 (71.9)	0.742
	Female	7 (31.8)	15 (68.2)	
Weight (Kg)	≤ 20	12 (26.1)	34 (73.9)	0.514
	> 20	13 (32.5)	27 (67.5)	
Place of Living	Urban	7 (14.9)	40 (85.1)	0.001
	Rural	18 (46.2)	21 (53.8)	
Type of Cerebral Palsy	Spastic Quadriplegia	12 (41.4)	17 (58.6)	0.471
	Spastic Diplegia	5 (20.8)	19 (79.2)	
	Spastic Hemiplegia	5 (21.7)	18 (78.3)	
	Dyskinetic	1 (33.3)	2 (66.7)	
	Hypotonia	2 (28.6)	5 (71.4)	

Bi-variate correlation analysis employing Pearson's correlation between age and QOL scores revealed a positive and statistically significant relationship with correlation coefficient 0.295 showing $p=0.006$, and the

details are drawn in figure 1.

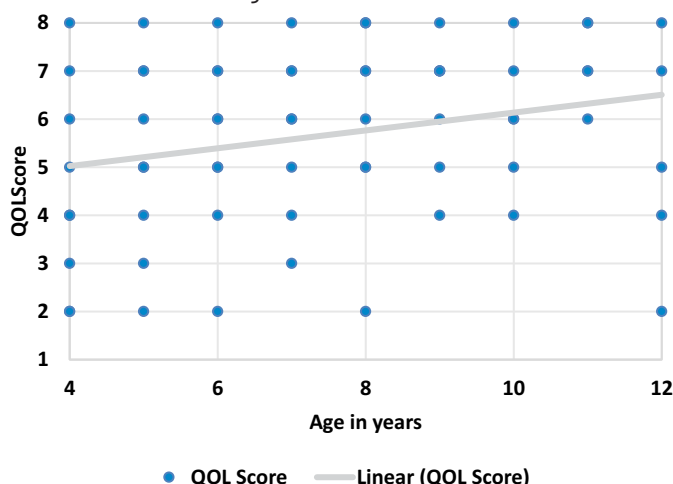


Figure 1: Relationship of Age and QOL Scores in Children with Cerebral Palsy

DISCUSSION

This study assessed psychosocial Quality of Life (QOL) among children with Cerebral Palsy (CP) in a tertiary care center in Bahawalpur, Pakistan. We observed that 29.1% of the children had high psychosocial QOL, while 70.9% had low QOL. Most psychosocial issues identified by parents had persisted for more than a year, and a notable proportion of these problems caused distress to the child (37%) and significantly affected family wellbeing (42%) [13]. Several international studies have also documented a high psychosocial burden among children with CP and their caregivers. An Iraqi study reported poor QOL in 92% of children and high psychosocial burden in over half of mothers [14]. Hend M, in 2021 evaluated various prenatal, perinatal, and postnatal risk factors contributing to the development of cerebral palsy in children [15]. These findings align with previous studies showing that children with CP often experience diminished quality of life, particularly in psychosocial domains. Nurani Gharaborghe et al., in 2015 reported a significant association between gross motor function and overall QOL among children with CP aged 4–12 years, indicating that physical limitations can directly influence psychosocial well-being [16]. Similarly, Tella et al., in 2011 highlighted poor health-related QOL in Nigerian children with CP, emphasizing the broader impact of the disorder on daily functioning and social participation [17]. Although the present results generally align with these international observations, it is important to interpret such comparisons with caution due to significant contextual differences in healthcare infrastructure, social support, and socioeconomic status. Early identification and intervention for CP may be hampered by limited healthcare resources and awareness in the present setting, potentially delaying support and impacting QOL scores,

especially among younger children. In this study, children aged 9–12 years appeared to have better QOL than those aged 4–8, possibly reflecting late recognition of CP or delayed access to services, a pattern that may not be as pronounced in regions with more robust early intervention systems. Age-related differences in HRQOL have been variably reported in the literature, with some studies from Nigeria showing a significant impact of age, while other studies, including those from the United States and elsewhere, have not found a consistent relationship between age and QOL in CP [17–19]. Gender was not found to impact QOL in this study, which is consistent with findings by Bjornson *et al.*, in the United States, but contrasts with an Indian study reporting greater impairment among males [20]. The study's findings are supported by prior research highlighting the multifactorial influences on the quality of life in children with cerebral palsy. Bjornson *et al.*, noted that youth with CP self-reported significantly lower health status and QOL compared to their typically developing peers, particularly in physical and social domains [20]. In an Indonesian population, Lestari *et al.*, identified that factors such as functional ability, parental education, and access to therapy were significantly associated with health-related QOL [21]. Similarly, Vila-Nova *et al.*, emphasized that parents of school-aged children with CP often reported lower QOL scores, particularly in domains related to emotional well-being and social participation [22]. Unique etiologies, such as congenital Zika virus infection, have also been linked with more severely impaired QOL, as demonstrated by Marques *et al.* [23]. In addition to child-specific factors, caregiver burden plays a pivotal role; Tedla *et al.*, in 2023 found that the QOL of caregivers is intricately tied to the child's disability severity and available support systems [24]. A local study by Hanif *et al.*, in 2023 also confirmed that CP significantly compromises multiple dimensions of QOL in Pakistani children, aligning with these study's observation of low psychosocial QOL in a majority of cases [25]. Such discrepancies may reflect local cultural attitudes toward gender and disability, as well as diversity in family and societal support systems. This study utilized the CP-QOL-Child questionnaire for QOL assessment, which is internationally validated and has been employed in studies from Iran, Nigeria, and the United States [16–20]. Regardless of the specific assessment instrument, the literature consistently describes a discernible impact of CP on children's QOL worldwide [17, 18, 20–25]. However, direct comparison of results across countries must be done cautiously due to the aforementioned contextual differences.

This study's limitations include its single-center design, modest sample size, and the lack of detailed assessment of parental, familial, or socioeconomic factors that may

influence QOL. Additionally, the specific regional context may limit the generalizability of these findings within or outside Pakistan. Future studies should consider multicenter designs and broader assessment of environmental, parental, and social variables to better understand the determinants of QOL in children with CP.

CONCLUSIONS

CP affects psycho-social QOL in high proportion of children. Younger age, urban residential affiliation were found to be significant association with low QOL scores.

Authors' Contribution

Conceptualization: MMN, SAT, SAS, RI

Methodology: MMN, SAT, IA

Formal analysis: IA

Writing and Drafting: MMN, SAT, SAS, RI

Review and Editing: MMN, SAT, IA, SAS, RI

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



Impact of Endoscopic Thoracic Sympathectomy among Hyperhidrosis Patients at A Tertiary Care Center

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ABSTRACT

Hyperhidrosis is characteristically termed as excessive sweating excessively even during normal situations. **Objectives:** To assess the dynamics of sweating in patients with hyperhidrosis before and after treatment with Endoscopic Sympathectomy (ETS). **Methods:** This pre-post intervention research was carried out at the Thoracic Surgery Unit of Lady Reading Hospital, Peshawar, from January 2023 to December 2024. Patients presenting with sweating of either gender, between 18 to 60 years of age, diagnosed with primary hyperhidrosis, were included in the study. Patients having secondary hyperhidrosis, female with symptoms of menopause, patients having generalized sweating, with severe or multiple co-morbidities such as pulmonary or cardiac issues, chronic illness (uncontrolled) or with any neurological condition were excluded from the study. SPSS version 23.0 was used for data analysis. Paired Student t-test was applied for sweating parameters before and after ETS, keeping $p < 0.05$ statistically significant. **Results:** The study included 53 patients with a mean age of (34.55 ± 8.72) years, nearly equally distributed by gender. Axillary hyperhidrosis was the most common type (43.4%), and most patients had HDSS grades 3 or 4. Post-ETS, all sweat parameters showed significant improvement. Notably, BSR reduced to 0.09 ± 0.07 mg/min/cm², PSR to 0.2 ± 0.17 mg/min/cm², SV to 0.07 ± 0.05 mg/cm², and ST to (12.28 ± 10.8) seconds. These findings demonstrate that ETS effectively reduces the severity and extent of sweating in patients with hyperhidrosis. **Conclusions:** A significant reduction in sweating parameters of patients with hyperhidrosis undergoing Endoscopic Thoracic Sympathectomy.

INTRODUCTION

Hyperhidrosis is characteristically termed as sweating excessively even during normal situations [1]. This results in perspiration more noticeably in extremities like armpits, hands, soles of feet and sometimes even face. This can occur intermittently or continuously, severely affecting routine daily activities [2]. The global prevalence of hyperhidrosis shows much variability, with recorded rates varying from as low as 1 % to as high as 16.7 % [3]. The frequency depends upon research from different populations as well as regions. The variations are postulated to have influences of climatic conditions, genetic factors and lifestyle differences [4]. For the treatment of hyperhidrosis, currently, medicinal treatment

shows resistance; only surgical treatment is recommended [5]. Surgical treatment includes a procedure known as Endoscopic Sympathectomy (ETS), which is carried out by making small incisions in the chest of the patient via thoracoscopy [6]. Based on the surgeon's experience and type of hyperhidrosis, the sympathetic nerve trunk is severed using electric cautery that is linked to hyperhidrosis. This tends to reduce or halt abnormal stimulation of the gland effectively [7]. This makes ETS the preferred mode of treatment, having evident outcomes [8]. Nevertheless, compensatory hyperhidrosis (CH) is one of the few but frustrating adverse effects reported post-operatively [9]. In CH, various anatomic regions start



sweating [10]. The most frequent adverse effect occurs on the chest, abdomen, groin and back. CH prevalence ranges very widely from 3 % to 98 % [11]. In addition to causing physical discomfort, CH leads to change in clothes more frequently, and causes the avoidance of certain activities. Coupled with all factors, it leads to substantial and unnecessary psychological distress, social withdrawal and anxiety [12]. In severe CH (SCH), patients might experience excessive as well as persistent sweating, interfering with activities of daily life and work, causing a substantial reduction in overall health and regret over choosing surgical treatment [13]. ETS is carried out by using a perspiration meter for measuring sweat volume (SV) before and after surgery. This is done for assessing indications and the effect of treatment. The etiology of hyperhidrosis is unknown [14]. Primary hyperhidrosis is a condition by itself, resulting from sympathetic hyper stimulation. Secondary hyperhidrosis is caused by various medical conditions such as neurological issues, endocrine disease, hematological malignancy, chronic infection, drugs and neuroendocrine tumor [15]. For many patients, the condition has a devastating social impact and emotional distress, leading to embarrassment and a reduction in quality of life. Nonetheless, patients prefer medicinal treatment to surgical treatment, which leads to either a delay in attaining proper treatment and therefore the severity of the condition increases [16]. Other causes of delay in being diagnosed and treated are misunderstanding of the patient on behalf of the disease, fearing a lack of medicinal treatment or fear of surgery, while it is the only option [17].

Despite Endoscopic Thoracic Sympathectomy (ETS) being an effective surgical treatment for hyperhidrosis, there remains limited evidence on postoperative sweating patterns and compensatory hyperhidrosis, particularly in terms of objective pre- and post-treatment sweat dynamics. The wide variability in reported outcomes and complications highlights a lack of standardized assessment and understanding of treatment effects. This study aimed to assess the dynamics of sweating in patients with hyperhidrosis before and after treatment with Endoscopic Sympathectomy (ETS).

METHODS

This pre-post intervention study was carried out at the Thoracic Surgery Unit of Lady Reading Hospital, Peshawar (Reference No: 377/LRH/MTI) from January 2023 to December 2024. Patients presenting with sweating of either gender, between 18 to 60 years of age, diagnosed with primary hyperhidrosis, were included in the study. Patients having secondary hyperhidrosis, females with symptoms of menopause, patients having generalized sweating, with severe or multiple co-morbidities such as pulmonary or cardiac issues, chronic illness (uncontrolled)

or with any neurological condition were excluded from the study. Informed consent was obtained from each patient before their inclusion in the research. The sample size was calculated using the Open Epi online software, keeping the hypothesized frequency of hyperhidrosis at 8.85 % as reported in a study; the sample size came out to be 53 at a 80% confidence level [18]. Due to constraints in resources and limited availability of patient sample size, the confidence level was kept at 80%. Because at a 95% confidence level, the sample size had come out to be 124; however, this sample was not feasible for us. This is why it was kept at 80%. Population size was kept as 1,000,000 as fpc (finite population correction factor), as it is used generally when calculating sample sizes. Primary hyperhidrosis was confirmed by the clinician after excluding all possible causes of hyperhidrosis (secondary). The term secondary hyperhidrosis was used when excessive sweating takes place, which was not idiopathic but was due to an underlying condition or medication side effect. Diseases of the spinal cord (including CNS), thyroid disease, chronic infections like tuberculosis or HIV-associated disorders, auto-immune diseases, neuroendocrine tumors or hematological malignancies. The HDSS was used for objectively measuring primary hyperhidrosis severity. It helps in assessing hyperhidrosis severity on the basis of the extent of excessive sweating associated with impairment of routine activities. Severity of hyperhidrosis was rated by the patients as follows [6]: 1- Underarm sweating was never noticeable and never interferes with daily activities, 2- Underarm sweating is tolerable but sometime interferes with daily activities, 3- Underarm sweating was barely tolerable and frequently interferes with daily activities, 4- Underarm sweating is intolerable and always interferes with daily activities. After ethical approval and taking informed consent from the patients, data were collected, which included baseline demographics, clinical signs and symptoms and any treatment received before being advised for ETS. Any treatment before surgical advice, including topical antiperspirant, anti-cholinergic or iontophoresis, etc., was also recorded. The symptom severity was recorded before and after ETS. ETS was performed under general anesthesia for each patient. Intubation was of the double-lumen variety. A single-staged bilateral ETS using two-port VATS (video-assisted thoracoscopic surgery) was carried out using single lung ventilation with the patient kept in the lateral decubitus position. Incision of the thoracoscopic port was in the mid-axillary line, incised at the 6th intercostal space. The instrument port was incised at 3rd intercostal space in the anterior axillary line. The sympathetic chains were transacted at the 3rd and 4th level of ribs using electro-cautery, and extending to the 5th rib if there was the presence of axillary hyperhidrosis. At the lower rib border, special care was considered for

avoiding any injury to the intercostal bundles (neurovascular). The trunk's exact spot was identified via surrounding landmarks like the arch of aorta arch and the azygous arch. The 1st rib was another vital landmark, where the pulse of the subclavian artery could be felt in a closed C-shape ring. To prevent bleeding or hyperemia, unnecessary palpation of the sympathetic chain was avoided as much as possible. SPSS version 23.0 was used for analyzing the data. Data included were age, gender, Hyperhidrosis severity scale (HDSS), basal sweat rate (BSR), start sweat rate (SR), peak sweat rate (PSR) and sweat time (ST). Comparison of demographics and various variables pre- and post-ETS was carried out using a paired student t-test, keeping p-value of ($p < 0.050$) as statistically significant after testing the normality of data using the Shapiro-Wilk test (for limited sample size). The result of normality testing came back insignificant ($p > 0.050$), suggesting that the data were normally distributed, and so a paired t-test was then applied.

RESULTS

The study included 53 patients undergoing Endoscopic Thoracic Sympathectomy (ETS) for hyperhidrosis. The mean age of participants was (34.55 ± 8.72) years. Gender distribution was almost equal, with 26 (49.06%) male and 27 (50.94%) female. Regarding the site of hyperhidrosis, 23 patients (43.4%) had axillary hyperhidrosis, 11 (20.75%) had palmar hyperhidrosis, 9 (16.98%) had plantar hyperhidrosis, and 10 (18.87%) had genital hyperhidrosis. The Hyperhidrosis Disease Severity Scale (HDSS) showed that 5 patients (9.43%) were at level 2, 25 (47.2%) at level 3, and 23 (43.4%) at level 4, with no patients categorized at level 1 (Table 1).

Table 1: Baseline Demographics of Patients Undergoing ETS (n=53)

Variables		Frequency (%) / Mean $\pm$ SD
Mean Age		34.55 $\pm$ 8.72
Gender	Male	26 (49.06 %)
	Female	27 (50.94 %)
Site of Hyperhidrosis	Axillary	23 (43.4 %)
	Plantar	9 (16.98 %)
	Palmar	11 (20.75 %)
	Genital	10 (18.87 %)
HDSS	1	0
	2	5 (9.43 %)
	3	25 (47.2 %)
	4	23 (43.4 %)

Following ETS, significant reductions were observed across all measured sweat parameters. The BSR (Baseline Sweat Rate) decreased from a mean of 1.1 ± 0.5 mg/min/cm² to 0.09 ± 0.07 mg/min/cm² ($p < 0.001$). PSR (Peak Sweat Rate) was reduced from 2.62 ± 0.81 to 0.2 ± 0.17 mg/min/cm² ($p < 0.001$). Sweat Volume (SV) decreased substantially from 5.2 ± 2.97 to 0.07 ± 0.05 mg/cm² ($p < 0.001$). The Sweat Time

(ST) also significantly decreased from 236.76 ± 94.2 seconds to 12.28 ± 10.8 seconds ($p < 0.001$). Similarly, the SR start (Sweat Rate at initiation) dropped from 2.01 ± 0.78 to 0.1 ± 0.06 mg/min/cm² ($p < 0.001$), indicating a marked treatment impact of ETS on sweat parameters (Table 2).

Table 2: Comparison of Sweat Parameters Before and After ETS (n=53)

Sweat Parameters	Prior to ETS	After ETS	p-Value
BSR (mg/min/cm ²)	1.1 $\pm$ 0.5	0.09 $\pm$ 0.07	<0.001
PSR (mg/min/cm ²)	2.62 $\pm$ 0.81	0.2 $\pm$ 0.17	<0.001
SV (mg/cm ²)	5.2 $\pm$ 2.97	0.07 $\pm$ 0.05	<0.001
ST (s)	236.76 $\pm$ 94.2	12.28 $\pm$ 10.8	<0.001
SR start (mg/min/cm ²)	2.01 $\pm$ 0.78	0.1 $\pm$ 0.06	<0.001

DISCUSSION

In this research, a comparison of sweat parameters was made before and after ETS in patients diagnosed with primary hyperhidrosis in which medical treatment had failed. A significant reduction in sweat parameters was observed in patients undergoing ETS. Since sweating differs in its terms, localization, factors, etc., diagnosing local hyperhidrosis necessitates objective evaluation and assessment of sweating quantitatively by using a highly reliable technique. Quantitative assessment of sweating parameters is vital in the evaluation of temporal aspects of sweating disorders [19]. A study recommended the use of the SKN-2000 device for measuring the flow volume-compensating ventilation capsule perspiration meter that works by entering air into the capsule and then measures the difference in humidity in-between prior to and after bringing air into the capsule [20]. The meter contains a servo system which controls airflow volume, which depends on the CV, allowing high responsiveness and objectively measuring hyperhidrosis [21]. A similar problem was used in our study as well for inducing emotional stress and sweating. Another study reported demonstrated all stimuli induced sweating amongst hyperhidrosis patients in comparison to patients without hyperhidrosis. Furthermore, the study reported that the difference due to mental arithmetic, such as emotional stimuli, was the highest [22]. In yet another study, it was reported that different types of emotional sweating take place even among non-hyperhidrosis individuals; however, the phenomenon is substantially larger among hyperhidrosis patients [23]. Similar to the findings of our research, sweating was measured prior to ETS and right after ETS and then over time. However, the study used VapoMeter for comparison of transepidermal water loss till 1-year post-resection in either T3 or T4 sympathetic ganglia and observed that sweating was substantially decreased among both groups of patients 1-year post-surgery. In general, it is regarded that characteristically prolonged ST

is a more authentic measure of pre-operative hyperhidrosis patients than high PSR [24]. Similarly, in our study as well, we found elevated BSR, prolonged ST and an increase in PSR among hyperhidrosis patients pre-operatively. As predicted, post-operatively, all parameters of sweating reduced significantly to almost nil.

This study is limited by its relatively small sample size and short follow-up period, which may not fully capture long-term recurrence of sweating after ETS. Additionally, being a single-center study with a specific patient population may limit the generalizability of the findings. Future multicenter studies with larger cohorts and longer follow-up durations are recommended to evaluate the long-term durability of ETS outcomes and to standardize objective sweating assessment methods in hyperhidrosis patients.

CONCLUSIONS

The study concludes that Endoscopic Thoracic Sympathectomy (ETS) leads to a significant reduction in sweating parameters in patients with primary hyperhidrosis who are resistant to medical treatment. These findings support ETS as an effective therapeutic option for severe cases. However, further long-term, large-scale studies are needed to confirm durability of outcomes.

Authors' Contribution

Conceptualization: FK

Methodology: MAK, FK

Formal analysis: MAK

Writing and Drafting: MAK, TA

Review and Editing: MAK, FK, TA

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



Spectrum of Fabricated Injuries Presenting in Lahore General Hospital, Lahore

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ABSTRACT

Among the various types of injuries, fabricated injuries, those intentionally caused or exaggerated for personal gain, such as to facilitate insurance claims, commit criminal acts, or avoid legal consequences, present unique challenges in forensic analysis. **Objectives:** To identify, classify, and evaluate the various forms of fabricated injuries encountered in the forensic clinic of Lahore General Hospital, Lahore. **Methods:** A retrospective cross-sectional study was carried out at the Forensic Medicine and Toxicology Department of Lahore General Hospital, Lahore. Data were collected from medico-legal registers. The data included the number of individuals, age, sex, nature of injury and site of injury. From all medico-legal injuries, only fabricated injuries in individuals 18 years and above of both sexes were included in the study. SPSS version 25.0 was used for statistical analysis. **Results:** Male-dominated among all fabricated injuries across all age groups, comprising 83.63% (189/226) of total cases, while female made up 16.37% (37/226). The highest frequency of fabricated injuries was seen in the 21-25 years' age group (21.97% total). Most of the male had sharp weapon injuries 100/113 (88.5%), and the scalp was the site bearing the maximum fabricated injuries with 51.3%. Female had blunter weapon injuries than sharp weapon injuries. Missing teeth due to blunt weapon dominated among all blunt force injuries. **Conclusions:** A holistic strategy is necessary to address the issue of fabricated injuries, which involves enhancing examiner qualifications, establishing uniform procedures, and promoting prompt and accurate reporting.

INTRODUCTION

In forensic medicine, fabricated injuries pose a serious problem since they are wounds that are purposefully created or mimicked to deceive medical examiners, law enforcement, or court officials [1]. These injuries can be self-inflicted or caused by others at the self-request, frequently to avoid legal accountability, getting paid, or to hide maltreatment [2]. Identification and medicolegal evaluation of faked injuries becomes more difficult on account of their wide range, which includes superficial abrasions, incised wounds, contusions, lacerations, and even firearm injuries that resemble real trauma [3-5]. To avoid issues in the medical and forensic domains, it is

crucial to accurately identify such injuries. Children are also prone to self-inflicted injuries. Children from large, single-parent households, poor socioeconomic level families, and families with less education were more susceptible to self-harm [6]. Clinically, faked injuries frequently have the following characteristics: regular shape, parallel or crossing patterns, position on easily accessible body areas, lack of defensive wounds, and garment damage. Sharp objects like knives, razors, glass fragments, or scissors may be used to cause these injuries, which usually avoid painful or sensitive locations [7]. In order to differentiate fake injuries from real ones, a



thorough clinical examination, a thorough history-taking process, and confirmation with police and forensic reports are necessary. This distinction is essential for maintaining judicial correctness and avoiding the abuse of legal and medical resources [8]. The Lahore General Hospital, which is well-known in Pakistan for its forensic and scientific investigations, is crucial in identifying and handling fake injuries. The significant patient drift at the institution provides special information about the frequency and nature of those injuries. Self-inflicted injuries recorded in roughly 5.3% of total medico-legal cases at Lahore General Hospital represent a significant workload [9]. People with low socioeconomic status are more prone to self-inflicted injuries [10, 11]. According to demographic surveys, particularly young adult male exhibits a higher occurrence of both real and fake injuries; their heightened exposure to random events like violence and accidents or to incentives like avoiding punishment or winning over others is often linked to this vulnerability [12]. With its large patient base, Lahore General Hospital is a great place to look at the range of fake injuries. Prior research carried out at comparable facilities in Pakistan has revealed different trends in injury kinds and how they relate to demographic characteristics such as age, sex, and financial standing [9]. Even though the medico-legal field is becoming more aware of fabricated injuries, there is a dearth of thorough information and regional research on the demographic trends, causes, and clinical manifestations of fake injuries in Pakistan, especially at large public hospitals like Lahore General Hospital. The current study reflects more recent trends in the spectrum of fabricated injuries. There is a lack of region-specific insights because the majority of current research seeks to generalize findings or concentrate on populations from other countries, like the study conducted by Kumar *et al.* was in a different culture [12].

There is limited local data on the detailed patterns and characteristics of fabricated injuries in Pakistan, particularly from major hospitals like Lahore General Hospital. This gap restricts effective identification and management of such cases in forensic practice. This study aimed to identify, classify, and evaluate the various forms of fabricated injuries encountered in the forensic clinic at General Hospital Lahore.

METHODS

A retrospective cross-sectional study was conducted at the Forensic Medicine and Toxicology Department of the Lahore General Hospital, Lahore. Both male and female aged 18 and above with fabricated injuries were included in the study. All other injuries and children were excluded from the study. 226 cases of fabricated injuries were recorded from the medicolegal registers for the year 2023. Data collection was done from 1st July 2023 to 30 June

2024. Ethical approval was obtained from ethical review committee of Post Graduate Medical Institute Ameer Ud Din Medical College (Ref No. 7254 PFMI/AMC). The minimum sample size calculated was 77 by following the formula: $n = (Z^2 \times P \times (1-P)) / d^2$. Where: n = required sample size, Z = Z-score corresponding to the desired confidence level (e.g., 1.96 for 95% confidence), p = estimated proportion of the attribute in the population (5.3%) [9]. d = desired margin of error (e.g., 0.05 for $\pm 5\%$). The Statistical Package for Social Sciences (SPSS) version 25.0 was used to analyze the data. Data included age, sex, types of injuries, weapon used and sites of injuries. A chi-square and t-test were done for statistical analysis. The following factors were taken into account when examining the traits of fabricated cases. They are usually incised but may be of any nature. They are superficial, parallel, and multiple of the same depth at the initiating and terminating points. They are seen on easily accessible non-vital parts of the body. Clothes are not cut, and if cut, it does not correspond with the nature of the wound. History is also inconsistent with injury [13].

RESULTS

The highest frequency of fabricated injuries was observed in the 21-25 years' age group (21.97% total), followed by the 18-20 years (18.83%) and 31-35 years (19.28%) groups. Male dominated the injury counts across all age groups, comprising 83.63% (189/226) of total cases, while female made up 16.37% (37/226). Female injury percentages tended to be higher in older age groups (e.g., 26-30, 31-35, 36-40) compared to younger groups, despite lower absolute counts. Out of all cases, 83.63% (189/226) were male. The age categories with the highest total counts were 21-25 (21.97%) and 18-20 (18.83%). Middle-aged groups had a larger percentage of female (26.47%) despite having fewer female overall. Younger individuals (18-40 years old) account for the majority of instances, Table 1.

Table 1: Age and Gender Distribution of Fabricated Injuries

Age Group (Years)	Male Count, n (%)	Female Count, n (%)	Total Count, n (%)
18-20	38 (20.1%)	3 (11.8%)	42 (18.8%)
21-25	45 (23.8%)	3 (11.8%)	49 (22%)
26-30	25 (13.2%)	4 (14.7%)	30 (13.4%)
31-35	36 (19.0%)	5 (20.6%)	43 (19.3%)
36-40	19 (10.0%)	6 (26.5%)	28 (12.6%)
41-45	8 (4.2%)	5 (17.6%)	14 (6.3%)
46-50	5 (2.6%)	3 (5.9%)	7 (3.1%)
51-55	7 (3.7%)	2 (2.9%)	8 (3.6%)
56-60	4 (2.1%)	3 (8.8%)	7 (3.1%)
61-65	1 (0.5%)	1 (2.9%)	2 (0.9%)
66-70	0 (0.0%)	1 (2.9%)	1 (0.4%)
71-75	1 (0.5%)	1 (2.9%)	2 (0.9%)
Total	189	37	226

113 people were hurt by sharp weapons overall. 88.5% of

injuries are male (100/113). 11.5% of injuries are female (13/113). The most frequent site of damage (58 instances, 51.3% of sharp injuries) is the scalp. Other typical locations are the front of the chest (9), left arm (8), and left forearm anterior (15). The two most common injuries in women are to the left little finger (4) and the left forearm anterior (6), table 2.

Table 2: Injuries Caused by Sharp-Edge Weapons

Site	Nature of Wound	Male	Female	Total
Front of Chest	Skin Deep, Incised wound	9	0	9
Left Little Finger	Abraded Swelling	3	4	7
Left Forearm anterior	Skin Deep, Incised Wound	9	6	15
Left arm	Skin Deep, Incised Wound	8	0	8
Face	-	1	1	2
No external injury	-	1	0	1
Middle finger	-	3	0	3
Scalp	Skin Deep, Incised	56	2	58
Shoulder	-	3	0	3
Hand	-	5	0	5
Foot	-	2	0	2
Total	-	100	13	113

There were 113 blunt weapon injuries overall. Injuries to men: 78.8% (89/113). Injuries among women: 21.2% (24/113). The most frequent damage site, with 27 cases (21 men and 6 female), is no outward injury (missing teeth). Other frequently visited locations include the hand (22), right index finger (12), and right little finger (18). Compared to men, women experience more injuries to their middle fingers and hands, table 3.

Table 3: Injuries Caused by Blunt Weapon

Site	Nature of Wound	Female	Male	Total
Left Little Finger	Abraded Swelling	0	11	11
Right Little Finger	Mild Swelling	2	16	18
Right Index Finger	Abrasion	1	11	12
Face	-	2	8	10
No External Injury	Missing Teeth	6	21	27
Middle Finger	Swelling	3	1	4
Hand	-	8	14	22
Nose	Nasal Bone Fracture	2	7	9
Total	-	24	89	113

Critical value of chi-square at $\alpha=0.05$ was approximately 19.675, while the calculated Chi-square was 24.96, which was bigger than the critical value, which means there was a statistically significant association between age group and sex. T-test results: Test 1: Sharp Weapon Injuries by Gender. $t=1.64$, $p=0.116$. No statistically significant difference in sharp weapon injury counts between male and female across body sites ($p>0.05$). Test 2: Blunt Weapon Injuries by Gender. $t=3.46$, $p=0.0038$. There was a statistically significant difference between male and female in blunt weapon injuries by site ($p<0.01$). Male have

significantly blunter injuries than females.

DISCUSSION

The present study found a predominance of males in cases of fabricated injuries, affecting both sharp and blunt force trauma. Specifically, sharp weapon injuries showed a higher male proportion (88.5%) compared to blunt weapon injuries (78.8%). These findings align well with recent regional research, notably the comprehensive observational study by Hussain *et al.* in Sialkot, Pakistan, who reported that male constituted 75% of fabricated injury cases, with most incidents occurring in rural areas and predominantly in the evening or night. Hussain *et al.* also noted that blunt weapons accounted for 77% of injuries. Both studies consistently report that fabricated injuries commonly involve easily accessible body parts such as the upper limbs, head, nasal area, and fingers, which are typical target sites for self-infliction or fabrication [8]. Further corroborating the male predominance, a cross-sectional study conducted by Munir *et al.* at Sheikh Zayed Medical College, Rahim Yar Khan, showed that 72.1% of blunt and sharp force trauma cases were male, supporting the observed high prevalence of men in such injuries in our cohort [14]. This male preponderance corresponds with global trends indicating greater male involvement in violent trauma. Notably, no stab or firearm wounds were recorded in our study. This contrasts with findings by Mock *et al.* who reported neck and abdomen as common sites for self-inflicted stab wounds [15], and Ali and Khan, who documented self-inflicted gunshot injuries [4]. This discrepancy may be due to regional, cultural, or reporting differences. Regarding age distribution, the current study confirms that fabricated injuries are more frequent in younger individuals, particularly those aged 18 to 40 years, which aligns with findings by Devassy and PS, who reported a higher frequency of intentionally self-caused injuries among younger populations [16]. However, contrasting gender-related findings were observed in studies such as Peterson *et al.* who reported a female predominance in self-inflicted injuries, which differs from our results [17]. On the other hand, Oladunjoye *et al.* found a male predominance in self-inflicted injuries, consistent with our findings [18]. Site-specific patterns of injury in this study show a predominance of wounds on non-vital and easily accessible body parts, with the scalp being the most frequent site for sharp injuries, and the absence of external injuries (e.g., missing teeth) being common in blunt trauma. Nishimura *et al.* similarly reported that self-inflicted injuries commonly involve the abdomen, followed by limbs, with fewer on the chest, noting that older individuals tend to inflict injuries on the face more frequently [19]. While the pattern of accessible site targeting is consistent, our study

diverges from others in fracture distribution: we observed a higher incidence of fractures of the right little finger and nasal bones in blunt trauma cases, whereas Singh et al. identified the tibia as the most commonly self-fractured bone in India [20].

This study was limited by its single-center design and reliance on medico-legal records, which may be subject to underreporting or documentation bias. Additionally, lack of psychological evaluation and forensic verification of intent limited deeper assessment of true fabrication patterns. Future studies should incorporate multi-center forensic and psychiatric assessments to better validate fabricated injury patterns and explore underlying behavioral and sociocultural factors.

CONCLUSIONS

It was concluded that the majority of fabricated injuries involved young adult males and were most commonly inflicted using sharp objects on accessible body parts, particularly the scalp. A statistically significant gender difference was observed in blunt trauma cases. These findings emphasize the need for enhanced forensic awareness and standardized assessment protocols to detect fabricated injuries early and ensure justice in medicolegal contexts.

Authors' Contribution

Conceptualization: ZI

Methodology: ZI, AK

Formal analysis: MA

Writing and Drafting: GM, KM, HA

Review and Editing: ZI, MA, GM, KM, AK, 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



Hypophosphatemia in Critically ill Children: Insight from a Case Control Study

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ABSTRACT

Hypophosphatemia is a common yet under-recognized electrolyte abnormality in critically ill children. Early detection and treatment of hypophosphatemia can help avoid complications and enhance outcomes in critically ill children. **Objectives:** To determine the frequency of hypophosphatemia at the time of Pediatric Intensive Care Unit (PICU) admission and throughout the PICU stay, and to evaluate the need for serial phosphate level monitoring. **Methods:** This case-control study was carried out in the PICU at Ziauddin University Hospital, North Campus, from March to September 2019. Data were collected from 136 (68 cases and 68 controls) patients. At enrollment, each participant underwent a thorough clinical examination. Baseline laboratory investigations were performed according to institutional PICU protocols. **Results:** On Day 1, 61.7% of cases had hypophosphatemia, rising to 80% by Day 3. Serum phosphate levels were significantly lower in cases than controls at both admission (3.42 ± 1.20 vs. 4.71 ± 0.70 mg/dL) and Day 3 (3.08 ± 0.74 vs. 4.62 ± 0.70 mg/dL), both $p < 0.001$. Cases had a significantly longer duration of illness before admission (10.02 ± 11.99 vs. 5.37 ± 4.74 days; $p = 0.004$) and PICU stay (4.35 ± 2.44 vs. 3.49 ± 1.41 days; $p = 0.01$). **Conclusion:** It was concluded that hypophosphatemia is common among critically ill children and often develops after admission. A single phosphate measurement at admission is insufficient for detecting all cases. Therefore, a series of phosphate measurements during the PICU stay is recommended.

INTRODUCTION

Phosphorus in all its forms is a fundamental element of the tissues and is required for many fundamental functions. It is involved in various physiological processes, including cell signalling, energy metabolism, and is a vital component of cell membranes and bones [1]. Most of the phosphorus is found intracellularly or inside the bones, while less than 1% is in plasma. There is an age-related as well as diurnal variability in the phosphorus concentration. A high concentration of phosphorus in childhood is required to promote growth. Regarding diurnal variation, there is a peak in phosphorus levels during sleep [2, 3]. Hypophosphatemia may present with a range of clinical symptoms, including irritability, altered mental status, seizures, coma, and neuromuscular dysfunction such as rhabdomyolysis. It may also be associated with hemolysis, abnormal liver enzyme levels, and bone marrow

suppression affecting erythrocytes, platelets, and white blood cells [2, 3]. Severe hypophosphatemia can impair cardiac muscle performance, weaken respiratory muscles, and potentially lead to multi-organ dysfunction [4]. Despite the routine measurements of serum calcium, sodium, and potassium in critically ill children, phosphorus is not routinely monitored, particularly in asymptomatic cases of hypophosphatemia [5]. Hypophosphatemia has been documented as a contributing risk factor for decreased cardiac output, trouble in weaning off from the ventilator, respiratory failure, cardiac arrhythmias and increased death rate in septic patients [6-9]. Early diagnosis and aggressive treatment of hypophosphatemia may altogether diminish the risk of arrhythmias and improve prognosis [10]. Studies showed that hypophosphatemia occurred in most of the patients (56%) during their PICU



stay [11]. One study found that 60.2% of the patients developed hypophosphatemia from the time of admission to the seventh day [12]. Another study found that the prevalence of low phosphorus levels was 44.4% on Day 1, rising to 63.9% on Day 3, and then gradually declining to 56.9% on Day 7 and 42.8% on Day 10 [13]. Hypophosphatemia was found to be prevalent with infections and an increased number of starvation days in children and associated with poor outcomes in children admitted to the PICU [8]. One study found infections (dengue fever, enteric fever) as the most common risk factor for hypophosphatemia in 38.2% of patients, followed by respiratory diseases (pneumonias, bronchiolitis, bronchial asthma, pleural effusion, interstitial lung diseases) in 26.4%, followed by sepsis in 5.9%, central nervous system (CNS) infection in 5.9%, and poisoning in 5.9% of patients [14]. Hypophosphatemia is a common yet under-recognized electrolyte abnormality in critically ill children. Early detection and treatment of hypophosphatemia can help avoid complications and enhance outcomes in critically ill children.

This study aimed to report the frequency of hypophosphatemia in critically ill children both at the time of admission and during PICU stay. Also, to demonstrate that a single phosphate level measurement at admission is insufficient, as many children who had normal levels on Day 1 developed hypophosphatemia by Day 3. It also aims to recommend routine serial monitoring of serum phosphate levels in PICU settings.

METHODS

This case-control study was conducted in the Intensive Care Unit of the Pediatric Department, Ziauddin University Hospital, North campus, from March to September 2019. Study approval was obtained from the ethical review committee of Ziauddin University Hospital via reference code 0410818LKPED, and written informed consent was obtained from all participants before their inclusion in the study. The sample size was calculated using the Open Epi sample size calculator (version X.X; www.openepi.com) for unmatched case-control studies. This study is based on assumptions on data reported by Meneses *et al.* [15], which showed a prevalence of acute respiratory disease of 66.0% in children with hypophosphatemia (exposed group) and 40.6% in those with normal phosphatemia (unexposed group). Assuming a two-sided confidence level of 95%, a power of 80%, an exposure ratio of 1:1, and using these proportions, the corresponding odds ratio was approximately 2.86. Based on these parameters, the required sample size was calculated to be 136 participants in total (68 per group). Children aged 1 month to 16 years admitted to the PICU were included in the study if they had a minimum PICU stay of 48 hours and at least two serum

phosphate level readings available during admission. Children were classified as cases if they had low serum phosphate levels and as controls if they had normal serum phosphate levels. Patients were excluded if they had known chronic kidney disease or parathyroid disorders, known genetic or metabolic phosphate disorders, were receiving phosphate supplementation before admission, or had incomplete records or were discharged within 48 hours. Children were defined as cases if they had hypophosphatemia, defined as serum phosphorus levels less than 3.8 mg/dL in children younger than 2 years, and less than 3.5 mg/dL in those older, measured at the time of admission or day 3. Children were defined as controls if they had normophosphatemia, defined as serum phosphorus levels equal to or above 3.8 mg/dL in children younger than 2 years, and equal to or above 3.5 mg/dL in those older, measured at the time of admission or day 3. At enrollment, each participant underwent a thorough initial evaluation that included a detailed clinical history, physical examination, and vital signs assessment. Baseline laboratory investigations were performed according to institutional PICU protocols. Complete blood count (CBC) was performed using an automated hematology analyser (Sysmex XN-1000, Sysmex Corporation, Japan). Arterial blood gas (ABG) analysis was conducted using a blood gas analyser (ABL800 FLEX, Radiometer Medical, Denmark). C-reactive protein (CRP), serum electrolytes, serum creatinine, blood urea nitrogen (BUN), serum aminotransferases, alkaline phosphatase, magnesium, calcium, and phosphorus were measured using an automated chemistry analyzer (Cobas c501, Roche Diagnostics, Germany). Vitamin D levels and parathyroid hormone (PTH) were assessed using chemiluminescence immunoassay kits on a Cobas e411 analyser (Roche Diagnostics, Germany). All tests were performed according to the respective manufacturers' protocols. Specimens for bacterial culture were collected as needed: two aseptic blood samples in aerobic/anaerobic bottles, one urine sample (clean-catch or catheter) in a sterile container, and one tracheal aspirate via suction into a sterile tube. All specimens were processed using standard microbial organism detection protocols in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. Serum phosphorus levels were measured at two points on admission and on the third day of hospitalization and analyzed in the institutional clinical laboratory. Serum phosphorus levels less than 3.8 mg/dL in children younger than 2 years, and less than 3.5 mg/dL in those older, were used to define hypophosphatemia. Infection was diagnosed based on clinical signs of infection, increased white blood cell count and positive bacterial culture. Respiratory disease was diagnosed on clinical signs and

abnormal radiological findings such as pulmonary infiltrates or consolidation. Sepsis was diagnosed on ≥ 2 SIRS criteria with confirmed infection. SIRS criteria were confirmed by monitoring body temperature, heart rate, respiratory rate, and white blood cell (WBC) count. Body temperature was measured using a digital thermometer, heart rate and respiratory rate were monitored clinically, and WBC count was measured through CBC. Diabetic ketoacidosis was diagnosed on elevated blood glucose $>200\text{mg/dL}$, decreased venous $\text{pH} < 7.3$ or bicarbonate $< 18\text{ mmol/L}$, and ketonuria or ketonemia. Blood glucose, bicarbonate, and serum ketones were measured using an automated chemistry analyser (Cobas c501, Roche Diagnostics, Germany). Venous blood gas analysis for pH and bicarbonate levels was performed using a blood gas analyzer (ABL800 FLEX, Radiometer Medical, Denmark). In all hypophosphatemic patients, a spot urinary sample was obtained to calculate the fractional excretion of phosphorus (FePO_4), aiding in determining renal phosphate handling. Children identified with hypophosphatemia were treated with intravenous phosphate supplementation in the form of potassium phosphate. The dose and rate of administration were determined by the PICU team based on individual patient parameters. Electrolyte levels were closely monitored during treatment to ensure safety and therapeutic efficacy. Parathyroid hormone (PTH) levels were also measured in selected hypophosphatemic patients when clinically indicated, to assess potential secondary causes. Strict adherence to inclusion and exclusion criteria, data collection in a pre-designed structured proforma was maintained throughout the study to minimize bias and control for potential confounding variables. Data quality was assured by double-checking records, following standardized sample collection procedures, and performing all tests from a single laboratory. The primary dependent variable was serum phosphate level, which was utilized to define the critically ill patients into cases (hypophosphatemia) and controls (normophosphatemia). Independent variables included demographic characteristics (age and gender), clinical variables (duration of illness before admission and diagnosis on admission), and clinical outcomes (use of mechanical ventilation and duration of PICU stay). Data analysis was conducted using SPSS software, version 21.0. Continuous variables were summarized using either mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on the distribution. Categorical variables were expressed as frequencies and percentages. To compare continuous variables, independent t-tests were utilized, while the Chi-square test was applied for categorical variables. A p-value less than 0.05 was regarded as statistically significant.

RESULTS

A total of 136 children were admitted to the ICU with critical illness, classified either into the case group (68 children with hypophosphatemia) or the control group (68 children with normal phosphate levels). In the study population, the age distribution showed that 52.9% of cases were below 2 years of age compared to 44.1% in controls, while 47.1% of cases and 55.9% of controls were aged 2 years or above. However, the difference was not statistically significant ($p=0.300$). Gender distribution was nearly equal across both groups, with no significant difference observed ($p=0.600$) (Table 1).

Table 1: Age and Gender Distribution in Case and Control Groups

Variables	Category	Case (n=68)	Control (n = 68)	Chi-square Value	p-value
Age (Years)	2	36 (52.9%)	30 (44.1%)	1.06	0.300
	≥ 2	32 (47.1%)	38 (55.9%)		
Gender	Male	34 (50.0%)	37 (54.4%)	0.265	0.600
	Female	34 (50.0%)	31 (45.6%)		

Among the 68 children classified as cases, hypophosphatemia was present in 61.7% cases on Day 1 and increased to 80% by Day 3, showing a progressive decline in phosphate levels in the case group. Thus, the overall frequency of hypophosphatemia among cases during PICU stay was 100% by design, with a significant proportion developing it after admission. Serum phosphate levels were significantly lower in cases than controls at both admission ($p < 0.001$) and Day 3 ($p < 0.001$). The mean duration of illness before hospital admission was significantly longer in the case group (10.02 ± 11.99 days) compared to the control group (5.37 ± 4.74 days), with a statistically significant difference ($p=0.004$) (Table 2).

Table 2: Phosphate Findings and Duration of illness Before Admission in Case and Control Groups

Variables	Case (n=68)	Control (n=68)	p-Value
Phosphate Findings	Day 1 New Cases	42 (61.7%)	26 (38.3%)
	Day 3 Total Cases	55 (80%)	-
	Serum Phosphate at Admission	3.42 ± 1.20 (0.95–6.81)	4.71 ± 0.70 (3.54–6.27)
	Serum Phosphate Day 3	3.08 ± 0.74 (1.18–4.87)	4.62 ± 0.70 (3.59–6.7)
	FE Phosphate at Admission	17.84 ± 12.11 (0.53–65.75)	-
	FE Phosphate Day 3	17.87 ± 14.84 (1.71–66.76)	-
Duration of illness Before Admission		10.02 ± 11.99 (1–90)	5.37 ± 4.74 (1–30)
			0.004

The average length of PICU stay was significantly longer in the case group compared to the control group (4.35 versus 3.49 days; $p=0.010$), indicating a notable association between hypophosphatemia and prolonged critical care. However, the duration of mechanical ventilation did not differ significantly between groups (3.38 versus 3.40 days;

$p=0.90$), suggesting that hypophosphatemia did not affect ventilation duration (Table 3).

Table 3: PICU Stay and Mechanical Ventilation in Case and Control Groups

Variables	Case (n=68)	Control (n = 68)	p-Value
Length of PICU Stay	4.35 ± 2.44 (2-20)	3.49 ± 1.41 (2-10)	0.010
Mechanical Ventilation (n=20 and 10)	3.38 ± 1.69 (1.5-9)	3.40 ± 2.41 (1-9)	0.900

The primary diagnoses were similar between both groups, with infections and respiratory conditions being the most common in both. Among cases, 44.1% had infections and 41.1% had respiratory conditions, while in controls, respiratory disease was slightly more prevalent at 52.9%, and infections were seen in 39.7%. Infection was present in 57.4% of the case group compared to 42.6% of the control group, suggesting a higher occurrence among patients who developed hypophosphatemia ($p=0.080$) (Table 4).

Table 4: Diagnosis at Admission in Case and Control Groups

Diagnosis	Case, n (%)	Control, n (%)
Infection	30 (44.1%)	27 (39.7%)
Respiratory Disease	28 (41.1%)	36 (52.9%)
Sepsis	5 (7.4%)	3 (4.4%)
Diabetic Ketoacidosis	5 (7.4%)	2 (2.9%)
Chi-square Value	—	—
P-value	2.944%	0.4%
Infection		
Yes	39 (57.4%)	29 (42.6%)
No	29 (42.6%)	39 (57.4%)
Chi-square Value	—	—
p-value	2.941%	0.08%

DISCUSSION

The findings of this study revealed a significant association between hypophosphatemia and adverse clinical parameters in critically ill children. Hypophosphatemia was present in 61.7% of cases on Day 1 and increased to 80% by Day 3, showing a progressive decline in phosphate levels in the case group. Serum phosphate levels were also significantly lower in cases than controls at both admission ($p<0.001$) and Day 3 ($p<0.001$). Our study findings are similar to the findings of previous studies that also find a high frequency of hypophosphatemia in children. A study by El Shazly *et al.* reports that hypophosphatemia was present in 42% of critically ill children on day 1 and increased to 62% on day 7 [16]. A study by Springer *et al.* reports that hypophosphatemia ranged from 27.2% to 37.5% critically ill children within three days of admission [17]. Another study by Shah *et al.* reports that hypophosphatemia was reported in 71.6% critically ill children within 10 days of admission [18]. Another study by Lusteau *et al.* found that hypophosphatemia was diagnosed in 41% critically ill children at PICU admission and then increased to 46%

during the stay [19]. All similar studies report that hypophosphatemia mostly worsens after PICU admission in critically ill children, primarily due to increased renal phosphate excretion. However, our study reports stable fractional excretion of phosphate on Day 1 and Day 3 (17.84 versus 17.87), indicating that factors of critical illness are responsible for hypophosphatemia. Another significant finding of this study was the longer length of PICU stay (4.35 versus 3.49 days; $p=0.01$) in the case group compared to the control group, indicating a significant association between hypophosphatemia and prolonged critical care. Our study findings are similar to the findings of previous studies that also find a longer length of PICU stay in critically ill children with hypophosphatemia. A study by El Shazly *et al.* reports the 8-day PICU stay in normophosphatemia children and 10-day PICU stay in hypophosphatemia children ($p<0.001$) [16]. Another study by Shah *et al.* also reports that hypophosphatemia was associated with prolonged PICU stay of > six days in critically ill children [18]. Another study by Shah *et al.* reports the 4-day PICU stay in Normophosphatemia children and 7-day PICU stay in Hypophosphatemia children ($p=0.001$) [20]. All similar studies report that hypophosphatemia is significantly associated with longer length of PICU stay because hypophosphatemia worsens clinical status and delays the recovery of critically ill children. Another non-significant finding of this study was the similar duration of mechanical ventilation (3.38 versus 3.40 days; $p=0.0$) in the case group compared to the control group, indicating a non-significant association between hypophosphatemia and duration of mechanical ventilation. In contrast to our study findings, Lusteau *et al.* report the significant association of mechanical ventilation with hypophosphatemia. Duration of mechanical ventilation was significantly higher with hypophosphatemia than normophosphatemia (109 versus 67 hours; $p=0.007$) [19]. The difference was observed in the duration of mechanical ventilation due to different factors such as sample size, patient age, and their underlying diagnosis, which can change the phosphate-related respiratory compromise. No statistically significant differences in the distribution of initial diagnosis and infections between groups were evident ($p=0.4$ and 0.08 , respectively), although a greater prevalence of infections and respiratory pathologies was apparent in the hypophosphatemic group. All in all, these data add weight to the importance of routine serum phosphate measurement in critically ill children, especially those with prolonged episodes of illness or infections. Early identification and correction of hypophosphatemia is likely to reduce the time in PICU and enhance overall patient care [21, 22].

This study was limited by a relatively small sample size and short follow-up duration, which may affect the

generalizability of the findings. Additionally, underlying causes of hypophosphatemia and disease severity were not fully explored, which could influence clinical outcomes. Future studies should include larger cohorts with detailed evaluation of disease severity and underlying causes to better understand the clinical impact of hypophosphatemia.

CONCLUSIONS

It was concluded that hypophosphatemia is a common metabolic disturbance among critically ill children, which often worsens from the day of admission to day three of PICU stay. These findings of our study highlight that a single serum phosphate measurement at admission is insufficient for detecting all cases of hypophosphatemia. Therefore, a series of phosphate measurements during the PICU stay is recommended. This underscores the clinical value of routine serial phosphate monitoring rather than relying solely on admission values. Based on this evidence, it is recommended that pediatric intensive care protocols incorporate regular phosphate assessments to facilitate early detection and timely correction, potentially reducing PICU stay and improving outcomes.

Authors' Contribution

Conceptualization: LK

Methodology: LK, MI, FZ¹

Formal analysis: MI

Writing and Drafting: LK, MI, FZ¹, FZ²

Review and Editing: LK, MI, FZ¹, FZ²

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 and Risk Factors of Urinary Dysfunction in Post-Cesarean Patients

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ABSTRACT

Urinary dysfunction (UD) following cesarean section (CS) is a significant but underexplored maternal health issue. While vaginal delivery is traditionally associated with pelvic floor disorders, emerging evidence suggests cesarean delivery may also pose risks. **Objectives:** To determine the prevalence of UD and its associated risk factors among post-CS women in Peshawar, Pakistan. **Methods:** This cross-sectional study was conducted at Peshawar Institute of Medical Sciences, Peshawar, including 195 postpartum women who underwent CS between January to March 2024. Participants were contacted via telephone and assessed using a standardized proforma, including the International Prostate Symptom Score (IPSS) to evaluate urinary symptoms. Statistical analysis was performed using SPSS version 25.0. To identify the potential risk factors, logistic regression was performed. **Results:** The prevalence of UD was 31 (15.8%). Common symptoms included urgency (74.2%), incomplete bladder emptying (54.8%), and urinary frequency (41.9%). Stress urinary incontinence was observed in 38.7%. Significant risk factors included age >35 years ($p<0.001$), emergency CS ($p=0.001$), operating time >60 minutes ($p<0.001$), baby weight >4 kg ($p=0.001$), and BMI >30 kg/m² ($p<0.001$). Emergency CS was the strongest predictor (OR=6.31, $p<0.001$). **Conclusions:** Urinary dysfunction is a notable concern following cesarean delivery. Emergency CS, obesity, and prolonged surgery are key risk factors. Early identification and preventive strategies may improve postpartum care outcomes.

INTRODUCTION

Urinary dysfunction (UD) has a wide range of symptoms affecting the lower urinary tract. The lower urinary tract symptoms (LUTS) are categorized into storage, voiding, and post-micturition symptoms like nocturia, urgency, increased frequency, incontinence, incomplete bladder emptying, changed urine stream, and post-void dribbling [1]. It is a notable health concern that is frequently observed during pregnancy [2]. The most commonly seen symptom is urinary incontinence (UI) with a prevalence of 18.6% to 75% during pregnancy and 6% to 31% in the postpartum period [3]. The most prevalent type of UI during pregnancy is stress urinary incontinence (SUI), with a mean prevalence of 41% (18.6–60%) and rises with

gestational age. Together with hormonal changes, the expanding uterus and fetal weight put strain on the pelvic floor muscles (PFM), which weakens the PFM and impairs its supporting and sphincteric function. This leads to urethral sphincter incompetence by increasing urethral and bladder neck movement [4]. The meta-analysis of studies published between 1998 to 2020 based on postpartum UI reports a prevalence of 31%. The studies found an initial decline at three months postpartum, but then an increase to 32% during one year of post-delivery. SUI is the frequently reported (54%) postpartum UI [5]. The risk factor for urinary dysfunction, like UI, includes an emergency cesarean section (CS) followed by instrumental



vaginal delivery, vaginal delivery, and elective CS [3]. Studies demonstrate that vaginal deliveries are associated with a longer-term risk of UI and pelvic organ prolapse (POP) than Cesarean sections. Potential risk factors for pelvic floor disorders (PFDs) include urinary incontinence during pregnancy, older age at delivery, high BMI, multiple gestation, and mode of delivery, highlighting the complex interrelation between delivery mode and pelvic floor function [6, 7]. However, some studies reported no significant difference in the prevalence of UI among CS and vaginal delivery [8, 9].

Due to inconsistency in the literature, further research studies are needed to confirm the result. Through prospective evaluation of post-cesarean patients, this study will shed light on the burden of LUTS and its predictors, facilitating a better understanding of postpartum urinary health. The necessity for this research is highlighted by the absence of inclusive, context-related studies on post-cesarean urinary dysfunction, especially in areas such as Peshawar, where accessibility to healthcare and maternal health behaviours differ. Knowledge of the prevalence and determinants of postpartum LUTS will guide clinical recommendations, enhance patient counseling, and assist in creating targeted preventive and therapeutic interventions to improve the quality of life in affected women. This study aimed to assess the prevalence of urinary dysfunction in women in Peshawar, after cesarean delivery and determine risk factors associated with its development.

METHODS

This cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, Peshawar Institute of Medical Sciences, Peshawar. A total of 195 post-CS patients were included in the study. The sample size was calculated using Open Epi software. The calculation was based on a prevalence of 14.9% for urinary leakage during sneezing or coughing among post-CS women, as reported in a previous study [8]. A 95% confidence level and a 5% margin of error were used to ensure statistical precision. The study was initiated after obtaining approval from the hospital research committee under (Ref# PIMC/DMR/19). The data of 195 women having either emergency or elective CS from January to March 2025 were retrieved from hospital electronic records and included in the study through a consecutive sampling technique based on the inclusion criteria. The inclusion criteria were: women of the postpartum period, aged 18 to 45 years, and no prior history of urinary dysfunction before pregnancy. Women with failed trial of labor leading to CS, history of severe postpartum complications, like sepsis or uncontrolled postpartum hemorrhage, obstetric fistula or known pelvic organ prolapse before pregnancy, neurological conditions

affecting bladder function (e.g., multiple sclerosis, spinal cord injury), or history of recurrent UTIs requiring long-term treatment were excluded. Patients were then contacted telephonically to participate in the study after being identified by the study's criteria. Consent was obtained from each patient after explaining the study's goal. A standardized questionnaire proforma was used to collect data. Baseline demographic information, like age, number of prior births, body mass index (BMI), and whether the cesarean was an emergency or scheduled, was included. The IPSS scale was used to inquire about urinary problems like urgency, leakage, trouble emptying the bladder, weak urine stream, or frequent urination. Data were collected by the researchers themselves. All data were treated with the utmost confidentiality and used exclusively for research. Urinary dysfunction (UD) was defined as difficulty in normal bladder function experienced by women following cesarean section, including a range of symptoms, like frequent urination, urgency, leakage, difficulty in emptying the bladder, weak urine stream, or post-void dribbling. For this study, Urinary Tract Symptoms (UTS) were categorized into storage symptoms (e.g., increased frequency, nocturia, urgency, and urinary leakage), voiding symptoms (e.g., hesitancy, weak stream, straining, and prolonged urination), and post-micturition symptoms (e.g., incomplete bladder emptying and dribbling). Additionally, urinary incontinence was assessed and classified into three types: Stress Urinary Incontinence (SUI), characterized by leakage during physical exertion; Urgency Urinary Incontinence (UUI), marked by sudden, intense urges followed by leakage; and Mixed Urinary Incontinence (MUI), involving features of both SUI and UUI. SPSS version 25.0 was used for analysis purposes. Mean $\pm$ Standard deviation or Median (IQR) was calculated for the numerical/quantitative variable. Frequencies and percentages were calculated for categorical/qualitative variables. Post-stratification chi-square test or Fisher Exact Test was applied, keeping p-value ≤ 0.050 as statistically significant. Binary logistic regression analysis was performed to identify the potential risk factors among all.

RESULTS

Among 195 post-caesarean postpartum women, 31 (15.8%) developed urinary dysfunction (UD). Key factors significantly associated with UD included age >35 years ($p < 0.001$), emergency CS ($p = 0.001$), operating time >60 minutes ($p < 0.001$), and delivery of a baby weighing more than 4 kg ($p = 0.001$). Obesity (BMI >30) was also linked to UD, with significantly higher rates in the affected group ($p < 0.001$) (Table 1).

Table 1: Demographics and Clinical Characteristics of Patients

Variables	Urinary Dysfunction (n=31)	Non-Urinary Dysfunction (n=164)	p-Value
Age (Years)	32.8 ± 1.27	29.9 ± 0.91	<0.001
Age ≤35 Years	18 (58.1%)	121 (73.8%)	0.209
Age >35 Years	13 (41.9%)	43 (26.2%)	0.181
BMI (kg/m ²)	27.7 ± 2.17	28.3 ± 3.31	0.119
BMI ≤30 kg/m ²	21 (67.7%)	148 (90.2%)	0.002
BMI >30 kg/m ²	10 (32.3%)	16 (9.8%)	<0.001
Parity	2.48 ± 2.1	1.94 ± 1.5	0.134
Emergency CS	19 (61.3%)	29 (17.7%)	0.001
Blood loss (>800ml)	6 (19.4%)	14 (8.5%)	0.019
Operating time >60 Min	14 (45.2%)	23 (14%)	<0.001
Baby Birth Weight >4g	8 (25.8%)	15 (9.1%)	0.001
Diabetes	11 (35.5%)	8 (4.8%)	0.319
Hypertension	13 (42%)	19 (11.6%)	0.209

Among the 31 women who developed urinary dysfunction after caesarean section during postpartum time, the most commonly reported symptom was urinary urgency, affecting 23 (74.2%) patients. Incomplete bladder emptying was reported by 17 (54.8%) women, while increased urinary frequency (≥8 times/day) was noted in 13 (41.9%) patients. Weak urinary stream occurred in 11 (35.5%), and both nocturia and straining during urination were reported by 9 women each (29.0%). Post-micturition dribbling was also seen in 9 cases (29.0%). Regarding urinary incontinence, stress urinary incontinence (SUI) was present in 12 (38.7%) patients, urgency urinary incontinence (UUI) in 8 (25.8%), and mixed incontinence (both SUI and UUI) in 4 (12.9%) women (Table 2).

Table 2: Different Symptoms of Urinary Dysfunction Post CS

Symptoms	Type	(n=31) Frequency (%)
Urine Storage Problems	Urine Frequency ≥8 Times	13 (41.9%)
	Urgency	23 (74.2%)
	Nocturia	9 (29.0%)
Voiding	Straining	9 (29%)
	Weak Stream	11 (35.5%)
Post-Micturition	Incomplete Emptying	17 (54.8%)
	Dribbling	9 (29.0%)
Urinary Incontinence (UI)	Stress UI (SUI)	12 (38.7%)
	Urgency UI (UUI)	8 (25.8%)
	Mixed (SUI + UUI)	4 (12.9%)

Logistic regression analysis identified emergency caesarean section as the strongest independent risk factor for urinary dysfunction, with women undergoing emergency CS having over six times higher odds of developing UD (OR=6.31, p<0.001). Prolonged operating time >60 min was also significantly associated with increased risk (OR=4.11, p=0.023). Although age >35 years (OR=0.651, p=0.051) and BMI >30 kg/m² (OR=0.509, p=0.062) did not approach statistical significance. Blood loss over

800 mL was also not significantly associated with UD (OR=0.721, p=0.096) (Table 3).

Table 3: Logistic Regression Analyses of Risk Factors for Urinary Dysfunction Post CS

Variables	Odds Ratio (OR)	95% CI	p-Value
Age > 35 Years	0.651	0.322 - 1.230	0.051
BMI > 30 kg/m ²	0.509	0.222 - 1.161	0.062
Emergency CS	6.31	3.791 - 9.857	<0.001
Blood loss >800ml	0.721	0.193 - 1.357	0.096
Operating time >60 min	4.108	1.835 - 6.029	0.023

DISCUSSION

This study aimed to assess the prevalence and associated risk factors of UD in women following CS. Among the 195 post-cesarean patients evaluated, 15.8% were found to have developed urinary dysfunction during the postpartum period. These findings offer important insight into a relatively underexplored area of maternal health, especially in the context of CS, a procedure whose effects on pelvic floor integrity and urinary health remain debated. Cesarean delivery has been considered protective against pelvic floor disorders such as urinary incontinence or retention when compared to vaginal delivery. However, some literature challenges this assumption and emphasizes the multifactorial nature of UD [6-10]. This study analyzes the prevalence, types, and associated risk factors for UD among 195 cohort of post-CS women. In this study, the prevalence of UD was 15.8%, with symptoms including urgency (74.2%), incomplete bladder emptying (54.8%), increased urinary frequency (41.9%), and stress urinary incontinence (38.7%). This prevalence is notably higher than figures reported in some large-scale studies. For instance, Dowais et al. reported a prevalence of 5.8% in CS patients and 6.9% in vaginal delivery patients, indicating a narrower gap and challenging the perception that CS confers substantial protection against urinary dysfunction [11]. The relatively higher prevalence in our study may be attributed to the inclusion of both elective and emergency CS, and shorter follow-up periods. The most common form of urinary dysfunction observed in our study was urgency, followed by incomplete emptying and frequency, with stress urinary incontinence (SUI) affecting over one-third of the affected patients. Similar findings were in a meta-analysis, which reported that SUI was the predominant symptom in postpartum women regardless of delivery mode (54%) [5]. Additionally, our study observed urgency urinary incontinence (25.8%) and mixed urinary incontinence (12.9%), in line with patterns described in studies on lower urinary tract symptoms (LUTS) [12-15]. Postpartum urinary retention (PUR), a serious yet often underdiagnosed condition, has also been reported in the literature following CS. Warner et al. and Zakzouk et al. note

a higher prevalence of PUR post-CS, often attributed to intraoperative bladder manipulation, epidural anesthesia, and temporary autonomic dysfunction [16, 17]. Though our study did not quantify PUR independently, many symptoms, like incomplete emptying, likely overlap with this clinical entity. Our findings showed that emergency cesarean section was a significant risk factor for UD, with an odds ratio of 6.31 ($p < 0.001$). This supports earlier findings by Khalil *et al.* and was consistent with the work of Khasanov *et al.* who proposed that emergency interventions may predispose to pelvic floor and nerve trauma, especially following prolonged obstructed labor before surgery [18, 19]. In contrast, Chen *et al.* found no significant difference in pelvic floor dysfunction based on the timing of CS, suggesting that intrapartum versus antepartum factors may not universally influence outcomes [20]. The divergence may reflect population-specific risk profiles, surgical conditions, or perioperative care differences.

This study was limited by its single-center design and relatively short postpartum follow-up period, which may not capture late-onset urinary dysfunction. Additionally, lack of pre-pregnancy baseline urinary status and urodynamic confirmation may have led to misclassification of symptoms. Future studies should include longitudinal, multi-center designs with baseline pelvic floor assessment and objective urodynamic testing to better evaluate the long-term impact of cesarean section on urinary dysfunction.

CONCLUSIONS

The findings of this study highlight that urinary dysfunction is a common postoperative issue following cesarean delivery, particularly in emergency cases and in patients with identifiable risk factors such as high BMI, prolonged surgery, and macrosomic infants. While cesarean delivery has traditionally been viewed as a protective measure against pelvic floor trauma, this assumption should be re-evaluated in light of evidence showing comparable or even higher UD prevalence in certain CS populations. Future research should focus on preventive strategies, objective diagnostic modalities, and comparative studies between delivery modes. Early screening and postpartum pelvic floor rehabilitation may be key to improving maternal urinary health outcomes.

Authors' Contribution

Conceptualization: SS

Methodology: SS, SBK

Formal analysis: SS, HH

Writing and Drafting: BA, SS, H, ZI

Review and Editing: BA, SS, H, HH, ZI, SBK

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



Cytomorphological Spectrum of Breast Fine Needle Aspiration Cytology Using International Academy Cytology Yokohama System- A Retrospective Study in the Tertiary Care Center of Sahiwal

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ABSTRACT

Breast carcinoma is also a very widespread and upsetting cancer that pertains to women, and the incidence of the same is also high in developing countries. Breast cancer is one of the most common malignancies women are exposed to, and its occurrence is particularly high in third-world countries. Fine needle aspiration cytology (FNAC) is a good diagnostic tool when it comes to the detection of early breast lesions. **Objectives:** To evaluate the role of FNAC in the screening and assessment of breast lumps to identify breast cancer in the resource-poor Sahiwal Division. **Methods:** This retrospective cross-sectional study included 392 females presenting with palpable breast lumps. After obtaining informed consent, FNAC was performed, and the aspirated material was used to prepare and stain slides for cytological examination. The data were collected from clinical records and then analyzed. **Results:** Out of 392 female patients, the majority of breast lesions (40.05%) were found in C5; malignant category followed by 26.78% in C2 (benign), 21.93% of lesions in C3 (atypical), and 10.52% in C4 (suspicious for malignancy) categories. Most of the patients (39.84%) were aged 41 and above, and 143 patients (36.48%) were seen in category 5 whereas the duration of lesion according to history of disease for the majority of cases (36.48%) can be seen from 7 to 12 months in reporting category 5 (40.86%). **Conclusions:** The fine needle aspiration cytology (FNAC) is associated with fast, trustworthy, and economical means of initial classification of palpable breast growths on the basis of the standardized IAC system.

INTRODUCTION

Breast cancer is one of the most distressing and prevalent cancers among females after cervical cancer [1]. It accounts for approximately 18.4% of all cancers worldwide. The incidence is even more in developing countries. While in developed countries, due to early diagnosis and accessible diagnostic measures, it's under control. Being one of the major causes of mortality in women, it is very

significant to differentiate between benign and malignant lesions of the breast and several other reactive conditions mimicking malignant ones [2]. Pakistan ranks as the fifth Asian country where the number of females affected by breast carcinoma is increasing with every passing year. Pakistan currently has the highest death rate, which is 25.2/100,000 alone due to breast cancer alone, and one in



every 9 women has the risk in their lifetime of getting diagnosed with breast carcinoma [3]. Many patients present with an advanced stage of disease owing to several factors, such as social circumstances and low socio-economic status. Breast cancer is now considered a global burden posing as a major public health concern. It is also one of the leading causes of mortality and morbidity in women in African countries, where the incidence rate of 2.7 cases was seen in every 100,000 females [4]. Triple assessment is used worldwide for investigating a breast mass, which includes physical examination, radiological investigations such as ultrasound and mammography, and Fine needle aspiration cytology, which is a very valuable pre-operative assessment technique. It has two main objectives; firstly, to confirm of radiological and clinically benign lesions, which then avoid unnecessary surgical interventions. Thus, the diagnostic accuracy of diagnosing breast lesions is greatly increased by the combination of palpation (clinical examination), mammography, and cytology [5, 6]. In developing countries like Pakistan with limited resources, FNAC is considered to be a rapid, reliable, and cost-effective method of diagnosing breast carcinomas in palpable lumps. In India, similarly, which is also a developing country, the diagnostic accuracy of FNAC was found to be very high (97%) with 98% specificity and 94.5% sensitivity [7]. Due to an increase in demand for FNACs and increasing experience of our surgeons, the incidence and prevalence of breast carcinoma seem to be increasing. But still, there is seen to be paucity in data available, like disease (breast lesions), risk factors causing progression to carcinomas, epidemiology, and distribution of disease patterns [4].

Despite breast cancer being a major public health concern with high morbidity and mortality in Pakistan, there is limited locally available data on the diagnostic categorization of palpable breast lesions using standardized systems such as the IAC Yokohama classification. This study aims to determine the crucial role of FNAC in categorizing and screening palpable breast lumps in female patients according to the standardized IAC Yokohama system, as presented at Sahiwal Teaching Hospital in the Sahiwal division. As there are very limited resources for early diagnosis of palpable breast lesions, it is imperative to develop a technique that is cost-effective and requires little expertise.

METHODS

The study was a descriptive, retrospective, cross-sectional study that was done at Sahiwal Teaching Hospital, Sahiwal. The Institutional Review Board approved the study (No. 110/IRB/SLMC/SWL). Information was collected by retrieving the medical records of female patients who had presented to the hospital with palpable

lumps in the breast between 1 January 2020 and 31 December 2023. The projected sample size of 344 was calculated using the OpenEPI online calculator with a margin of error of 5 and is believed to have a 95 percent confidence level [2]. In total, 392 female patients with palpable breast lesions were enrolled, including those of any age presenting with breast lumps at Sahiwal Teaching Hospital, Sahiwal, Pakistan. Patients in whom an adequate aspirate was obtained. Patients with breast imaging done with reported mass lesions. Exclusion criteria included male patients with breast swellings, Female patients having bleeding disorders, and Female patients having recurrent malignant tumors or who were already undergoing chemo-radiotherapy. After having taken written informed consent, the breast lump was cleaned using aseptic techniques. After palpation and examination of the lump, an aspirate was taken by using 23 and 25-Gauge needles 1.0 to 1.5 inches long, creating negative pressure. Each patient had approx. 6 -10 slides. All aspirated material was placed on slides, spread at the frosted end using a glass spreader to prepare smears, and processed for staining. Giemsa staining of air-dried slides was done to examine cytological characteristics, and three or more slides were fixed using 95 percent alcohol and stained with hematoxylin and eosin (H&E) to estimate the nuclear morphology. A histopathologist/cytopathologist viewed the stained specimens under 20xs and 40x objectives, and results were classified based on the International Academy of Cytology Yokohama System for Reporting Breast FNAC, which included inadequate (C1), benign (C2), atypical (C3), suspicious of malignancy (C4), and malignant (C5) [8]. Patient data, including demographic details, clinical history (age, pain, mobility, duration, and site of lesion), examination findings, and cytological diagnosis, were extracted from archived records using a pretested data collection form. Data analysis through the use of SPSS version 20.0 was conducted. The quantitative variables (age, lesion duration) were presented in the form of mean and standard deviation, and the frequency and percentages were used to describe the qualitative variables (IAC categories). Results obtained with the Shapiro-Wilk test showed that age and duration of lesion were non-normally distributed ($p < 0.05$), and so, wherever possible, non-parametric tests were used (Kruskal-Wallis test). Categorical variables age group, lesion duration, and IAC categories were tested using the Chi-square test with $p < 0.05$ as the level of significance.

RESULTS

Out of 392 female patients presenting with palpable breast lumps, the majority of breast lesions (40.05%) were found in C5; malignant category followed by 26.78% in C2 (benign), 21.93% of lesions in C3 (atypical), and 10.52% in C4

(suspicious for malignancy) categories, Figure 1.

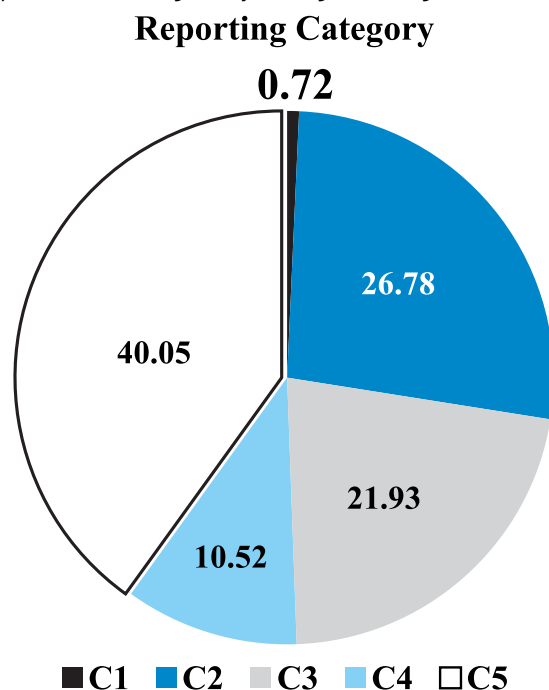


Figure 1: Distribution of Reporting Categories of Breast Lesions according to the IAC Yokohama system (n=392)

C1; insufficient material (Giemsa Stain, 10X) is shown, figure 2.



Figure 2: C1; Insufficient Material (Giemsa Stain, 10X)

C2; Benign (Giemsa stain, 20x) is shown, figure 3.

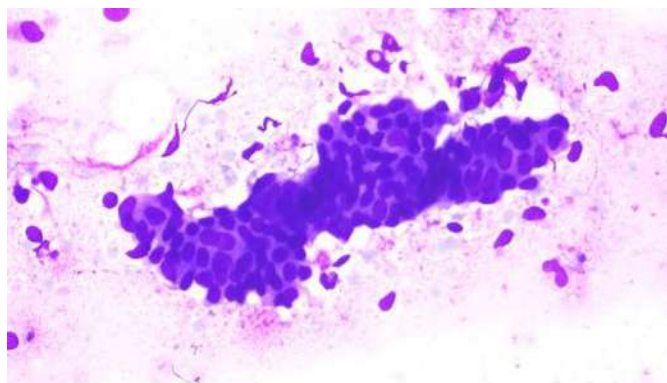


Figure 3: C2; Benign (Giemsa stain, 20x)

C3; Atypical (Giemsa stain, 20x) is shown, figure 4.

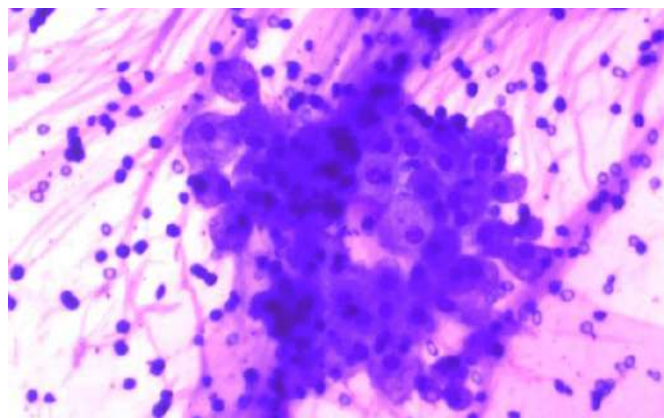


Figure 4: C3; Atypical (Giemsa stain, 20x)

C4; Suspicious of malignancy (Giemsa stain, 20x) is shown, figure 5.

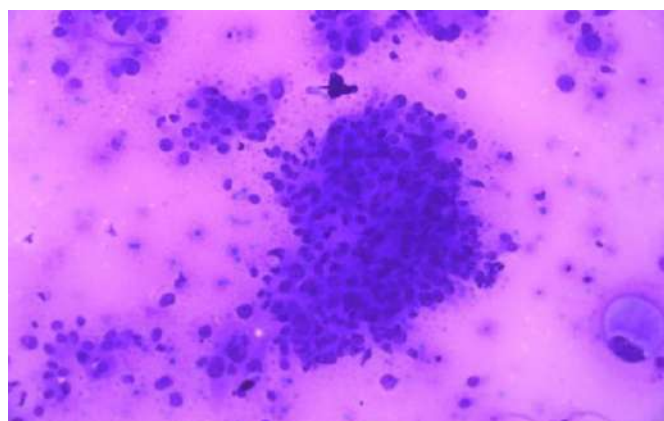


Figure 5: C4; Suspicious of Malignancy (Giemsa stain, 20x)

C5; Malignant (Giemsa stain, 40x) is shown, figure 6.

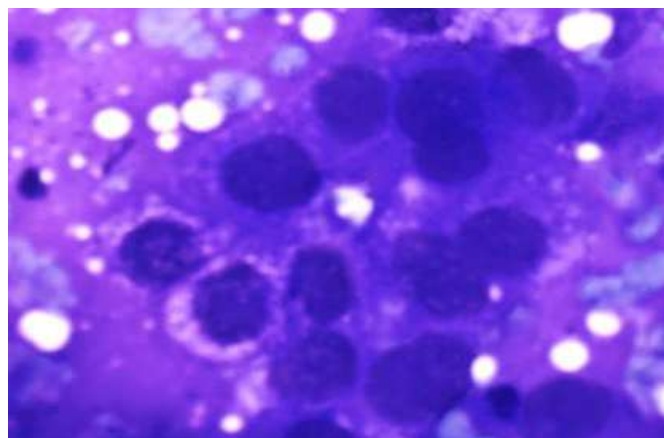


Figure 6: C5; Malignant (Giemsa stain, 40x)

The age group ranged between 15-78 years. Most of the patients (39.84%) were aged 41 and above, and 143 patients (36.48%) were seen in category 5. The reporting categories' correlation with age distribution was analyzed using the Chi-square test and found to be statistically non-significant (p -value=0.712), indicating no strong

association between age group and reporting category, table 1.

Table 1: Age Group of Patients at Presentation of Different Categories of Breast Lumps(n=392)

Reporting Category	Less than 20 Years	21-30 Years	31-40 Years	41-50 Years	51 and Above Years	Total	p-Value
C1	14 (29.17%)	10 (20.83%)	8 (16.67%)	11 (22.91%)	5 (10.42%)	48 (12.24%)	p=> 0.700
C2	12 (17.39%)	18 (26.08%)	11 (15.94%)	21 (30.44%)	7 (10.15%)	69 (17.60%)	
C3	13 (18.57%)	11 (15.71%)	13 (18.58%)	19 (27.14%)	14 (20%)	70 (17.86%)	
C4	12 (19.35%)	15 (24.20%)	10 (16.13%)	16 (25.80%)	9 (14.52%)	62 (15.82%)	
C5	31 (21.68%)	28 (19.58%)	30 (20.98%)	27 (18.88%)	27 (18.88%)	143 (36.48%)	
Total	82 (20.92%)	82 (20.92%)	72 (18.37%)	94 (23.98%)	62 (15.82%)	392	

The duration of the lesion, according to the history of disease for the majority of cases (42), can be seen from 7 to 12 months in the reporting category 5. The post-stratification correlation between the categories of reporting and duration of the lesions was statistically significant (p-value<0.001). Upper outer quadrant (58.3%), upper inner quadrant (33.4%), and central part of the breast (8.3%) were found to accommodate the highest number of patients with breast carcinomas with a lump (Table 2).

Table 2: Frequency of Duration of Lesion Groups with Reporting category(n=392)

Reporting Category	Less than a Month	1-3 Months	4-6 Months	7-12 Months	More than 1 Year	Total	p-Value
C1	4 (4.40)	7 (5.10)	2 (3.05)	8 (8.39)	2 (2.05)	23 (5.87%)	p=<0.001
C2	12 (17.22)	34 (19.97)	20 (11.94)	14 (32.83)	10 (8.04)	90 (22.96%)	
C3	18 (20.47)	20 (23.75)	6 (14.19)	51 (39.03)	12 (9.55)	107 (27.30%)	
C4	13 (11.48)	5 (13.32)	10 (7.96)	28 (21.89)	4 (5.36)	60 (15.30%)	
C5	28 (21.43)	21 (24.86)	14 (14.86)	42 (40.86)	7 (10.00)	112 (28.57%)	
Total	75 (19.13%)	87 (22.19%)	52 (13.27%)	143 (36.48%)	35 (8.93%)	392	

DISCUSSION

Nowadays, one of the leading causes of mortality in females is breast carcinoma all around the world, especially in a developing country, Pakistan. It is increasing at an alarming rate due to late diagnosis and scarce resources. Therefore, early detection is very important, and FNAC is found to be more reliable, cheaper, and quicker in diagnosing palpable breast lesions. In order to plan proper protocol for treatment and management, FNAC plays an important part in distinguishing benign and malignant breast tumors [9]. At present, it is also insisted upon to go for core needle biopsies directly to reach a definitive diagnosis and get receptor studies done. These

include Estrogen and progesterone receptors and HER2 neu, which are done as part of prognostic studies and disease management. But in countries like Pakistan, where the resources are already limited, FNAC and cell preparation combined from the material aspirated can also help in proceeding to definitive management, increasing its diagnostic accuracy and having receptor studies done as well without even requesting tissue biopsies [10]. In our current study, the prevalence of benign and malignant breast lumps was seen by using cytological categories of IAC Yokohama System in addition to post-stratification correlation of reporting categories with age groups as well as durations of lesions, the studies of which are not much available. According to our study of 392 patients, the cytological examination of palpable breast lumps showed 26.78% of patients in the C2 (Benign) and 40.05% in C5 (Malignant) categories which is opposed to the studies done by Sarfraz *et al.* and Rehan *et al.* with 50% and 64.5% of patients in C2 and 30% in C5 categories in both studies respectively [11, 2]. The youngest age group in our study presented with palpable breast lumps was less than 20 11 15 years, which is found to be by the study done by Roheen *et al.* in Medinah Teaching Hospital of Faisalabad [12] and Panwar *et al.* a study conducted in Central India [13]. respectively. Similarly, the age distribution ranged between less than 20 to greater than 50, which also may be seen according to the study done by Rehan *et al.* which was 14-85 years and 14-86 years in another study of Bangladesh done by Rahman *et al.* [2,14]. In another done by Chandawale *et al.* the benign breast lesions were present in a younger demographic age group, and malignant lesions occurred in middle to elderly patients; these findings are similar to the data in our present study [15]. As compared to a study conducted by Shrestha *et al.* and Tripath *et al.* the majority of cases occurred within the age bracket of 31-40 years and 41-50 years [16, 17]. Correlation of reporting of cytological categories compared with duration of lesions is found in a very low number of studies. Based on our findings, most of the breast lesions in C2 (34) were found within 1-3 months and that in C5 (malignant) category took place in 7- 12 months duration but this is not reflected by the study conducted by Umat *et al* where most of the palpable breast lesions in C2 (32 patients) occurred in less than 1 month and that in C5 [13] took less than a year [18]. Breast cancer has emerged as a major health issue, as the rate of its occurrence around the world has shocked people. Hence, early detection has to be the main priority, especially among young women, who are increasingly likely to survive [19]. FNAC has never been perfect in terms of making the right diagnosis of breast disease, as was relatively invasive. The clinical assessment done carefully should make it complement the histopathological

diagnosis in different settings [20].

This study was limited by its single-center design and lack of histopathological correlation for all cytological cases, which may affect diagnostic validation of FNAC categories. Additionally, incomplete availability of clinical follow-up and receptor status data restricted assessment of long-term outcomes and prognostic accuracy. Future studies should include multi-center designs with routine histopathological confirmation and integration of receptor studies to improve diagnostic accuracy and prognostic utility of FNAC in breast lesions.

CONCLUSIONS

Fine-needle aspiration cytology provides an efficient, cost-effective, and accurate means of initially categorizing palpable breast lesions following the standardized IAC classification system. This approach not only enables timely management of treatment but also plays a crucial role in screening programs at breast clinics. This study highlighted that the majority of palpable breast lumps in female patients were malignant (C5), with a significant correlation between lesion duration and reporting category.

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Authors' Contribution

Conceptualization: RAL, MUS

Methodology: QUAT

Formal analysis: SS, FBS

Writing and Drafting: SS, FBS, OW, MUS

Review and Editing: RAL, QUAT, SS, FBS, OW, MUS

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

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Original Article



Comparative Analysis of Endocarditis in Congenital Heart Disease Patients Across Age Groups

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ABSTRACT

Infective endocarditis remains a serious complication in patients with congenital heart disease, yet age-related differences in presentation and outcomes are not well understood. **Objectives:** To evaluate age-stratified clinical characteristics, microbiological profiles, and in-hospital outcomes of infective endocarditis (IE) in patients with congenital heart disease (CHD), with emphasis on diagnostic patterns and mortality predictors. **Methods:** This cross-sectional analytical study was conducted at the Department of Cardiology, Quaid-e-Azam Medical College, Bahawalpur, from March 2024 to March 2025. A total of 113 patients with CHD and definite IE, diagnosed per modified Duke criteria, were enrolled through non-probability consecutive sampling. Patients were stratified into two groups: ≤ 18 years ($n=57$) and >18 years ($n=56$). Data on demographics, clinical variables, blood culture results, inflammatory markers, echocardiographic findings, and in-hospital outcomes were collected. **Results:** Septal defects were significantly more common in children (61.4%) versus adults ($p=0.0288$). Adults exhibited higher mean creatinine (1.21 ± 0.42 mg/dL vs 0.96 ± 0.28 mg/dL, $p=0.032$) and vegetation size (10.4 ± 4.2 mm vs 8.6 ± 2.9 mm, $p=0.031$). In-hospital mortality was 12.4%. Vegetation size >10 mm and prosthetic material presence were significant mortality predictors (adjusted OR=4.23, 95% CI: 1.63-10.99, $p=0.001$; and OR=3.45, 95% CI: 1.19-9.83, $p=0.009$). Blood culture positivity reduced mortality risk (adjusted OR=0.53, 95% CI: 0.22-0.91, $p=0.001$). **Conclusions:** Adult CHD patients with IE presented with more advanced disease and higher mortality risk, especially with prosthetic material and large vegetations.

INTRODUCTION

Endocarditis remains a life-threatening complication among individuals with underlying structural heart diseases, particularly congenital heart disease (CHD), which predisposes patients to abnormal intracardiac flow and endocardial injury [1]. Infective endocarditis (IE), though relatively rare in the general population, carries substantial morbidity and mortality in CHD patients, especially in low-resource settings where diagnostic and therapeutic facilities are limited [2, 3]. In countries like Pakistan, with a high birth prevalence of CHD (reported between 8-12 per 1,000 live births) and inadequate access to early surgical correction or routine follow-up, the risk of

developing endocarditis is markedly increased [4]. Endocarditis in CHD patients exhibits diverse clinical manifestations and outcomes across different age groups [5]. The pathophysiological mechanisms vary by age due to evolving cardiac anatomy, immune response, and exposure to risk factors such as catheterization, dental procedures, or prosthetic materials [6, 7]. Children with cyanotic CHD or septal defects often experience earlier and more aggressive forms of endocarditis, while adults are frequently affected due to long-standing uncorrected anomalies or prosthetic valve complications [8]. In recent years, researchers from wealthy nations have studied the



symptoms, types of IE and common bacteria found in children with CHD [9, 10]. Follow-up treatment is also not good enough for many patients [11, 12]. That's why we need to look into how endocarditis in CHD affects people in Pakistan in terms of their medical history, symptoms and lab findings [13].

This study aimed to compare the clinical presentation, microbiological profile, and echocardiographic findings of infective endocarditis in children versus adults with CHD at a tertiary care center in Pakistan, and assess treatment modalities and short-term outcomes, including complications and in-hospital mortality.

METHODS

The descriptive cross-sectional study was organized at the Department of Cardiology in Quaid-e-Azam Medical College, Bahawalpur, Pakistan, from March 2024 to March 2025. Ethical approval was obtained from the Institutional Review Board of Quaid-e-Azam Medical College, Bahawalpur (Approval number: 2459 /DME/QAMC Bahawalpur). The research included patients diagnosed with IE or CHD and looked at similarities and differences in these patients' characteristics depending on their age. Exclusion criteria encompassed patients with acquired heart diseases without congenital anomalies, those with incomplete medical records, and individuals who declined consent. A sample size of 113 was determined based on established prevalence data and practical considerations. A nationwide case-control study cumulative lifetime incidence of infective endocarditis (IE) of approximately 8.5% among patients with congenital heart disease [14]. This figure was considered a realistic baseline incidence for calculating sample size. Using standard formulas for prevalence studies at a 95% confidence level and a 5% margin of error, the minimum required sample size was estimated to be approximately 120. A slightly lower sample of 113 was selected due to logistical limitations, while still allowing for statistically acceptable subgroup analyses by age and CHD severity. This sample represents the complete set of available cases during the defined timeframe at the study center, ensuring comprehensive data coverage for the research objectives. The diagnosis of congenital heart disease (CHD) was confirmed based on prior echocardiographic reports and clinical documentation available in the patients' medical records. Infective endocarditis (IE) was diagnosed according to the modified Duke criteria, using a combination of clinical, microbiological, and echocardiographic findings. Non-probability consecutive sampling was employed to recruit participants meeting the inclusion criteria. Laboratory investigations included complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and blood cultures. All patients underwent routine laboratory

testing at the time of admission or initial evaluation. Complete blood counts (CBC) were performed using an automated hematology analyzer (e.g., Sysmex XN-Series), which measured hemoglobin levels, total leukocyte count, and platelet count. Erythrocyte sedimentation rate (ESR) was determined by the Westergren method, following standard laboratory protocols. C-reactive protein (CRP) levels were measured using an immunoturbidimetric assay on a fully automated biochemistry analyzer (e.g., Roche Cobas or equivalent). For microbiological diagnosis, blood cultures were collected under sterile conditions from two separate venipuncture sites before the initiation of antibiotic therapy. Samples were inoculated into aerobic and anaerobic culture bottles and incubated in an automated blood culture system (e.g., BACTEC or BacT/ALERT). Positive cultures were further sub-cultured and identified using standard biochemical tests and, where available, automated identification systems such as VITEK 2. Data were entered and analyzed using SPSS version 23.0. Descriptive statistics were calculated for all variables. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using means and standard deviations or medians with interquartile ranges, depending on data distribution. The Chi-square test or Fisher's exact test was used to compare categorical variables between groups (e.g., children vs. adults). For continuous variables, independent-samples t-tests or Mann-Whitney U tests were applied based on normality. A p-value of <0.050 was considered statistically significant.

RESULTS

This study provided a detailed comparative analysis of endocarditis among patients with congenital heart disease across different age groups, yielding several important findings. The study presents the frequency distribution and chi-square test results of categorical variables, including gender, type of congenital heart disease, previous surgery, prosthetic material, and type of infective endocarditis, stratified by age group (≤ 18 years and > 18 years) (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Population by Age Group

Variables	Category	≤ 18 Years (n=57)	> 18 Years (n=56)	Total (n=113)	p- Value	Unadjusted OR (95% CI)
Gender	Male	29	32	61	0.933	1.03 (0.51-2.07)
	Female	28	24	52		Ref
Type of CHD	Septal Defect (VSD/ASD)	35	21	56	0.028	2.56 (1.20-5.47)
	Valve Abnormality	8	16	24		Ref
Previous Surgery	Yes	17	22	39	0.103	0.63 (0.29-1.38)
	No	40	34	74		Ref

Prosthetic Material	Yes	11	16	27	0.756	0.89 (0.38-2.08)
	No	46	40	86		Ref
Type of IE	Native Valve	35	33	68	0.672	1.19 (0.55-2.57)
	Prosthetic Valve	13	14	27		Ref

Chi-square or Fisher's exact test was used for categorical comparisons; unadjusted odds ratios with 95% confidence intervals are reported. A p-value <0.050 was considered statistically significant.

Findings compare the inflammatory markers and microbiological results between patients with positive and negative blood cultures, with Mann-Whitney U test applied for non-normally distributed data. The findings emphasize the importance of early culture sampling before empirical therapy to enhance diagnostic yield (Table 2).

Table 2: Microbiological and Inflammatory Profile by Culture Positivity

Variables	Culture Positive (n=79)	Culture Negative (n=34)	p-Value	Unadjusted OR (95% CI)
Prior Antibiotic Use	21 (26.6%)	23 (67.6%)	0.003	3.41 (1.51-7.68)
CRP >10 mg/L	65 (82.3%)	23 (67.6%)	0.017	2.26 (1.12-4.98)
ESR >30 mm/hr	60 (75.9%)	22 (64.7%)	0.210	1.70 (0.72-3.97)
Organism Identified	Staph (30.4%), Strep (23.9%), Others	-	-	-

Chi-square or Fisher's exact test was used for categorical comparisons; unadjusted odds ratios with 95% confidence intervals are reported. A p-value <0.050 was considered statistically significant.

Results summarize the distribution of key continuous variables such as CRP, ESR, hemoglobin, creatinine, and vegetation size across pediatric and adult age groups (Table 3).

Table 3: Continuous Variable Comparison Between Age Groups

Variables	Age ≤18 Years (Mean ± SD / Median [IQR])	Age >18 Years (Mean ± SD / Median [IQR])	p-Value	Test Used
Vegetation Size	8.6 ± 2.9 mm	10.4 ± 4.2 mm	0.031	t-test
CRP	15.4 (10-21) mg/L	17.2 (12-26) mg/L	0.088	Mann-Whitney U
ESR	39 (25-55) mm/hr	42 (30-67) mm/hr	0.114	Mann-Whitney U
Creatinine	0.96 ± 0.28 mg/dL	1.21 ± 0.42 mg/dL	0.032	t-test
Hemoglobin	10.8 ± 1.9 g/dL	10.2 ± 2.1 g/dL	0.106	t-test

Independent-samples t-test was used for normally distributed variables; Mann-Whitney U test for non-normally distributed variables. A p-value <0.050 was considered statistically significant for all comparisons.

Findings display in-hospital outcomes (discharge, death, transfer, LAMA) and factors associated with mortality using logistic regression. Odds ratios are reported for vegetation size, prosthetic material, and culture status (Table 4).

Table 4: Outcome Analysis and Risk Predictors

Variables	Deaths (n=14)	Survivors (n=99)	p-Value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Vegetation >10 mm	10 (71.4%)	27 (27.3%)	0.001	4.85 (1.91-12.3)	4.23 (1.63-10.99)
Prosthetic Material	7 (50%)	20 (20.2%)	0.009	3.92 (1.36-11.31)	3.45 (1.19-9.83)
Culture Positive	8 (57.1%)	71 (71.7%)	0.001	0.49 (0.18-0.83)	0.53 (0.22-0.91)

Chi-square or Fisher's exact test was used; unadjusted and adjusted odds ratios with 95% confidence intervals are shown. A p-value <0.050 was considered statistically significant.

To enhance the clarity and focus of the results in line with the study's aims, the study summarizes key variables associated with differences in prevalence, outcomes, and clinical characteristics between pediatric and adult patients with congenital or acquired heart disease (Table 5).

Table 5: Summary of Significant Diagnostic Findings and Mortality Predictors

Variables	Group with Higher Prevalence	p-Value	OR (95% CI)	Interpretation
Septal Defects (VSD/ASD)	Pediatric Group (≤18 Years)	0.028	2.56 (1.20-5.47)	Age-related pattern in CHD type
Valve Abnormalities	Adult Group (>18 Years)	-	Ref	More common in adults
Creatinine	Adult Group (>18 Years)	0.032	-	Suggests a more advanced disease
Vegetation Size (>10 mm)	Adult Group, Mortality Cases	0.001	4.23 (1.63-10.99)	Strong independent predictor of mortality
Prosthetic Material	More Frequent in Adults, Deaths	0.009	3.45 (1.19-9.83)	Associated with worse outcomes
Culture Positivity	Protective (More in Survivors)	0.001	0.53 (0.22-0.91)	Early identification is linked with a better prognosis
Prior Antibiotic Use	Higher in Culture -Negative Cases	0.003	3.41 (1.51-7.68)	Associated with lower culture yield

Statistical tests used include chi-square, Fisher's exact test, t-test, Mann-Whitney U, and logistic regression. ORs represent unadjusted or adjusted associations; p-values <0.050 were considered statistically significant.

DISCUSSION

The study presented a comprehensive analysis of infective endocarditis (IE) in patients with congenital heart disease (CHD), stratified by age, within a Pakistani tertiary care context. A strong impact of socioeconomic factors on disease presentation and outcomes was also observed, along with a mortality rate of 12.4%, aligning with global trends [14-16]. The findings of this study align with research conducted in Europe, which emphasizes the importance of obtaining blood cultures before initiating antibiotic therapy [17, 18]. Similar observations have been reported in East Asian studies, where patients with culture-negative endocarditis often had prolonged

empirical antibiotic use before diagnosis, leading to delays and suboptimal treatment choices [19]. The association identified between vegetation size and increased mortality in this study is consistent with previous research from Western cardiac centers, where vegetations larger than 10 mm, particularly in patients with prosthetic valves, were linked to higher complication rates and worse outcomes [20]. Additionally, the protective effect of culture-positive endocarditis noted in our study mirrors patterns seen in multicenter studies from North America, where early identification of the causative organism allowed for more precise antimicrobial therapy and improved clinical outcomes.

This study was limited by its single-center design and relatively small sample size, which may limit the generalizability of the findings to other populations. Additionally, incomplete availability of microbiological data (including prior antibiotic exposure affecting culture results) and lack of long-term follow-up restricted assessment of treatment outcomes and recurrence. Future studies should include multi-center cohorts with standardized early blood culture protocols and long-term follow-up to better evaluate microbiological patterns and outcomes in infective endocarditis associated with congenital heart disease.

CONCLUSIONS

This study identified clear age-related differences in the clinical presentation, management, and outcomes of infective endocarditis (IE) among patients with congenital heart disease (CHD) in Pakistan. Strengthening healthcare infrastructure and awareness at the community level may significantly improve outcomes for CHD patients with IE in low-resource settings.

Authors' Contribution

Conceptualization: MN

Methodology: FUR, MAZ

Formal analysis: US, IA

Writing and Drafting: UM

Review and Editing: MN, FUR, US, UM, MAZ, IA

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

Conflicts of Interest

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Original Article



Clavicular Hook Plate Removal: A Necessity or A Myth?

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ABSTRACT

Timely fixation of fractures of the clavicle or acromioclavicular joint dislocation is rising in popularity vs conservative management. This is primarily due to potential complications, such as impingement, which may result in chronic pain and limited shoulder mobility. **Objectives:** To find the cause and number of hardware removals among clavicular fractures. To assess whether clavicular plates caused any after effects when they were left in. **Methods:** A Total of 156 patients treated by hook plate for either fracture of distal clavicular fracture or treatment of acromioclavicular joint dislocation were enrolled from January 2024 to April 2024 in the Orthopedic Department of Gurki Trust Teaching Hospital. All patients were followed for 12 months postoperatively. Clinical results were gauged using different scores. **Results:** There were 107 male and 49 female. At follow up patients in group I were n=50 (64.5%), while group II had only n=15 (19.2%) patients who underwent hook plate removal. The pain VAS scale had a significant p-value of 0.0035 among both groups. The SST score was statistically significant with a p-value of 0.0026. On the last follow-up visit, the mean VAS, SST, and Constant-Murley scores had insignificant p-values, respectively, in both groups. **Conclusions:** Clavicular fracture or acromioclavicular joint dislocation fixation by using hook plates is a safe and reliable mode of treatment. Patients operated with hook plates for distal clavicular fractures are more comfortable, while those treated for acromioclavicular joint dislocation are keener for its removal.

INTRODUCTION

Clavicle fractures and dislocation of the acromioclavicular joint are relatively common shoulder girdle injuries. The incidence of clavicular fracture is not so common, with 50 fractures per 100,000/ year, with distal clavicle fracture accounting for 18% to 25% of all clavicular fractures [1]. However, sports acromioclavicular (AC) joint dislocation is a relatively common injury and constitutes about half of all the shoulder injuries [2]. Depending on the nature of the injury and the percentage of the soft tissue involved, clavicular fractures can be treated operatively or non-operatively [3]. The adverse events that are increasing in non-operative treatment include symptomatic nonunion or stiffness of the shoulders, but it remains the gold standard in non-displaced or minimally displaced fractures. The operative treatment is considered in the presence of

comorbid neurovascular injury, open fractures or fractures with high risk of displacement with skin perforation, or shoulder girdle fractures with significant crushing. Due to studies showing a greater number of complications, surgeons are supporting prompt and definitive fixation for fracture configurations as compared to the conservative approach, which has previously been quite promising. This operative treatment has substantially gained in popularity in the past decade [4]. Research shows that plate fixation with bone graft is one of the reliable and best methods for clavicular fractures. The internal fixation is so firm that early mobilization can be started [5]. Other methods that can be used are K-wire, coracoclavicular (CC) screw, and tight loop [6]. Other than them, AC joint fixation with pins, clavicular plate, tension band wire, and with the modified



Weaver-Dunn procedure, almost alone and occasionally with fixation using a washer and screw, are mostly adopted. Each alternative has merits and demerits. Similarly, a hook plate is preferred by many people, but there are also advantages and disadvantages of the same [7]. Hook plate denies this kind of rotational movement. Wider hook plates or the right size of hook plate treatment can lead to much better results. The commonest being that it may cause erosion by increasing the pressure of the hook under the body of the acromion [8, 9]. Although the hook plate design is such that it allows free movement at the AC joint, especially during elevation and rotation, it does not interfere with the biomechanics of the AC joint, but it can result in impingement and inflammation [10, 11]. Complications such as osteolysis, calcification have also been documented [12]. Limited data is available internationally on the management of the hook plate of AC joint dislocation and distal clavicle fractures. Moreover, literature shows very few studies have been done in Pakistan comparing acromioclavicular joint dislocation with distal clavicular fracture. This study will also help the attending orthopedic surgeon to redefine timelines for the removal of hook plates and explore more options, weighing the pros and cons. Lastly, the surgeons must educate patients regarding the standard protocols for its removal since they are lost to follow-up, and they feel it is unnecessary. Consequently, they might face complications thereafter [13]. The study was enlightening and eye-opening for patients as well as surgeons. Moreover, the demonstration of such sequels can help surgeons to become more amicable with such modalities of treatment, as they are considered relatively new methods, at least in our locality and regions. Despite various operative techniques for clavicular fractures and acromioclavicular (AC) joint injuries, including hook plate fixation, there is limited local evidence comparing outcomes, complications, and the necessity of hardware removal, particularly in Pakistan where follow-up and standardized management protocols are often inconsistent. This lack of data creates uncertainty regarding optimal timing for implant removal and the long-term effects of retained hardware. This study aimed to find the cause and number of hardware removals among clavicular fractures. To assess whether clavicular plates caused any after effects when they were left in.

METHODS

A prospective cohort study on 156 patients (by consecutive sampling technique) treated by hook plate for either fracture of the distal clavicle or treatment of acromioclavicular joint dislocation in the Orthopedic Department of Ghurki Trust Teaching Hospital, Lahore. The patients were enrolled from January 2024 to April 2024

after taking formal consent and approval from the Institutional Review Board Committee (Ref No. 2024/01/R-46). Patients who had multiple fractures or complications during surgery were excluded. The sample size was calculated by using the following formula, keeping the incidence of acromioclavicular joint injury as 11 % of all shoulder injuries [14] with an error margin of 5%: $n = \frac{N \times E^2}{E^2 + x}$. The total number of patients was divided into 2 groups with an equal number of 78 patients in each. Group I had hook plate fixation for AC joint dislocation, whereas those who got it for distal clavicle fracture were referred to as group II. Statistical analysis was undertaken using SPSS Statistics version 24.0. Quantitative variables, including age of patients, scores from pain visual analogue, simple shoulder test, and Constant-Murley, were presented as mean $\pm$ standard deviation. Qualitative variables, including gender, no of patients who underwent removal of the hook plate and its causes, were presented in the form of frequency and percentages using chi-square test. After finding out the normality of data using the Shapiro-Wilk test, the t-test was applied to determine the p-value, with a value less than 0.05 considered statistically significant. Results were drawn using the simple shoulder test, pain visual analogue scale (VAS) and Constant-Murley scores. The follow-up time of the patients was 12 months after the operation for the study, while the mean follow-up time was 8 months and 19 days.

RESULTS

Hook plate treatment was applied to a total number of 156 adult patients enrolled in the study (78 third-Neer type II-fractures of the distal clavicle and 78 type III acromioclavicular dislocations). Out of the 156 patients, 107 were male and 49 were female, giving the male-female ratio of 2.1:1.9 (Figure 1).

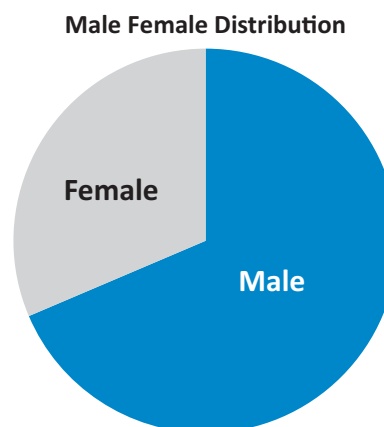


Figure 1: Male and Female Distribution

The mean age of the patients was 40.4 ± 3.45 years. About 67% of the injuries were right-sided, and 33% injuries were on the left side. Union of fractures was seen in 153 (98.56%) of the total patients. The patients were divided into groups,

with group I having hook plate fixation for AC joint dislocation, whereas those who got it for distal clavicle fracture were referred to as group II. Among those in group I, patients who got the hook plate removed were n=50 (64.1%). Whereas in group II, who were treated for third-Neer type II-fractures of the distal clavicle, only n=15 (19.2%) wanted the removal of the hook plate, while 80.8 % had no objection to retaining it. About 85% of the women in group I got plate removal vs 60% of the women in group II.

Table 1: Variables Showing Plate Removal in Group I and Group II

Variables	Group I	Group II
Mean Removal Time (Months)	4.5	7.6
Percentage of Women	85 %	60%
Plate Removal	64.1%	19.2%
3 Months	30.4%	15.1 %
6 Months	22.4%	2.6%
1 Year	11.2%	1.5%

The main causes for removal of the plate were the following: 15(30%) patients had restricted movement of the joint, and 28 (55 %) had pain because of impingement. Mechanical failure was observed in one of the patients (2.5%), and the plate was levered off the bone or eroded the acromion. About 06 patients (12.5%) wanted to get the plates removed due to hypertrophic scar tissue (Table 2).

Table 2: Distribution of Causes of Hook Plate Removal in Group I

Causes	n (%)
Restricted Movement of the Joint	15 (30%)
Pain Due to Impingement	28 (55%)
Mechanical Failure	1 (2.5%)
Hypertrophic Scar Tissue	06 (12.5%)
Total	50 (100%)

The reasons for the removal of the plate in group II were pain due to plate impingement. In 8 patients (33.33 %), and 5 of them (46%) had pain because of impingement. No plate was removed due to a mechanical failure in this group. Only 2 (13.33%) had to get the plates removed due to an increase in scar tissue (Table 3).

Table 3: Distribution of Causes of Hook Plate Removal in Group II

Causes	n (%)
Restricted Movement of A Joint	5 (33.33%)
Pain Due to Impingement	8 (46%)
Mechanical Failure	0 (0%)
Hypertrophic Scar Tissue	2 (13.33%)
Total	15 (100%)

However, on the last follow-up visit, the mean Visual Analogue Score between the two groups was (1.75 ± 1.99 vs. 1.89 ± 1.57), the simple shoulder test had (18.05 ± 1.16 vs. 15.72 ± 1.33), and the Constant-Murley scores were (89.50 ± 5.39 vs. 95.20 ± 5.57). The p-value was found to be insignificant ($p=0.423$, 0.340 , and 0.118) respectively in both groups (Table 4).

Table 4: Last Follow-Up Visit Between Groups

Follow-Up List	Group I (Mean $\pm$ SD)	Group II (Mean $\pm$ SD)	p-value
Visual Analogue Score	1.75 ± 1.99	1.89 ± 1.57	0.423
Simple Shoulder Test	18.05 ± 1.16	15.72 ± 1.33	0.340
Constant-Murley Scores	89.50 ± 5.39	95.20 ± 5.57	0.118

DISCUSSION

Our study had a male-to-female ratio of 2:1, probably because male is often more vulnerable to fractures of the distal clavicle and acromioclavicular joint dislocation due to road traffic accidents and sports injuries. A similar finding was seen in a study by Maliwankul et al. who stated the prominent causes of upper shoulder girdle as traffic accidents and sports injury [15]. The analysis using the VAS, SST and constant Murley scores demonstrated that favourable results were found when the hook plate was used for AC joint disruption or distal clavicular fractures. Martetschlager et al. reported similar results [16]. Our study showed union of fractures in 98.56% of patients. Kashii et al. reported a good union rate with the hook plate for clavicular fracture [17]. Thangaraju et al. and Reska et al. also reported a good union rate of 95% and almost no complications with dislocated distal clavicular fractures (Neer type II) who had interventional surgery with a hook plate [18, 19]. Our study showed that 64.5% patients in group I were keen for removal of the hook plate as compared to group II, in which only 19.2% were interested in removal. Similar results were observed by Oh et al. who stated that patients treated for AC joint dislocation wanted the hardware to be removed [20]. Our study showed that mean VAS, simple shoulder and Constant-Murley scores were insignificant in both groups; however, the VAS and SST had slightly raised values in group I as compared to group II, whereas Constant-Murley scores were higher in group II. This implies that group I had complications like pain and restricted movements due to the hook plate, which eventually led to its removal. On the other hand, patients in group II had better Constant Murley scores, showing better shoulder function despite the hook plate. Similar results Louwerens et al. and Hendrickx et al. showed same results [21, 22]. Thus, patients from group I who underwent plate fixation for AC joint dislocation were more adversely affected as compared to Group II, leading to its higher rate of removal in that group.

This study was limited by its relatively small sample size and single-center design, which may limit the generalizability of the findings. Additionally, short- to mid-term follow-up restricted assessment of long-term functional outcomes and late complications related to hook plate fixation. In our suggestion, hook plates can be removed if they cause effects like impingement. Their use in the older age group should be carefully done as per the given tendency of the

plate to lever off the bone. In other words, it is important to enlighten patients about the importance of implant removal and educate them about its removal.

CONCLUSIONS

Clavicular fracture or acromioclavicular joint dislocation fixation by using hook plates is a safe and reliable mode of treatment. The added advantage of it has a very low secondary surgery for implant removal or revision. Patients operated on with hook plates for distal clavicular fractures are more comfortable with them. On the other hand, those treated with a hook plate for acromioclavicular joint dislocation are more prone to removal due to various medical reasons.

Authors' Contribution

Conceptualization: UR

Methodology: UR, HR

Formal analysis: IA

Writing and Drafting: AW, SI, IA, AR

Review and Editing: UR, AW, SI, IA, HR, AR

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 Platelet-to-Lymphocyte Ratio and Neutrophil-to-Platelet Ratio as Diagnostic Markers in Dengue and Malaria

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ABSTRACT

Dengue fever and malaria are endemic febrile illnesses in South Asia that often present with overlapping clinical features. Accurate differentiation is essential for timely and appropriate treatment. Inflammatory biomarkers such as the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) may aid diagnostic decision-making. **Objectives:** To evaluate the role of PLR and NPR as diagnostic markers in distinguishing dengue fever from malaria in patients presenting with acute febrile illness. **Methods:** A cross-sectional comparative study was conducted at LUMHS, Hyderabad, over 5 months. A total of 116 patients (58 each with confirmed dengue and malaria) were enrolled using non-probability consecutive sampling. Clinical data and complete blood counts were collected. PLR and NPR were calculated and analyzed for diagnostic accuracy using SPSS version 21.0. ROC curve analysis determined optimal cutoffs, sensitivity, and specificity. **Results:** The mean PLR was significantly lower in dengue (109.7 ± 58.2) compared to malaria (131.6 ± 69.3) ($p=0.034$). NPR did not show a significant intergroup difference ($p=0.321$). At a cutoff of 73.89, PLR demonstrated moderate sensitivity (65.52%) and low specificity (36.21%). NPR showed high specificity (100%) but no sensitivity (0%) at a cutoff of 0.0500. **Conclusions:** PLR can be considered a modestly useful marker in differentiating dengue from malaria, while NPR lacks diagnostic sensitivity. These findings suggest that PLR, in conjunction with clinical evaluation, may support early differentiation between the two diseases.

INTRODUCTION

Dengue and malaria are among the most prevalent vector-borne febrile illnesses in tropical and subtropical regions, particularly affecting South Asian countries such as Pakistan. These diseases present with overlapping clinical features such as fever, malaise, and thrombocytopenia, posing significant challenges to differential diagnosis, especially in resource-limited settings [1, 2]. According to the World Health Organization (WHO), dengue cases have increased dramatically worldwide in the last two decades. In 2022 alone, more than 2.8 million dengue cases and over 1,200 deaths were reported from 70 countries, including South Asia [3]. Similarly, the WHO's World Malaria Report 2023 states that there were an estimated 249 million

malaria cases globally in 2022, with Pakistan contributing to over 900,000 confirmed cases, primarily caused by *Plasmodium vivax* and *Plasmodium falciparum* [4]. In Pakistan, both dengue and malaria remain endemic, with seasonal outbreaks peaking during the post-monsoon period. Sindh, Punjab, and Khyber Pakhtunkhwa are the most affected provinces. According to the National Institute of Health (NIH), Islamabad, over 75,000 confirmed dengue cases and 185 deaths were reported nationwide in 2022 [5]. Concurrently, malaria cases surged following the 2022 floods, with Sindh alone recording over 400,000 confirmed infections [6]. Given the clinical similarities and co-circulation of these diseases, there is a pressing need



for rapid, accurate, and cost-effective diagnostic tools, especially in rural and district-level healthcare centers lacking molecular diagnostics. Hematological indices derived from complete blood counts (CBC) have recently gained attention as adjunct markers for the early differentiation of infectious diseases. Among these, the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) have been proposed as accessible and inexpensive inflammatory biomarkers [7, 8]. PLR, calculated as the ratio of platelet count to lymphocyte count, reflects systemic inflammation and immune response. Elevated PLR has been reported in bacterial infections and some parasitic diseases, while decreased PLR is frequently observed in viral infections such as dengue due to profound thrombocytopenia and reactive lymphocytosis [9]. Conversely, NPR, a ratio of neutrophil count to platelet count, has been studied less extensively but may have potential in differentiating etiologies with varying neutrophil responses [10]. Despite growing international literature on PLR and NPR, evidence from Pakistan remains scarce and inconclusive. Few local studies have explored their utility in differentiating dengue from malaria, and none have established population-specific thresholds. Moreover, routine clinical reliance on NS1 antigen, IgM/IgG serology, or malarial smears may not be feasible in peripheral settings with limited lab support. Therefore, evaluating the diagnostic performance of PLR and NPR in a Pakistani cohort is not only timely but crucial for strengthening clinical decision-making and outbreak response strategies [11].

Although dengue and malaria are highly prevalent in Pakistan and share overlapping clinical features, there is limited local evidence on the use of simple hematological markers such as Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) for their early differentiation, particularly in resource-limited settings. This gap restricts timely diagnosis and appropriate management where advanced diagnostic tools are not readily available. This study aims to evaluate the role of PLR and NPR as diagnostic markers in distinguishing dengue fever from malaria in patients presenting with acute febrile illness.

METHODS

This cross-sectional comparative study was conducted at the Diagnostic and Research Laboratory of Liaquat University of Medical and Health Sciences, Hyderabad, in collaboration with the Department of Medicine at Liaquat University Hospital. The study was conducted over a 5-month duration from January 2025 to May 2025. The study was approved by the Ethical Review Committee of Liaquat University of Medical and Health Sciences, Jamshoro (Ref. No. LUMHS/REC/-563). A total of 116 adult patients (58 with

confirmed dengue fever and 58 with confirmed malaria) presenting with acute febrile illness were enrolled through non-probability consecutive sampling. The sample size was calculated using the WHO OpenEpi sample size calculator, based on an estimated odds ratio of 3.26 for the platelet-to-lymphocyte ratio (PLR) when comparing dengue to malaria [12]. Margin of error was 5%, confidence interval was at 90%, and a statistical power of 80% was used to calculate sample size. Patients aged 18 years or older with acute febrile illness of less than seven days and confirmed diagnosis of either dengue (NS1 antigen/IgM/IgG positive) or malaria (peripheral smear or rapid diagnostic test) were included, while those with co-infections, chronic hematologic or autoimmune disorders, or pregnancy were excluded. On arrival, overlapping symptoms commonly noted in both groups were fever, headache, myalgia, nausea, vomiting, and fatigue, with some also presenting with rash, retro-orbital pain, chills, and sweating, making initial differentiation difficult. Dengue was diagnosed based on clinical signs and confirmed by NS1 antigen or IgM/IgG serology, while malaria diagnosis was established using peripheral blood smear or rapid diagnostic test. After obtaining informed consent, demographic and clinical data were collected using a structured questionnaire. Blood samples were collected for complete blood count (CBC), from which the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) were calculated. PLR was determined by dividing platelet count by lymphocyte count and categorized as normal (100-200) or raised (>200). NPR was calculated by dividing neutrophil count by platelet count, with values <10 considered normal and >10 considered raised. Data were analyzed using SPSS version 21.0. Normality of continuous variables (WBC, PLR, and NPR) was assessed using the Shapiro-Wilk test before applying parametric tests. The data was normally distributed. Independent t-tests were used to compare the means of PLR and NPR between the dengue and malaria groups. Chi-square tests were applied to assess differences in proportions for categorical outcomes such as normal vs. raised PLR and NPR. Diagnostic accuracy of PLR and NPR was evaluated using Receiver Operating Characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated. Optimal cutoff thresholds were derived to determine sensitivity and specificity. A p-value of <0.050 was considered statistically significant.

RESULTS

The mean age of participants in both groups was comparable, with 38.8 ± 11.2 years in the dengue group and 39.1 ± 10.7 years in the malaria group. Gender distribution was nearly equal across both groups. Most participants resided in urban areas, with 62.1% in the dengue group and 58.6% in the malaria group. The mean duration of

symptoms was slightly shorter in dengue patients (3.2 ± 1.6 days) compared to malaria patients (3.4 ± 1.8 days). Similarly, the mean hospital stay was marginally shorter in dengue cases (5.6 ± 2.1 days) versus malaria (6.1 ± 2.4 days) (Table 1).

Table 1: Descriptive Demographics and Clinical Features

Variables	Dengue (N=58)	Malaria (N=58)
Mean Age (years)	38.8 $\pm$ 11.2	39.1 $\pm$ 10.7
Gender		
Male	30 (51.7%)	31 (53.4%)
Female	28 (48.3%)	27 (46.6%)
Residence		
Urban	36 (62.1%)	34 (58.6%)
Rural	22 (37.9%)	24 (41.4%)
Mean Duration of Symptoms (days)	3.2 $\pm$ 1.6	3.4 $\pm$ 1.8
Mean Hospital Stay (days)	5.6 $\pm$ 2.1	6.1 $\pm$ 2.4

The mean WBC, neutrophil, lymphocyte, and platelet counts were similar between groups. However, the mean PLR was lower in dengue patients (109.7 ± 58.2) than in malaria patients (131.6 ± 69.3). A raised PLR (>200) was seen in 22.4% of dengue cases and 32.8% of malaria cases. NPR values remained low in both groups, with very few cases crossing the revised cutoff (>0.050), suggesting limited diagnostic utility for this marker (Table 2).

Table 2: Hematological Parameters and Ratios

Parameters	Dengue (N=58)	Malaria (N=58)
Mean WBC (cells/ μ L)	5408 $\pm$ 1472	5523 $\pm$ 1521
Mean Neutrophils	2950 $\pm$ 802	2983 $\pm$ 789
Mean Lymphocytes	1775 $\pm$ 491	1810 $\pm$ 502
Mean Platelet Count	148200 $\pm$ 29650	151800 $\pm$ 31000
Mean PLR	109.7 $\pm$ 58.2	131.6 $\pm$ 69.3
PLR Status		
Normal (100-200)	45 (77.6%)	39 (67.2%)
Raised (>200)	13 (22.4%)	19 (32.8%)
Mean NPR	0.020 $\pm$ 0.006	0.021 $\pm$ 0.007
NPR Status		
Normal (≤ 0.0500)	56 (96.6%)	57 (98.3%)
Raised (> 0.0500)	2 (3.4%)	1 (1.7%)

Statistical analysis revealed a significant difference in PLR between dengue and malaria groups ($p=0.034$), whereas the difference in NPR was not statistically significant ($p=0.321$), indicating PLR as a potentially useful discriminative marker (Table 3).

Table 3: Inferential Statistics for PLR and NPR

Parameters	Mean $\pm$ SD (Dengue)	Mean $\pm$ SD (Malaria)	p-Value
PLR	109.7 $\pm$ 58.2	131.6 $\pm$ 69.3	0.034
NPR	0.020 $\pm$ 0.006	0.021 $\pm$ 0.007	0.321

PLR at a cutoff of 73.89 yielded a sensitivity of 65.52% and specificity of 36.21%, indicating moderate diagnostic

performance. NPR demonstrated 100% specificity but 0% sensitivity, limiting its clinical applicability (Table 4).

Table 4: Diagnostic Accuracy of PLR and NPR

Markers	Optimal Cutoff	Sensitivity	Specificity
PLR	73.89	65.52%	36.21%
NPR	0.0500	0.00%	100.00%

DISCUSSION

The findings demonstrate that PLR was significantly lower in dengue patients compared to those with malaria ($p=0.034$), whereas NPR showed no statistically significant difference between the two groups. ROC analysis revealed that PLR demonstrated modest diagnostic accuracy, with a sensitivity of 65.52% and specificity of 36.21%. Although NPR demonstrated 100% specificity, its sensitivity was 0%, which limits its practical diagnostic utility. Our findings are consistent with studies from other endemic regions. Alsedig et al. reported significantly lower PLR values in dengue compared to malaria and endorsed its potential as a cost-effective diagnostic marker [13]. Iqbal et al. also observed reduced PLR values in dengue patients and suggested its usefulness in early diagnosis in resource-limited settings [14]. Similarly, Previous studies highlighted the utility of PLR in distinguishing viral from bacterial infections, including dengue and malaria, though with only moderate performance, similar to our results. One aspect not explored in our study is whether combining PLR with other hematological indices, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), or red cell indices, could enhance diagnostic accuracy. Recent studies have proposed such integrated approaches to improve the reliability of differentiating febrile illnesses, and future research may benefit from evaluating multi-marker strategies. A multicenter study by Karunaratna et al. [15] suggested that variations in lymphocyte responses, despite similar thrombocytopenia patterns, may explain differences in PLR between dengue and malaria. In contrast, our study did not find significant variation in NPR between the groups, consistent with the findings of Iqbal et al. [16], who also reported poor diagnostic accuracy for NPR in distinguishing viral and parasitic infections. The potential for PLR and NLR to vary with disease severity has been acknowledged in earlier literature. Obeagu [17] highlighted how the diagnostic performance of these markers fluctuates depending on malaria severity and host immune response. However, our study did not assess the relationship of PLR or NPR with clinical severity, which is a limitation. Incorporating this dimension in future studies may provide deeper insights into their prognostic value. Our findings also support the conclusion by Kabir et al. [18], who emphasized that PLR should be integrated with clinical assessment and rapid

diagnostic tests due to its limited specificity. The pathophysiological basis of PLR differences likely relates to dengue's characteristic lymphocytosis and marked thrombocytopenia, whereas malaria typically induces neutrophilia with relatively stable platelet counts [19, 20]. This mechanism explains the PLR shift observed in dengue and the relatively unchanged NPR across both conditions. This study has several limitations. The relatively small sample size and exclusion of pediatric patients may reduce generalizability, especially in endemic regions where children are disproportionately affected. The use of non-probability consecutive sampling further limits the representativeness of the findings. Additionally, reliance on single-time-point blood samples may have reduced diagnostic accuracy, whereas serial PLR measurements could provide greater insight, as suggested by Hossain *et al.* [21]. Finally, the sensitivity and specificity values of both PLR and NPR were relatively low, which reduces their standalone clinical utility.

This study was limited by a relatively small sample size and the exclusion of pediatric patients, which may affect the generalizability of the findings. Additionally, reliance on single time-point measurements and not assessing disease severity may have reduced the diagnostic accuracy of PLR and NPR. Future studies should include larger, multicenter populations with severity stratification and combined hematological markers to improve diagnostic performance.

CONCLUSIONS

In conclusion, PLR appears to be a useful supplementary marker in differentiating dengue from malaria, particularly in resource-limited settings. However, it should not be used in isolation; PLR must be interpreted alongside clinical presentation and serological findings to enhance diagnostic accuracy. NPR, due to its poor sensitivity, showed limited clinical utility. Further large-scale prospective studies are necessary to validate these findings and establish more robust cutoff values for broader clinical application.

Authors' Contribution

Conceptualization: SN

Methodology: SN, IDU, SM, AG, AR

Formal analysis: SN, SK, AR

Writing and Drafting: SN, IDU, SM, AG, SK

Review and Editing: SN, IDU, SM, AG, SK

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 Series



Histopathological and Radiological Findings in Nasolabial Cysts

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ABSTRACT

Nasolabial cysts are relatively rare, non-odontogenic soft tissue cysts that are usually found in the nasolabial fold, just beneath the nasal ala. **Objectives:** To analyse the clinical, histopathological, and radiological features of nasolabial cysts and evaluate their association with symptom duration, cyst size, and bone remodelling. **Methods:** This retrospective case series study included 10 patients diagnosed with nasolabial cysts. Patient data, including age, gender, ethnicity, cyst size, location, and duration of symptoms, were collected. Radiological assessments focused on bone remodelling and scalloping through computed tomography (CT) scans. Histopathological examination of excised cysts assessed the type of epithelial lining. Statistical analysis was performed to evaluate associations between cyst characteristics, symptom duration, and radiological findings, using Pearson's correlation and Chi-square tests. **Results:** The mean age of patients was 44.9 years, with a male predominance (60%). A significant association was found between longer symptom duration and the presence of bone changes on CT ($p=0.03$), and a moderate positive correlation existed between cyst size and symptom duration ($r=0.32$, $p=0.009$). **Conclusions:** It was concluded that nasolabial cysts can lead to bone remodelling when symptoms persist for extended periods. Early diagnosis and treatment are critical in preventing complications. Further research is needed to explore minimally invasive treatment approaches for managing nasolabial cysts.

INTRODUCTION

Nasolabial cysts are relatively rare, non-odontogenic soft tissue cysts that are usually found in the nasolabial fold, just beneath the nasal ala. These cysts are also referred to as nasoalveolar or Klestadt's cysts in some literature. They are different from other common facial cysts because of their origin, which is believed to be from the remnants of the embryonic nasolacrimal duct [1]. Most cases are discovered incidentally, as many patients do not present with obvious symptoms. However, in some instances, individuals may develop visible swelling in the nasolabial region, experience nasal obstruction, or suffer from localized pain and infection. When symptoms do occur, they can be quite uncomfortable and may interfere with

daily activities or lead to cosmetic concerns that affect the patient's overall well-being [2]. In terms of demographic trends, these cysts are seen more often in women, particularly those in their middle age, which suggests a possible hormonal or developmental predisposition. Moreover, studies and clinical observations have shown that nasolabial cysts are more frequently encountered in Asian populations compared to others [1, 3]. Even though these cysts are benign and don't have malignant potential, their anatomical location close to vital facial structures can lead to both aesthetic issues and functional impairments if the cyst enlarges or becomes secondarily infected. From a histopathological point, the nasolabial cysts are usually



lined with pseudostratified columnar epithelium that contains mucus cells called goblet cells. In many cases, it can also be squamous metaplasia, but it does not happen very much [4]. This type of epithelial lining gives support to the theory that it is coming from the nasolacrimal duct. Accurate histology evaluation is very important to distinguish nasolabial cyst from other cyst lesions which also in the same area, like odontogenic or dermoid cyst and other non-odontogenic growths. This difference needs to be avoided to prevent misdiagnosis and help doctors treat correctly. Diagnosis imaging has a big role in detecting and understanding nasolabial cysts. CT scans and MRIs are the main tools doctors use in clinics nowadays to diagnose this case. A CT scan is good for knowing the real size and where exactly the cyst is, also shows if bones near the cyst have changed or been damaged because the cyst has been pressing long time [5]. But MRI is better for soft tissue imaging, and it is good when you want to see how the cyst is touching the other tissues around. Also, it helps to prove the lesion is not an odontogenic one, which helps again in diagnosis [6]. Even now, when better tools for diagnosis and surgery are there, the knowledge in books and articles about nasolabial cyst is still limited. Most time, it is only some case reports or very few case series. Still, there is a big missing part in the study that tells us fully about what is seen in the radiology and histology of these cysts. We need more studies like that to better understand, develop diagnostic methods, and help give better treatment to people. So, this study wants to help by showing a few patients who have a nasolabial cyst. We mainly look at their scan results and tissue exam findings. When we combine this with what we see in real patient cases, the study wants to show a clearer picture of how this cyst behaves, how to find it, and how to manage it. This will help doctors to make diagnoses more correctly and choose better treatment plans for people who have it.

Despite nasolabial cysts being well-described as rare benign lesions, there is limited comprehensive evidence integrating their clinical presentation with radiological and histopathological features, as most existing literature is restricted to isolated case reports and small case series. This lack of consolidated data makes accurate diagnosis challenging and may lead to misclassification with other facial cysts. This study aimed to analyze the clinical, histopathological, and radiological features of nasolabial cysts and evaluate their association with symptom duration, cyst size, and bone remodeling.

METHODS

The purpose of this retrospective case series study was to examine the radiological and histological characteristics of nasolabial cysts. All patients involved in the study gave their informed consent, and the Ethical Consideration was

obtained from IRB # ATMC/IERC/13th (01-2023)/24 of Al-Tibri Medical College and Hospital, Isra University Karachi. The study comprised ten patients who received a nasolabial cyst diagnosis between January 24 and December 24. The following inclusion criteria were used to choose the patients: full radiological data availability, histopathological confirmation of nasolabial cysts, and clinical presentation of swelling in the nasolabial region. The study excluded patients with insufficient medical data and those who had previously undergone surgery for nasolabial cysts. The required sample size is 11 individuals. The patients' medical records were examined to gather information on their age, gender, and ethnicity as well as their clinical presentation, size, and location of cysts, length of symptoms, and modes of therapy. Pathology reports provided the histological data, while computed tomography (CT) scans provided the radiological data. Radiological Evaluation: The size, location, and extent of the cysts, together with any related bone remodeling or scalloping, were evaluated by reviewing the CT scans. Upon independent assessment of the CT scans by two radiologists, disagreements were settled by consensus. Histopathological Analysis: Cyst specimens taken following surgical excision were subjected to a histological investigation. The presence of mucin-secreting cells, pseudostratified columnar epithelium, and any indication of squamous metaplasia was evaluated in the cyst lining. Two pathologists examined each slide separately, and when they disagreed, they came to a consensus. The clinical and demographic features of the patients were compiled using descriptive statistics. The standard deviation (SD) of continuous data, such as the age and size of the cysts, was represented by the mean $\pm$ SD. Frequencies and percentages were used to represent categorical characteristics, such as gender, ethnicity, and histological results. The relationship between the length of symptoms and the existence of bone remodeling on CT scans was assessed using the Kruskal-Wallis test. Statistical significance was attained when the p-value was less than 0.05. Version 22.0 of the SPSS software was used for all statistical analyses.

RESULTS

The results of the study highlight several key findings related to nasolabial cysts. Descriptive statistics showed that the mean age of patients was 44.9 ± 12.1 years, with cysts averaging 2.8 ± 1.1 cm in size and a mean symptom duration of 3.7 ± 2.0 years (Table 1).

Table 1: Descriptive Statistics

Variables	Mean $\pm$ SD
Age (Years)	44.9 ± 12.1
Size of Cyst (cm)	2.8 ± 1.1

Duration of Symptoms (Years)	3.7 ± 2.0

Gender distribution was 60% male and 40% female, with a higher prevalence among the Sindhi ethnic group (50%). CT findings revealed that 50% of the patients had no bone changes, while 40% exhibited scalloping and 30% showed bone remodeling (Table 2).

Table 2: Frequency Distribution

Variables	Categories	Frequency (%)
Gender	Male	6 (60%)
	Female	4 (40%)
Ethnicity	Sindhi	5 (50%)
	Balochi	2 (20%)
	Urdu	3 (30%)
CT Findings	None	5 (50%)
	Scalloping	4 (40%)
	Remodeling	1 (10%)
Histopathology	Pseudostratified Columnar	4 (40%)
	Mucin-Secreting Columnar	3 (30%)
	Double-Layer Columnar and Cuboidal	1 (10%)
	Squamous Metaplasia	2 (20%)

A significant association was found between the duration of symptoms and CT findings ($p=0.030$), with longer symptom durations linked to scalloping or remodeling (Table 3).

Table 3: Association analysis between CT Findings and Duration of Symptoms

CT Findings	Mean Duration of Symptoms (Years)	H-Value	p-Value
None	2.2 ± 0.8	8.21	0.016
Scalloping	4.0 ± 1.2		
Remodeling	5.5 ± 0.9		

Kruskal-Wallis test was applied, $p\text{-value}<0.050$

However, there was no statistically significant difference in age between patients with and without CT changes ($p=0.060$), suggesting that age does not strongly predict bone involvement (Table 4).

Table 4: Relationship between Age Difference Based on CT Findings

CT Findings	Mean Age of Symptoms (Years)	t-Value	p-Value
None	38.6 ± 11.0	2.13	0.060
Scalloping/Remodeling	51.3 ± 9.6		

An independent t-test was applied, $p\text{-value}<0.050$

The correlation between cyst size and duration of symptoms was also significant ($r=0.32$, $p=0.009$), indicating that larger cysts were associated with longer symptom durations. Overall, the findings underscore the importance of early diagnosis and treatment to prevent complications like bone remodeling, particularly in patients with longer-standing cysts (Table 5).

Table 5: Correlation Between Cyst Size and Duration of Symptoms

Variable 1	Variable 2	Correlation Coefficient (r)	p-Value
Cyst Size (cm)	Duration of Symptoms (Years)	0.32	0.009

Pearson correlation coefficient $p\text{-value}<0.050$

DISCUSSION

This study provides a comprehensive analysis of the clinical, radiological, and histopathological features of nasolabial cysts, enhancing the existing understanding of this Rare but significant lesion. Nasolabial cysts are non-odontogenic developmental lesions arising from remnants of the embryonic nasolacrimal duct, typically presenting as a painless swelling in the nasolabial fold. In our cohort, the mean patient age was 44.9 ± 12.1 years, with a slight male predominance (60%). These findings align with previously reported trends, where nasolabial cysts commonly affect middle-aged individuals, particularly in Asian populations [2, 7]. CT imaging revealed maxillary bone remodeling in 30% of patients, scalloping in 40%, and no significant changes in 50%. These findings are in line with prior studies that have shown imaging, particularly CT, to be critical for preoperative planning and for evaluating bone involvement [5, 8]. Study found a moderate correlation ($r=0.32$, $p=0.009$) between cyst size and symptom duration, suggesting that larger cysts tend to be present for longer periods, a trend also noted in recent case reviews [9, 10]. The mean cyst size was 2.8 ± 1.1 cm, with an average symptom duration of 3.7 ± 2.0 years. Almutairi *et al.*, highlighted that nasolabial cysts may remain asymptomatic for extended periods but can gradually enlarge and compromise aesthetics and function [2]. Though a t-test comparing bone change presence with age produced a p-value of 0.06 (not statistically significant), patients with scalloping or remodeling were on average older (51.3 ± 9.6 years) than those without such features (38.6 ± 11.0 years). This implies that while age may play a role, symptom duration and cyst behavior are more likely to influence bone alterations [11, 12]. Overall, the current findings reaffirm that nasolabial cysts generally occur in the middle age group, with a slow-growing course and late onset of symptoms, supporting previous clinical observations [13, 14]. These cysts often go unnoticed until they attain sufficient size to cause visible facial asymmetry or nasal obstruction. Long-standing lesions are more prone to result in osseous changes, which have been previously documented by Yang *et al.*, [11] and Sato *et al.*, [15]. Advanced imaging modalities also play a critical role. While CT offers high-resolution bone detail, MRI, particularly with fat suppression techniques, can better define cystic content and rule out differential diagnoses [16]. In current study, prolonged symptom duration showed a strong correlation with radiological changes—specifically bone scalloping and remodeling on CT scans ($p=0.03$),

underscoring the importance of timely diagnosis and intervention, as emphasized in the systematic review by Sheikh et al., [17]. Histopathologically, all specimens demonstrated a pseudostratified columnar epithelial lining. Mucin cells were observed in 30% of cases, while squamous metaplasia was present in 20%, a pattern that supports earlier findings indicating that chronicity and local inflammation may influence epithelial transformation [18, 19]. Where MRI is unavailable, high-resolution ultrasound is a viable adjunctive diagnostic tool [20]. Histological evaluation remains pivotal in diagnosis, as seen in our study and those by Sheikh et al., and Ramos et al., where mucus-secreting cells and squamous metaplasia were variably present [17, 21]. This epithelial heterogeneity is consistent with the observations made by Ramos et al., and others, who found histologic variability based on the duration and infectious status of the cyst [21]. Early case reports, including Wesley et al., also emphasized similar patterns of long symptom latency and the importance of histological confirmation [22]. Regarding treatment, both sublabial excision and transnasal endoscopic marsupialization remain effective options. Current findings support existing literature suggesting that surgical technique selection should be based on surgeon expertise, lesion accessibility, and patient preference, with low recurrence rates reported for both methods [9, 21]. Moreover, psychological and cosmetic implications, particularly with bilateral or recurrent cysts, highlight the need for prompt surgical intervention [15, 22]. This study is limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings. Additionally, the lack of long-term postoperative follow-up limits assessment of recurrence rates and long-term surgical outcomes. More studies in the future should look at how treatment affects in the long term, and also at using less invasive techniques to manage this cyst.

CONCLUSIONS

It was concluded that even if nasolabial cysts are not very common, they still cause many difficulties in clinical practice. Especially when symptoms last for a long time, this study shows how important early diagnosis and management are to stop complications like bone changes. Findings also suggest that the best way to handle this cyst is using a team approach with imaging, histology, and clinical examination all together.

Authors' Contribution

Conceptualization: VKK, AMN

Methodology: VKK, SMMR, SK, SMAR, SBJ

Formal analysis: VKK, SMAR, SBJ, AMN

Writing and Drafting: SMMR, SK, FI, AMN

Review and Editing: VKK, SMMR, SK, SMAR, SBJ, FI, AMN

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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