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Conclusion should elucidate how the results communicate to the theory presented as the basis of the study and provide a concise explanation of the allegation of the findings.

ACKNOWLEDGEMENT

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Impact of Psychological and Social Determinants on Health

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The World Health Organization defines the Social Determinants of Health (SDH) as "the conditions under which people are born, grow, work, live, and age, as well as the broader set of forces and systems influencing the conditions of daily life". Psychosocial variables and social determinants both have an important role in determining a person's health and well-being. The psychological, social, and cultural dimensions of these issues can have an impact on a person's behavior and health. Stress, education, poverty, social exclusion, discrimination, and violence are a few examples of these psychosocial determinants. These elements can be protective or, on the other hand, raise the risk of physical and mental illness and lower people's quality of life. Social determinants of health are a combination of social, economic, and physical factors. They play a role in determining the patterns of illness, disease, and health that are observed in a population. They establish the circumstances in which people are conceived, develop, live, work, and age. Health and medical care, economic security, social and communal context, local geography and built environment, and education are all examples of social determinants of health. The connection between individuals and their social and physical environments frequently worsens poor health outcomes. Low socioeconomic position, unemployment, strained family ties, and hazardous neighborhoods have been shown in studies to have a significant negative impact on mental health. Additionally, those who suffer from severe psychological disorders are more probable to experience social segregation, poverty, food insecurity and housing uncertainty all of which can decrease quality of life and hamper rehabilitation. Pakistan experienced the largest gain among the SAARC nations between 2013 and 2018, increasing its happiness score by 26 points, and is expected to rank among the top 20 gainers globally in 2020 [2]. However, it lowers to 4.934from 2018-2020 and is ranked 105 out of 149 happiest countries. There could be a number of causes for this downward tendency. The need of the hour is to pinpoint the causes of Pakistan's declining happiness level. These findings would help policymakers get rid of or manage the factors contributing to people's lower levels of happiness. It is improbable to understate the importance of social and psychological factors in determining health. Healthcare systems and politicians may create initiatives that successfully promote well-being, lessen health inequities, and enhance overall health outcomes by understanding and addressing these variables. A healthier and more equal society must be built via comprehensive strategies that incorporate socioeconomic inequities and mental health care. In order to promote a more inclusive and sustainable society, the international community is making great progress towards reaching many Sustainable Development Goals (SDGs). We are covering several SDGs described by United Nations which include: SDG 1, “No Poverty”; SDG 2, "Zero Hunger"; SDG 3, "Good Health and Well-being"; SDG 4, "Quality Education"; SDG 5, "Gender Equality"; SDG 8, "Decent Work and Economic Growth" and SDG 10, "Reduced Inequalities". The elimination of poverty, hunger, and inequality, as well as the promotion of sustainable economic growth, are the top priorities behind these objectives. By achieving these objectives, we can collectively work towards a more sustainable and equitable future in which no one is left behind.

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Original Article

Frequency of Inferior Alveolar Nerve Damage After Open Reduction and Internal Fixation in Mandibular Fractures

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ABSTRACT

One of the most frequent injuries to the maxillofacial region is mandibular fracture. Numerous places experience fractures. The inferior alveolar nerve is often injured as a result of mandibular fractures. **Objective**: To ascertain how frequently patients in the oral and maxillofacial department of the Ayub Teaching Hospital in Abbottabad experienced inferior alveolar nerve injury following open reduction and fixation of a mandibular fracture. **Methods:** This was a Descriptive case series carried out at Oral and Maxillofacial Department, Ayub Teaching Hospital, Abbottabad after approval from the IRB of the institution and CPSP vide number (CPSP/REU/DSG-2018-010-2532). Using the formula to evaluate proportion with absolute precision and the following premises, the sample size was determined to be 96 using the WHO software for sample size computation in health studies: The expected percentage of inferior alveolar nerve injury following fixation in mandibular fracture is 45%, the confidence level is 95%, and the absolute precision is 10%. **Results**: The mean age of participants was 35.81±5.63 years with range from 26 to 45 years. Most common age group was 36-40 years and 41-45 years (n=26, 27.08%) followed by 26-30 years (n=23, 23.96%). There were 70 (72.92%) males and 26 (27.08%) females in the study. Majority (n=88; 91.67%) of the patients were given general anesthesia while the remaining (n=8; 8.33%) received local anesthesia. Perioperative inferior alveolar nerve injury was observed in 56 (58.33%) patients while permanent inferior alveolar nerve injury was diagnosed in 39 (40.63%) patients. **Conclusions**: Damage to inferior alveolar nerve is a frequent problem of open reduction and fixation of mandibular fracture. However, utmost care should be exercised to reduce its occurrence in patients with mandibular fracture.

INTRODUCTION

Mandible being the most prominent bone of the facial skeleton is the most susceptible area of fracture and trauma) [1]. It makes up 79.7% of facial fractures and the frequency of mandibular fracture is 67% in Pakistan [2]. The major factors of mandibular fractures include sports injuries, car accidents, fights etc. [3, 4]. A non-compressive mini plate fixation is the standard treatment because of its low complication rate [5]. Inferior alveolar nerve & lingual nerve are the most injured branches of trigeminal nerve in mandibular fractures [6, 7]. The Surgical reduction and fixation of the fracture results in damage of inferior alveolar nerve leading to sensory disturbances in the lower lip and the chin area, infection disturbed occlusion, impaired wound healing [8, 9]. Inferior alveolar nerve injuries after open reduction and fixation in mandibular fractures is the focus of this study. Fractures positioned amongst the mandibular foramen and mental foramen causes neurosensory variations in inferior alveolar nerve which may be due to the injury or because of open reduction and fixation [10, 11]. Inferior alveolar nerve

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injury is the common problem after surgical reduction and fixation of mandibular fracture [4]. It might be of temporary or permanent in nature affecting the normal routine [12-15]. The main causes of neurosensory changes postoperatively include handling of fracture segments, cutting of tissue, retraction of appliances and closeness of fracture segments with the inferior alveolar nerve [16]. The features that add to the nerve injury include site of the fracture, type of fracture, distance between the fragments, numbers of missing teeth and treatment used for reduction [9]. Patients with inferior nerve injury complain of sensory damage that may manifest as pain, paraesthesia, dysesthesia, hypoesthesia, hyperaesthesia and anaesthesia. Affected drinking, eating, talking abilities and lip biting are the major complains of the patients [1, 2]. The frequency of postoperative nerve damage is 0.6% to 92.3% [1-3, 7, 8]. While the reported frequency of permanent inferior alveolar nerve damage is up to 45% [2]. The study's goal was to ascertain how frequently patients in the oral and maxillofacial department of the Ayub Teaching Hospital in Abbottabad experienced inferior alveolar nerve injury following open reduction and fixation of a mandibular fracture.

METHODS

This was a Descriptive case series carried out at Oral and Maxillofacial Department, Ayub Teaching Hospital (ATH), Abbottabad after approval from the IRB of the institution and CPSP vide number (CPSP/REU/DSG-2018-010-2532). Using the formula to evaluate proportion with absolute precision and the following premises, the sample size was determined to be 96 using the WHO software for sample size computation in health studies: The expected percentage of inferior alveolar nerve injury following fixation in mandibular fracture is 45%, the confidence level is 95%, and the absolute precision is 10%. Patients of both genders aged between 20-50 years and gone under open reduction were involved in the study while Patients reporting with pathological mandibular fracture and those who were not keen to partake were omitted from the study. Well-versed consensus was taken from the patients after fulfilling the inclusion criteria. Data was collected from the Oral and Maxillofacial Surgery, ATH with the help of structured questionnaire via interview. The surgery was performed by an oral and maxillofacial surgeon. General Anaesthesia was given, mucoperiosteal flap was raised. Nerve was identified. Fractured segments reduction and fixation was done as per requirement of the situation. After the completion of surgery the patients were followed after one week, one month and three months of duration. Statistical analysis was performed by using SPSS version 26.0. Quantitative variables like age were described as mean ± standard deviation. Categorical variables like gender, type of anaesthesia, fragment manipulation, presence of preoperative inferior alveolar nerve injury, degree of fracture segment displacement, and type of fixation method were described as frequencies and percentages. Outcome variable was stratified by gender, age groups, fragment manipulation, type of anaesthesia, degree of fracture segment displacement and type of fixation method. Post stratification Chi square test was used at 5% level of significance.

RESULTS

The mean age of participants was 35.81±5.63 years with range from 26 to 45 years. Most common age group was 36-40 years and 41-45 years (n=26, 27.08%) followed by 26-30 years (n=23, 23.96%). There were 70 (72.92%) males and 26 (27.08%) females in the study. Majority (n=88; 91.67%) of the patients were given general anesthesia while the remaining (n=8; 8.33%) received local anesthesia. Fracture segment manipulation was required in 70 (72.92%) patients with fractured mandible while manipulation was not required in the remaining 26 patients. Open reduction and fixation were the mode of fracture fixation in majority (n=86; 89.58%), while closed reduction was required in 10 (10.42%) patients (Table 1).

Table 1: Frequency of gender, type of anesthesia, fragment manipulation, fracture segment displacement, fracture fixation method

Variables	Categories	N (%)
Gender	Male	70 (72.92)
	Female	26 (27.08)
Type of Anesthesia	General Anesthesia	88 (91.67)
	Local Anesthesia	8 (8.33)
Fragment Manipulation	Done	77 (80.21)
	Not Done	19 (19.79)
Fracture segment displacement	Present	70 (72.92)
	Absent	26 (27.08)
Fracture fixation method	Open Reduction & Fixation	86 (89.58)
	Closed Reduction & Fixation	10 (10.42)

Perioperative inferior alveolar nerve injury was observed in 56 (58.33%) patients while permanent inferior alveolar nerve injury was diagnosed in 39 (40.63%) patients (Table 2).

Table 2: Frequency of preoperative and post-surgical inferior alveolar nerve injury

Variables		N (%)
Perioperative IAN Injury	Present	56 (58.33)
	Absent	40 (41.67)
Post-Surgical IAN injury	Present	39 (40.63)
	Absent	57 (59.38)

No statistical association was found between post-surgical inferior alveolar nerve injury with gender (P=.838) and age (P=.286). The detailed statistics are shown in the

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Table 3.

Table 3: Frequency of inferior alveolar nerve injury stratified by gender and age group

Variables		IAN Outcome		p-value
		Yes	No	
		N (%)	N (%)	
Gender	Male	28 (40)	42 (60)	0.286
	Female	11 (42.3)	15 (57.7)	
Age Groups	26-30	7 (30.4)	16 (69.6)	0.838*
	31-35	12 (57.1)	9 (42.9)	
	36-40	9 (34.6)	17 (65.4)	
	41-45	11 (42.3)	15 (57.7)	

*Chi-square test

Similarly the difference for post-surgical inferior alveolar nerve injury among type of anesthesia (p=.851), fragment manipulation (p=.370), degree of fracture segment displacement (p=.793) and fixation method (p=.793) was not statistically significant. The details are shown in Table 4.

Table 4: Frequency of inferior alveolar nerve injury stratified type of anesthesia, fragment manipulation, degree of fracture segment displacement, fixation method

Variables		IAN Outcome		p-value*
		Yes	No	
		N (%)	N (%)	
Type of anesthesia	General	36 (40.9)	52 (59.1)	0.851
	Local	3 (37.5)	5 (62.5)	
Fragment manipulation	Yes	33 (42.9)	44 (57.1)	0.370
	No	6 (31.6)	13 (68.4)	
Degree of fracture segment displacement	Displaced	29 (41.4)	41 (58.6)	0.793
	Un-displaced	10 (38.5)	16 (61.5)	
Fixation Method	Open	36 (41.9)	50 (58.1)	0.793
	Closed	3 (30.0)	7 (70)	

*Chi-square test

DISCUSSION

The frequency of inferior alveolar nerve injury in study participants was 40.63%. A broad range of IAN injury has been reported in literature and it could be due to demographics of the study participants. In general, the occurrence of IAN injury was 33.7% beforehand management and 53.8% after management, according to a study from Singapore. In this investigation, 123 mandibular sides (43 bilateral) from 80 patients were examined. The most common causes of injuries were assault (33.8%), falls (31.3%), car accidents (25.0%), and sports injuries (6.3%). All condylar fractures (13.0%) lacked NSD, and 49.6% of the fractures elaborate the posterior mandible, which bears the IAN. Open reduction and internal fixation (ORIF; 74.8%), closed reduction and fixation (22.0%), and no treatment (3.3%) were the available options for treatment [1]. In dissimilarity, the follow up period for our study was very short and therefore, we were unable to determine recovery of the neurosensory deficit in our study population. In another investigation, the sharp/blunt differentiation method was used to assess the inferior alveolar nerve for neurological deficit following damage. The progression of brain recovery was evaluated over the observation period. This study comprised 52 patients with mandibular fractures affecting the ramus, angle, and body. The likelihood of neural injury to the inferior alveolar nerve was 42.3%; comminuted and displaced linear fractures were related with a higher risk of neural injury to the inferior alveolar nerve and a slower rate of recovery; and 91% of patients had their inferior alveolar nerve function return. Injuries to the inferior alveolar nerve are more common in cases of mandibular fractures affecting the ramus, angle, and body, as well as comminuted and displaced linear fractures [17]. In dissimilarity; we did not determine the mode / type of trauma to mandible and did not determine its relationship with the outcome. In contrast a seven-year retrospective study from China reported that in patients with mandibular fracture, 38 fractures (13%) had a worsened neurosensory status after treatment in areas supplied by IAN or mental nerve (MN) [2]. 209 patients with 293 fractures were examined in this study. Among the lingula and the mental foramen, there were 120 fractures (41%), and there were 173 fractures (59%) distal to the mental foramen. 211 (7%) of the samples had an offset of 5 mm or greater. A significantly significant risk (p 0.05) for postoperative deterioration of IAN/MN feeling was linked in a multivariate model to fracture displacement, operator inexperience, and two plate fixations [18]. In difference; our investigation did not find a statistically significant correlation amongst fracture displacement and IAN damage. Subjects with unilateral mandibular fracture reported within a day after injury were monitored over the course of a year in a prospective cohort study that included sixty patients cared for mandibular fracture. 52 patients (86.7%) were found to have a post-traumatic neurosensory deficit, albeit this number fell to 23.3% over the follow-up period. Angle fracture cases (33.3%) had abnormal postoperative neurosensory ratings that were substantially greater than body fracture cases (11.1%). 90% of body fracture cases had considerable recovery associated to 67% of mandibular angle fracture cases when non-recovered and recovered neurosensory scores were related by fracture location. Neurosensory recovery scores were statistically substantially higher in cases with less than 5mm fracture dislocation (90.6%) than in cases with more than 5mm fracture displacement (59.9%) [17]. In difference; the current study did not find any statistically significant association amongst IAN injury and fracture displacement. We did not take into account the location of mandibular fracture and its association with the outcome in our study population. The probability of IAN injury was 35% in a Lahore-based randomized controlled experiment

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that examined the frequency of inferior alveolar nerve impairment following reduction of open and close mandibular fractures [19]. In 21 patients (35%) with NS deficits or disturbances, 18 (60%) belonged to open reduction, while only three (10%) belonged to closed reduction. In the closed reduction cluster, there were 27 patients (90%) without any NS deficit, however in the open reduction cluster; twelve patients (40%) had an NS defect or disturbance. Researchers used the chi-square test to discover that patients in the closed reduction group had considerably smaller NS deficit than those in the open reduction cluster, with a p-value of 0.000 (0.0001) [20]. Even though in our analysis fewer patients underwent closed reduction, there was no discernible difference between the two fixation strategies in terms of the frequency of IAN injury.

CONCLUSIONS

Damage to inferior alveolar nerve is a frequent problem of open reduction and fixation of mandibular fracture. Utmost care should be exercised to reduce its occurrence in patients with mandibular fracture.

Authors Contribution

Conceptualization: AT
Methodology: AT, ZJ
Formal analysis: ZJ, MA
Writing-review and editing: SK, AJ, SAK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

A Comparative Analysis of Factors Affecting Uncontrolled Asthma among Paediatric Population in Urumqi vs Islamabad

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ABSTRACT

The prevalence of paediatric asthma, a serious worldwide health issue, varies greatly across different geographical areas. Particularly striking contrasts have been found between Islamabad, Pakistan, and Urumqi, China, prompting a comparison of the underlying causes of uncontrolled asthma. **Objective:** To determine and evaluate the variables influencing uncontrolled asthma in children in the populations of Urumqi and Islamabad. **Methods:** A comparative cross-sectional study on children with uncontrolled asthma aged 3 to 18 years old was carried out in Urumqi, China, and Islamabad, Pakistan. Analysis of hospital data were used to evaluate the uncontrolled factors related to patient's demographics, medical history, factors related to asthma control and living conditions and the environment. **Results:** In both cities, the study found important causes of uncontrolled asthma. Poor inhaler technique, raised BMI, environmental triggers such pollen allergies, poorly ventilated homes, and treatment non-compliance were also noted in both populations. In addition, the study indicated that uncontrolled asthma was present in 32% of paediatric patients in Urumqi and 56% of those in Islamabad for a variety of reasons. **Conclusions:** The results underscore the importance of context-specific interventions in managing paediatric asthma. Measures such as improving inhaler techniques, ensuring treatment compliance, healthy BMI and proper ventilation can significantly improve asthma control in paediatric populations of both Urumqi and Islamabad.

INTRODUCTION

The chronic inflammatory condition of the airways known as asthma continues to be a major public health concern on a global scale. Episodes of wheezing, chest tightness, shortness of breath, and coughing are common symptoms of the condition, which is controlled by a complex interaction of hereditary, environmental, and lifestyle variables. Developing nations are particularly affected by the disease's rising prevalence, which places a heavy burden on healthcare systems and the lives of those who are afflicted despite advances in our understanding and treatment [1, 2]. Asthma prevalence and severity are influenced by a variety of variables that varies depending on the region. Asthma occurrence has been linked to genetics, ethnicity, and the calibre of both indoor and outdoor surroundings. Given how much time individuals spend indoors and the possibility for exposure to a range of allergens and irritants, including dust mites, mildew, pet dander, and cigarette smoke, the indoor environment in particular has gained attention recently [3, 4]. Asthma prevalence has increased annually in China, where fast economic development has resulted in major changes to living conditions. These changes have had a considerable negative influence on children's physical health and placed a heavy financial strain on their families [1]. Due to its

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distinct physical and climatic features, Urumqi, the capital of the Xinjiang Uyghur Autonomous Region in northwest China, is a city of great significance. However, recent epidemiological surveys of asthma in children in Urumqi have been scarce, creating a knowledge gap in understanding the current situation and the risk factors contributing to the disease in this region. [5-8]. Children and adolescents are particularly prone to asthma attacks, which can cause them to miss school, require hospitalization, and in severe cases, even lead to death. Despite advancements in asthma management, many pediatric patients continue to suffer from uncontrolled asthma. Good asthma control is the main management goal according to current asthma management guidelines, as this decreases the risk of asthma exacerbations and improves the quality of life. [9]. However, uncontrolled asthma is still highly prevalent (26% in Western Europe) despite the availability of effective asthma treatment [10]. Several factors of uncontrolled asthma in children have been previously described such as age, male gender, maternal education level, exposure to indoor smoking, pet ownership and high use of short-acting ß2-agonists, incorrect inhaler technique, poor adherence to asthma medication and the presence of co-existing diseases. Many children with asthma have co-existing atopic diseases – including food allergy, allergic rhinitis, and atopic dermatitis – or recurrent respiratory tract infections which makes asthma uncontrollable [11-13]. The results of this study would significantly contribute in literature about asthma risk factors in developing countries, which has significant implications for public health planning and policy development. This research was built on a previous study conducted in August 2019, which investigated the prevalence of childhood asthma and indoor environmental risk factors in Urumqi across six districts, encompassing 8153 preschool children [14]. While in Islamabad the prevalence of childhood asthma is reported to be much higher than Urumqi i.e. 31.58% [8]. The current study has extended this research by comparing these findings with the situation in Islamabad, thus providing a broader perspective on the factors influencing asthma control in different geographical contexts.

METHODS

This comparative study was conducted in two cities, Urumqi, China, and Islamabad, Pakistan. The study aimed to investigate uncontrollable factors related to asthma among children aged 3-18 years in these cities. This study utilized data collected from hospital record databases at two major healthcare institutions, namely the First Affiliated Hospital of Xinjiang Medical University in Urumqi, China, and the Pakistan Institute of Medical Sciences in Islamabad, Pakistan. For both sites, the data collection period ran from 1st July 2021, to 31st December, 2022. A controlled period from 1st January to 30th June of 2021 was also taken into account for comparison. The datasets from Urumqi and Islamabad each contained 874 cases, while the dataset from Urumqi had 738 cases. Both in Urumqi, China, and Islamabad, Pakistan, the data gathering procedure was conducted in accordance with the same guidelines to maintain uniformity. Information about children's health status was gathered using a thorough proforma, with an emphasis on asthma symptoms in particular. The proforma contained questions on demographic information, BMI, medical history, history and treatment of allergies, family history of asthma and allergy, the number of follow-ups in the last 6 months, the number of asthma attacks in the last 6 months, the number of hospitalizations due to asthma in the last 12 months, the number of antibiotics used up to 12 months and possible triggering factors for asthma participation, use of corticosteroids, inhaler technique, forced expiratory volume in 1 second (FEV1) at first diagnosis, treatment for asthma, treatment compliance and information on living conditions and the environment like ventilation in house, quality of indoor air, the number of rooms in the house, and the number of people living in one room. Statistical analyses were performed using the SPSS software. Descriptive statistics were used to summarize the characteristics of the study population. The association between potential risk factors and asthma control was evaluated using logistic regression models, adjusting for potential confounders. Differences in asthma control and associated risk factors between the two cities were analyzed using Chi-square tests for categorical variables and t-tests for continuous variables. Ethical approval for the study was obtained from the respective local research ethics committees in both countries. Confidentiality of the participants' information was ensured throughout the study.

RESULTS

There were significant variations between the data of two cities. Data from Urumqi had a higher percentage of boys compared to Islamabad with a higher prevalence of overweight children. Moreover, there were more children in Urumqi with history of allergies, family history of allergies and a higher proportion of children receiving treatment for allergies compared to Islamabad (Table 1).

Table 1: Demographic variables

Variable	URUMQI N (%)	Islamabad N (%)
Age Group		
3-7 years	230 (26.35%)	195 (26.47%)
7-12 years	356 (40.74%)	289 (39.19%)
12-18 years	288 (32.91%).	254 (34.43%)

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Gender		
Boy	392 (44.85%)	431 (58.40%)
Girl	482 (55.15%)	307 (41.60%)
Height (cm)		
Mean ± SD	136.5 ± 12.3	138.2 ± 11.9
Weight (KG)		
Mean ± SD	31.4 ± 6.8	32.1 ± 6.5
BMI		
Mean ± SD	19.9 ± 3.7	17.3 ± 2.6
Underweight	104 (11.91%)	87 (11.79%)
Normal weight	446 (51%)	470 (63.67%)
Overweight	290 (33.2%)	157 (21.29%)
Obesity	34 (3.89%)	24 (3.25%)
Age at The Time of Diagnosis		
Mean ± SD	6.2 ± 2.1	6.4 ± 2.2
Gestational Age of The Child		
Mean ± SD	38.2 ± 1.9)	38.5 ± 1.8
Family History of Asthma		
Yes	502 (57.44%)	262 (35.50%)
No	372 (42.56%)	476 (64.50%)
Presence of Family Members with Asthma		
Yes	663 (75.85%)	173 (23.44%)
No	211 (24.15%)	565 (76.56%)

Medical history of participants shown in table 2.

Table 2: Medical history

Variable	URUMQI N (%)	Islamabad N (%)
History of Allergies		
Yes	562 (64.30%)	237 (32.11%)
No	312 (35.70%)	501 (67.89%)
Family History of Allergies		
Yes	566 (64.75%)	277 (37.53%)
No	308 (35.25%)	461 (62.47%)
Treatment for Allergies		
Yes	589 (67.36%)	179 (24.25%)
No	285 (32.64%)	559 (75.75%)
Number of Follow-Ups in the Last 6 Months		
0	81 (9.27%)	73 (9.89%)
1	205 (23.48%)	181 (24.53%)
2	341 (39.04%)	283 (38.36%)
3 or more	247 (28.21%)	201 (27.22%)
Number of Asthma Attacks in the Last 6 Months		
0	368 (42.10%)	76 (10.29%)
1	179 (20.48%)	193 (26.14%)
2	226 (25.89%)	312 (42.30%)
3 or more	101 (11.54%)	157 (21.27%)
Number of Hospitalizations in the Last 12 Months Due to Asthma		
0	679 (77.75%)	34 (4.61%)
1	134 (15.34%)	583 (78.99%)
2	46 (5.27%)	112 (15.18%)
3 or more	15 (1.72%)	9 (1.22%)
Allergen Test Results		
Positive	612 (70.02%)	295 (39.95%)
Negative	262 (29.98%)	443 (60.05%)
Allergen Test Results		
1	653 (74.71%)	295 (39.95%)
2	221 (25.29%)	262 (35.52%)
3 or more	0	181 (24.53%)
Prevalence of Uncontrolled Asthma		
Uncontrolled Asthma	32%	56%

Regarding factors related to asthma control, Urumqi and Islamabad exhibit differences in the reported triggering factors (Table 3).

Table 3: Factors Related to Asthma Control

Variable	URUMQI N (%)	Islamabad N (%)
Possible Triggering Factors for Asthma Participation		
Tobacco Smoke	234 (26.79%)	209 (28.35%)
Dust/Air Pollution	417 (47.73%)	149 (20.19%)
Flower/Pollen	168 (19.23%)	632 (85.64%)
Strong Odor	112 (12.83%)	95 (12.88%)
Child Exercise	385 (44.09%)	311 (42.16%)
Child Sports	279 (31.95%)	235 (31.86%)
Cold Air / Cold Weather	168 (19.23%)	144 (19.52%)
Medicines	197 (22.55%)	168 (22.77%)
Use of Corticosteroids		
Yes	563 (64.46%)	613 (83.06%)
No	311 (35.54%)	125 (16.94%)
Inhaler Technique		
Adequate	591 (67.62%)	45 (6.10%)
Inadequate	283 (32.38%)	693 (93.90%)
Age at The Time of Diagnosis		
Mean ± SD	78.5 ± 12.4)	77.2 ± 11.8)
Treatment for Asthma		
Yes	657 (75.23%)	558 (75.74%)
No	217 (24.77%)	179 (24.26%)
Treatment Compliance		
Good	721 (82.49%)	268 (36.33%)
Poor	153 (17.51%)	470 (63.67%)

Dust/air pollution is more commonly reported in Urumqi, while flower/pollen is reported more frequently in Islamabad. Furthermore, there are variations in the use of corticosteroids for asthma treatment, with higher usage in Islamabad compared to Urumqi. Moreover, Islamabad has a higher percentage of non-ventilated houses and a slightly higher proportion of houses with poor indoor air quality compared to Urumqi which may contribute to poor asthma control. 70.66% of the participants in Urumqi had good ventilation in their houses in comparison to the Islamabad. Air quality was measured by the presence of withering, discolorations, unpleasant smells in and around the houses. Good air quality was labelled where there was no smell, satisfactory was labelled when there was presence of foul smell occasionally while moderate air quality means presence of smell sometimes (Table 4).

Table 4: Living conditions and the environment

Variable	URUMQI N (%)	Islamabad N (%)
Ventilation in house		
Ventilated	592 (70.66%)	512 (58.64%)
Non-Ventilated	246 (29.35%)	362 (41.36%)

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Indoor Air Quality Index		
Good	195 (22.34%)	162 (21.97%)
Satisfactory	305 (34.91%)	264 (35.80%)
Moderate	237 (27.14%)	199 (26.97%)
Poor	87 (9.97%)	78 (10.57%)
Very Poor	38 (4.35%)	29 (3.93%)
Severe	12 (1.37%)	6 (0.81%)
Number of Rooms in The House		
1 - 3 rooms	642 (73.46%)	476 (64.53%)
4 - 6 rooms	232 (26.54%)	194 (26.25%)
7 or more rooms	0	68 (9.22%)
Number of people living in one room		
1	721 (82.49%)	108 (14.64%)
2	153 (17.51%)	420 (56.91%)
3 or more	0	210 (28.45%)

The table depicts the key factors related to uncontrolled asthma. The chief factor for uncontrolled asthma in Islamabad was reported to be of poor inhaler techniques, followed by Flower/pollen allergies and non-compliance to treatment compared to Urumqi, which has the chief factors of High BMI (Table 5).

Table 5: Factors relating to uncontrolled asthma

Factor	URUMQI (32%)	Islamabad (52%)
Poor Inhaler Techniques	32.38%	93.9%
	(Not Significant)	(p<0.05)
High BMI	37.09%	24.54%
	(Not Significant)	(Not Significant)
Non-Compliance to Treatment	17.51%	63.67%
	(p<0.001)	(p<0.005)
Flower/Pollen Allergy	19.23%	85.64%
	(Not Significant)	(p<0.001)
Poor Ventilation	29.35%	41.36%
	(Not Significant)	(Not Significant)

DISCUSSION

Asthma is a chronic disease that affects a large number of children worldwide [15]. Although it can occur at any age, it is primarily considered a childhood condition, with children being more susceptible than adults [16]. This disease imposes a significant burden on millions of children and their families, and its prevalence is on the rise [17]. While asthma cannot be cured, it can be managed effectively through adherence to a comprehensive medical management plan, including the treatment of coexisting conditions such as rhinitis, and by preventing exposure to environmental triggers [18]. Despite ongoing efforts, the exact reasons for the increasing prevalence of asthma remain unknown. Researchers have explored various factors, both genetic and environmental, in their quest to identify the risk factors associated with asthma. Some confirmed risk factors include a family history of asthma, personal history of allergic rhinitis, exposure to passive smoking during childhood, and living in smaller houses with inadequate ventilation and sunlight [19]. The present study aimed to identify and assess these factors in relation to asthma in 2 different cities i.e. Urumqi and Islamabad, representative of 2 countries China and Pakistan, respectively. In Urumqi, poor inhaler techniques account for 32.38% of asthma cases, while in Islamabad, it is significantly higher at 93.9% which was statistically significant. Such high prevalence of improper use of inhalers in Islamabad, is strongly suggestive of need of inhaler technique education and training for asthma patients as reported by the study conducted by Almomani *et al.*, in Jordan which yielded that only 13.4% of paediatric asthma patients were using inhalers appropriately [20]. Urumqi, high BMI contributes to 37.09% of uncontrolled asthma cases, but it is not statistically significant. Similarly, in Islamabad, high BMI is not a significant factor, accounting for 24.54% of asthma cases. While not significant, it is important to consider weight management as a part of overall asthma management, as obesity can impact respiratory health. The prevalence of obesity has reached epidemic levels in many populations in recent years and has been identified as a risk factor for asthma [21]. Furthermore, overweight and obese individuals tend to experience more severe asthma symptoms compared to those of normal weight [22]. High BMI among children is a modifiable risk factors which can be dealt with targeted interventions that improve asthma control and overall management. Non-compliance to treatment is a significant factor in both Urumqi and Islamabad. In Urumqi, it accounted for 17.51% of asthma cases. While in Islamabad, the non-compliance was reported to be at 63.67%. Low adherence is a significant contributor of poor asthma control which may be addressed through patient education, support systems, and interventions to improve asthma management outcomes [23]. Pollen allergy is reported to be a major cause for both allergic asthma and uncontrolled asthma [24]. In our study, in Urumqi 19.23% of participants identified flower/pollen as a triggering factor for asthma, while in Islamabad, a significantly higher percentage of 85.64% reported the same. Apart from pollen, other triggering factors were also assessed in the study. Other factors such as Tobacco smoke, strong odors, child exercise, child sports, cold air/cold weather, and medicines showed relatively similar prevalence rates between the two cities while dust/air pollution was reported as a triggering factor by a higher proportion of participants in Urumqi (47.73%) compared to Islamabad (20.19%), suggesting that air pollution may be more prevalent in Urumqi and could contribute to asthma exacerbations in that area. Dust/air pollution is reported to be a potent risk factor for respiratory problems [25]. These results highlight the need for targeted interventions to manage allergies and reduce exposure to allergens in both

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cities. The comparison between Urumqi and Islamabad reveals some variations in housing conditions and indoor air quality. Among children with uncontrolled asthma, poor ventilation was found present in 41.36% in Islamabad as compared to 29.35% cases in Urumqi. The differences in housing characteristics can influence indoor air quality and potentially increaring the risk of uncontrolled asthma as reported by Majeed *et al.,* [26]. These findings align with existing literature that details numerous risk factors for uncontrolled asthma and poor symptom control, including treatment adherence, environmental triggers, family history of asthma, and poor inhaler techniques. The high rates of uncontrolled asthma found in Urumqi and Islamabad are concerning. For example, in the United States, about 44% of children with current asthma had uncontrolled asthma from 2018 to 2020 [27]. The higher rates in Islamabad suggest a more significant burden of disease in that city, more likely to be attributed to controllable factors like compliance issues and use of inhaler techniques. Adherence to asthma medication is a critical aspect of controlling the disease. However, medication non-adherence is a significant concern, especially among urban minority patients. [28]. Several risk factors undermine medication adherence in children, including factors like male gender, non-Asian ethnic background, living in a larger household, older age at diagnosis, living in rural areas, and lower socio-economic status [29]. Both unintentional and intentional factors contribute to non-adherence, including lack of parental involvement, lack of access to appropriate medications, improper inhaler technique, child psychological distress, caregiver psychological distress, issues in family functioning, poor child and family understanding of asthma and asthma medications, and a lack of community support [30].

CONCLUSIONS

In both cities, the study found important causes of uncontrolled asthma. Poor inhaler technique, raised BMI, environmental triggers such pollen allergies, poorly ventilated homes, and treatment non-compliance were also noted in both populations. In addition, the study indicated that uncontrolled asthma was present in 32% of paediatric patients in Urumqi and 56% of those in Islamabad for a variety of reasons.

Authors Contribution

Conceptualization: MIA, LR
Methodology: LR
Formal analysis: MIA, YW
Writing-review and editing: YW

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Overweight, Obesity and its Associated Factors among Nurses at Tertiary Care Hospitals Karachi

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ABSTRACT

Overweight and obesity have been identified as considerable health risks worldwide. **Objective:** To identify the prevalence of overweight, and obesity and its association with demographic variables among nurses. **Methods:** A cross-sectional analytical study was conducted at Dr. Ruth KM Pfau Civil Hospital and Dow University Hospital Karachi over a period of six months of periods from March to August 2019. A total of 299 subjects of both genders were approached by the non-probability convenient sampling method. Chi-square test was applied to identify the associated factors. P-value ≤ 0.05 counted as significant. **Results:** Out of 299, half of the study nurses 149 (49.8%) were male. Among 299 participants, 75 (25.1%) of them were overweight or obese. While 13 (4.3%) were underweight and 211 (70.6%) were normal weight. Mean age, working experience, and BMI were found 29.52 ± 8.568, 7.35 ± 6.177, and 23.30 ± 3.148 respectively of the study nurses. Gender (p-value=0.003), educational status (p-value=0.002), and nature of the job (p-value=0.003) of the participants were found statistically significant with BMI. **Conclusions:** Present study concluded that the majority of study participants had normal BMI and a small number of study subjects were found obese. However, a quarter of nurses are recognized as overweight. Moreover, a significant association was established between BMI with gender, the nature of the job, and the education of nurses.

INTRODUCTION

Overweight and obesity is a relatively common health-related problem across the globe and it is persistently raising as a pandemic [1]. It has become a major risk factor for many non-communicable diseases such as cancer, hypertension, diabetes, musculoskeletal disorders, and cardiac diseases [2]. It is established that nearly 40% of the global adult population is overweight or obese [3]. It is disclosed that nurses primarily female nurses who work in night shift tend to be overweight or obese [4]. In Kenya, the rate of overweight and obesity among healthcare workers was 35% and 28.4% [5]. It is established that overeating, stress, anxiety, and inactivity can lead to obesity [6]. Obesity has been recognized as an emerging health issue in both developing and developed countries [7]. World Health

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Organization (WHO) predicted that non-communicable diseases will cause the greatest number of deaths in Southeast Asia and the Western Pacific Region by the year 2020 [8]. The prevalence of obesity was 40.3% reported in India [9]. In Bangladesh, 39% of participants were found overweight [10]. Pakistan is the 9th most obese nation in the world. Moreover, it is documented that around 26% of women in Pakistan suffer from the trouble of obesity while just 19% of the men are obese [11]. For a nurse, it is very necessary to maintain the quality and quantity of healthy life to achieve life's main goal [12]. Therefore, this research was performed to define the prevalence of obesity and its associated factors amongst nurses at Tertiary Care Hospitals, in Karachi.

METHODS

This Cross-sectional analytical study was carried out at Dr. Ruth KM Pfau Civil Hospital Karachi (CHK) and Dow University Hospital (DUH) Karachi. The study was accomplished in six months of periods from March to August 2019. OpenEpi version 3.0 was used to calculate the sample size with the proportion formula. It was calculated by taking 26.4% of the prevalence of overweight and obesity [13], a 95% level of significance, and a 5% margin of error. The calculated sample was 299 subjects of both genders. Subjects were approached by a non-probability convenience sampling method. Both gender male and female nurses, who were registered by Pakistan Nursing Council (PNC) and had one-year working experience were included in the study. Study protocols were approved by the Institutional Review Board of Dow University of Health Sciences, Karachi. Data were entered and analysed by using SPSS version 21.0. Quantitative variables like age, working experience, and BMI were presented with mean ± standard deviation. While, data of qualitative variables such as gender, marital status, religion, educational status, hospital, nature of the job, and shift duty were presented in frequency and percentages. Moreover, the Chi-square test was applied to determine an association between designation, gender, age, working experience, educational status, hospital, religion, marital status, duty shift, and nature of the job with the outcome variable. P-value ≤ 0.05 was considered as significant. Data Collection Tool: Adapted, validated tool was used for data collection. It was adapted from the previously published study conducted by Aryee *et al.*, in Ghana [13]. The written permission of using the questionnaire was granted.

RESULTS

Table 1 disclosed the socio-demographic characteristics of the study participants. In this study, there were 299 nurses, and the majority 272 (91%) of the study participants were staff nurses. Whereas, only 27 (9%) were either head nurses or team leaders of the duty shift. Approximately half of the study nurses 149 (49.8%) were male. Almost half 154 (51.5%) were unmarried. Three fourth 227 (75.9%) of the study subjects were Muslims. Two-thirds of 193 (64.9%) of the participants had an education or diploma in nursing. Out of 299 participants, 75 (25.1%) of them were overweight or obese. While 13 (4.3%) were underweight, and 211 (70.6%), were normal weight. Mean age, working experience, and BMI were found 29.52 ± 8.568, 7.35 ± 6.177, and 23.30 ± 3.148 respectively of the study nurses.

Table 1: Demographic information of the study participants

Demographic factor	N (%)
Designation	
Staff Nurse	272(91)
Head Nurse	21(7)
Other	6(2)
Gender	
Male	149(49.8)
Female	150(50.2)
Marital Status	
Single	154(51.5)
Married	144(48.2)
Divorced	1(0.3)
Religion	
Muslim	227(75.9)
Christian	67(22.4)
Hindu	5(1.7)
Education	
Diploma in Nursing	193(64.5)
BS. Nursing	103(34.4)
MS. Nursing	3(1)
Duty Shift	
Morning	125(41.8)
Evening	108(36.1)
Night	66(22.1)
Hospital	
CHK	165(55.18)
DUH	134(44.82)
Job Nature	
Single	211(70.6)
Double	13(4.3)
Duty with study	75(25.1)
BMI	
Underweight	13(4.3)
Normal	211(70.6)
Overweight	67(22.4)
Obese	8(2.7)
***Age**	29.52±8.568
***Working experience**	7.35±6.177
***BMI**	23.30±3.148
*Presented in form Mean ± SD; SD; Standard deviation	

Figure 1 exhibited the BMI according to gender. The study

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findings unveiled the majority of 114 (38.13%) females had normal BMI while 97 (32.44%) male subjects had normal BMI. Furthermore, 3(1%)males and 10(3.34%)females were found underweight. With respect to overweight, 42 (14.05) and 25(8.36%)were male and female respectively. As for as obesity concern, a rare number of females 1(0.33%) were obese whereas 7(2.34%)males were obese.

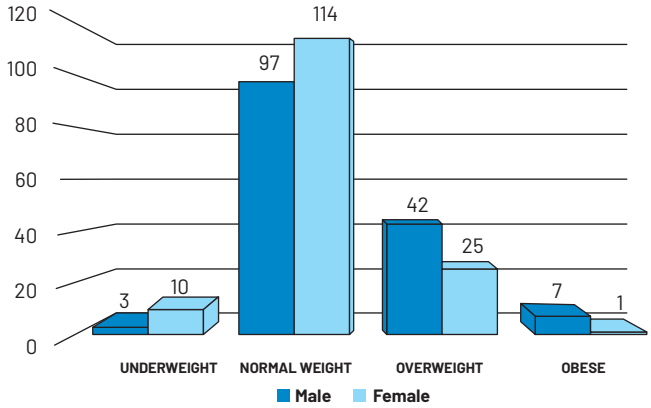

Figure 1: BMI of Study Participant According to Gender

Table 2 revealed the job and lifestyle-related questions from study participants. This table highlighted that the majority of nurses were working 6 days and 36 hours of duty per day. It is also notified that most (69.6%) nurses have time to sit during duty hours. One-third(63.5%)of the study subjects were also involved in some sort of activities like household etc along with duty. While only 77(25.8%) were involved in the exercise. Mostly 122 (40.8%) nurses were using a motorbike as a conveyance for duty, whereas, a few 20 (6.7%) were using the car. A huge number of the participants 254 (84.9%), 263 (88%), and 200 (66.9%) were taking fruits and snacks, always eating breakfast and using supper/dinner respectively.

Table 2: Job and lifestyle characteristics of study participant

Questions	N (%)
How many times do you come to work within a week?	
≤ 5 days	14(4.7)
6 days	268(89.6)
7 days	17(5.70)
Do you normally sit at desk at work?	
Yes	209(69.9)
No	90(30.1)
Average duty hours at work in a week	
<36 hours	4(1.3)
36 hours	236(78.9)
> 36 hours	59(19.7)
Do you work other than scheduled duty hours?	
Yes	80(26.8)
No	219(73.2)
Do you engage in other activities after work, like household, sports etc?	
Yes	190(63.5)
No	109(36.5)
Do you hold any special position at work?	
Yes	67(22.4)
No	232(77.4)
By what means do you come to work?	
By foot	39(13)
By cycle	36(12)
By motorcycle	122(40.8)
By car	20(6.7)
Other	82(27.4)
Do you engage in any form of exercise?	
Yes	77(25.8)
No	222(74.2)
Do you watch TV?	
Yes	126(42.1)
No	173(57.9)
How many times do you eat in a day?	
1	3(1)
2	62(20.8)
3	222(74.2)
4	12(4)
Do you normally take in fruits and snacks?	
Yes	254(84.9)
No	45(15.1)
Do you always take breakfast?	
Yes	263(88)
No	36(12)
Do you always take lunch?	
Yes	274(91.6)
No	25(8.4)
Do you always take supper/dinner?	
Yes	200(66.9)
No	99(33.1)
Do you normally skip meals?	
Yes	114(38.1)
No	185(61.9)

Table 3 showed the association of underweight, normal weight, overweight, and obesity with demographic variables. Gender variable was found statistically significant (p-value=0.003) with BMI. This table exhibits that male nurses are more overweight or obese as compared to female nurses. Moreover, the educational status of the participants was also found significant (p-value=0.002), diploma level nurses were found more obese as compared to a higher level of education. Overweight was also recorded as high in Dow University Hospital as compared to Civil Hospital; this variable is also statistically significant with BMI. Another variable that indicated a significant association with BMI was job nature (p-

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value=0.003). BMI recorded more than 25 in those nurses who were performing single jobs.

Table 3: Association of BMI with demographic variables

Parameter	According to BMI				Chi	p-value
	Underweight	Normal weight	Overweight	Obese		
	N	N	N	N		
Designation						
Staff Nurse	13	192	59	8	3.538	0.739
Head Nurse	0	14	7	0		
Other	0	5	1	0		
Age (year)						
20-30	8	108	30	4	3.102	0.796
31-40	2	44	19	1		
≥41	3	59	18	3		
Gender						
Male	3	97	42	7	13.949	0.003
Female	10	114	25	1		
Marital Status						
Single	8	113	29	3	7.593	0.269
Married	4	98	37	5		
Divorced	0	0	1	0		
Religion						
Muslim	10	157	53	7	8.572	0.199
Christian	3	51	13	0		
Hindu	0	3	1	1		
Education						
Diploma in Nursing	12	140	39	2	20.726	0.199
BS. Nursing	1	70	27	5		
MS. Nursing	0	1	1	1		
Hospital						
CHK	9	126	28	2	10.596	0.014
DUH	4	85	39	6		
Shift						
Morning shift	6	89	27	3	5.412	0.492
Evening shift	7	74	25	2		
Night shift	0	48	15	3		
Job Nature						
Single	8	145	55	3	19.711	0.003
Double	0	6	6	1		
Duty with study	5	60	6	4		
Family member overweight						
Yes	3	62	24	2	3.088	0.798
No	9	141	42	6		
Don't Know	1	8	1	0		

*p-value ≤ 0.05 was considered as significant

DISCUSSION

In the present study, the mean age of study participants was 29.52 ± 8.568 years. The study results are similar to a study performed in Pakistan by Badil et al., reported mean age of the study participant was 27.1 ± 7.412 years [14]. The findings of this study exhibited that more than two-thirds 70.6% of nurses had normal BMI, 4.3% were underweight and 22.4% were overweight which is comparable with the study accomplished in Hong Kong by Wong et al., showed 68% had normal BMI, 11.9% reported underweight and 20.1% were overweight [15]. Moreover, the mean BMI of this study was 23.30 ± 3.148 kg/m2 which is consistent with a study carried out in Korea by Kim et al., revealed a 20.9 ± 2.5 kg/m2 BMI among nurses [16]. In the present study, 2.7% of nurses were obese. On the other hand, the prevalence of obesity was higher compared with nurses in the UK at 25.12% [17], Scotland at 29.4% [18], and South Africa at 51.6% [19]. A very small number of female nurses 1 (0.33%) was found obese in this study. These findings are contradicted by a study conducted in Saudi Arabia that established a large number of female nurses 30.6% were obese [20]. Additionally, the study conducted in Pakistan, showed 13.8% of female nurses were obese [14]. In another study, the author observed 27% of female nurses were obese [21]. Current study findings showed a statistically significant association between BMI with gender (p-value= 0.003). This study's finding is consistent with previous research [22]. In addition, the present study results revealed a significant association between BMI with education (p-value= 0.002) and the nature of the job (p-value =0.003). These study results are comparable with the study conducted in Peru, in which education and the nature of jobs had significant associations [23]. On the other hand, dissimilar results were found in the study conducted in China which unveiled that obesity was significantly associated with female gender, and fast-food intake [24].

CONCLUSIONS

The study concluded the majority of nurses had normal BMI and a small number of study nurses were found obese. However, a quarter of nurses are recognized as overweight. Furthermore, a significant association was established between BMI with gender, the nature of the job, and the education of nurses.

Authors Contribution

Conceptualization: JA
Methodology: R, SA
Formal analysis: FS, YA
Writing-review and editing: JA, B, R, FS, YA, GQ

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Effectiveness of Muscle Energy Technique and Manipulation in The Management of Non-Specific Backache; A Randomized Control Trial

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ABSTRACT

Backache is the most common musculoskeletal impairment in general population worldwide. **Objective:** To evaluate the effectiveness of MET and manipulation in the management of non-specific backache. **Methods:** After getting the REC approval from The Neurocounsel Clinic, Islamabad this study was initiated. Duration of study was 6 months from September 20, 2022 to March 19, 2023. Simple convenient sampling technique was done for data collection and total 30 patients of both genders between age of 18-50 years old who had backache due to mechanical cause or had no comorbidity of any kind. Those patients who had a) Lumber disc disease, b) Spondylolisthesis, c) previous back surgery, d) cardiac disease, e) pain <3 on NPRS, f) Parkinson disease were excluded. Two equals (n=15 each) were formed named as group A (MET) and group B (Manipulation). 3 sessions/ week for 3 weeks were given to each group along with heating pad (10minutes). SPSS version-22 was used for data analysis. NP test was used for between groups analysis and level of significance was kept $p<0.05$. **Results:** The mean age of patients in group A was 28.25 ± 5.53 whereas of group B it was 34.73 ± 10.66. Between groups analysis revealed that there was no significant difference ($p>0.05$) between both groups. **Conclusions:** It was concluded from the result of current study that both MET and manipulation are equally effective in the pain reduction and QoL enhancement in NSLBP sufferers.

INTRODUCTION

Backache, is the most common musculoskeletal impairment in the general population worldwide [1, 2]. More than 85% of individuals experience backache one in their life time. Around 30-39% of this condition resolves within 2-3 weeks and in remaining individuals it becomes a chronic morbidity [3, 4]. According to the global burden of disease (GBD), this is placed at 6th rank among 290 musculoskeletal conditions which results in greater socioeconomic burden [5]. Due to this the level of productivity and work-related activities of the sufferers are impacted the most which in turn affects the healthcare cost in billions of dollars annually [6]. Non-specific low

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back pain (NSLBP) arises due to many reasons such as muscular insufficiency, muscular imbalance, faulty mechanics, postural impairment and inadequate supply of blood to muscles [7, 8]. There are many interventions in literature which are commonly employed to the treatment of this disease. First line management includes the pharmacological intervention in which muscle relaxants (tizanidine), NSAIDs (Ibuprofen), opioids, antidepressants and pregabalin are mainstream drugs which are used [9, 10]. Non-pharmacological intervention includes the physical therapy and bed rest with lifestyle modifications. In physical therapy there are many methods which are used to treat the NSLBP such as manual therapy exercises (MET), manipulation, kinesio tape, braces, stretches and modalities. In modalities most frequently used are SWD, Microwave diathermy, Interferential currents, TENS, NMES, Ultrasound and low laser [11, 12]. One of the effective techniques invented by Fred Mitchell was the muscle energy technique which is used to reduce the muscle spasm (muscle relaxation) and increases the muscle elasticity as well as strength. This technique has two basic components, one is post isometric relaxation and post facilitation stretch. This technique is most commonly used intervention in physical therapy for the management of backache even patient can perform this exercise at home. Many studies have reported that MET is as efficacious as manipulation of lumber spine to enhance the ROM, pain reduction and disability alleviation [13]. Manipulation is another technique which is used by many physiotherapists in the LBP management. Manipulation induces the relaxation of mobility restricted area by unlocking the facet joints of affected region of spine. As a result, relaxation and ROM gain occurs instantly. It has been reported in literature that manipulation has the same effects as of NSAIDs because it as neurophysiological effects [14]. As reported by Salman *et al.*, in their study that MET and manipulation are effective in the management of non-specific neck pain, both of these techniques could be used for the management of non-specific backache as no such intervention in combination had been used in literature for this condition [15]. The purpose of this study was to evaluate the effectiveness of MET and manipulation in the pain management and quality of life enhancement in NSLBP individuals.

METHODS

Current RCT (Randomized control-trail) was initiated after getting approval from the ethical review committee of The Neurocounsel Clinic Islamabad. The duration of this study was six months from 20th September 2022 to 19th March 2023. Sample size was calculated by Epitool which came as 30. Simple convenient sampling technique was done for recruitment of patients in current study. Both genders between age of 18-50 years old were included in this study who had backache due to mechanical cause or had no comorbidity of any kind. Following individuals were excluded from the study a) Lumber disc disease, b) Spondylolisthesis, c) previous back surgery, d) cardiac disease, e) pain <3 on NPRS, f) Parkinson disease. Two equal groups (n=15) were formed. Group A (interventional group) received muscle energy technique along with 10 minutes of heating pad to low back area. In MET, PIR technique was employed at the rate of 6-10 stretches, each stretch was of 15 seconds following a 10 seconds relaxation 2 times a day for 3 session per week for 3 weeks. Group B (Control group) was given lumber spine manipulation (HVLA thrust technique) 1x/day for 3 session per week with a total 3 weeks of interventions along with 10 minutes of heating pad to lower back area. Total 9 sessions were incorporated in this study and results were evaluated on the basis of pain, quality of life and disability by use of following tools, a) NRPS, b) EQ-5D-5L (QoL). Evaluations were done at baseline and after end of study. SPSS version 22.0 was used for the statistical analysis of data. Normality of data were checked by use of Shapiro Wilk test. As our data were non-normally distributed, we used non-parametric tests (Man-Whitney U test) for between groups analysis. $p<0.05$ was kept as level of significance in this study with CI=95%.

RESULTS

Total 30 patients were included in current study. Two equal groups of 15 patients in each group were formulated. The frequency of age between 18-30 years of patients in group A was 09(60.1%) whereas in group this frequency was 06(40.2%). The frequency of participants in between age group of 31-40 & 41-50 years in group A was 04(26.6%) & 02(13.3%) while in group B this frequency of participants was 03(19.6%) and 06(40.2%) respectively. From the perspective of gender distribution, it was found that there were 08(53.3%) of males and 07(46.7%) females in group A while such distribution in group B was found that the frequency of male participants was 06(39.7%) and of females it was 09(60.3%). Marital status distribution in current research showed that there were 05(33.3%) singles in group A while in group B 08(53.3%) patients were single and married patients in group A were 10(66.7%) whereas in group B there were 07(46.7%) (Table 1).

Table 1: Frequency distribution

Variable	Groups	Frequency (%)
Age		
18-28	A	09(60.1)
	B	06(40.2)
31-40	A	04(26.6)
	B	03(19.6)
41-50	A	02(13.3)
	B	06(40.2)

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Gender		
Male	A	08(53.3)
	B	06(39.7)
Female	A	07(46.7)
	B	09(60.3)
Marital Status		
Single	A	05(33.3)
	B	08(53.3)
Married	A	10(66.7)
	B	07(46.7)

The mean age of patients in group A was 28.25 ± 5.53 whereas of group B it was 34.73 ± 10.66. (Table 2).

Table 2: Descriptive Statistics

Variable	Groups	Mean ± SD
Age	A	28.25 ± 5.53
	B	34.73 ± 10.66

As our data were non-normally distributed which was demonstrated by Shapiro wilk test ($p<0.05$), so we performed Man Whitney U test (NPT) to analyze the difference between groups. The descriptive statistics were illustrated in the form of median and interquartile range (IQR). On the basis of numeric pain-rating Scale (NPRS), in group A median and IQR at baseline was 7(3) while in group B it was 6(2). After the 3 weeks of intervention both groups median and IQR values reduced to 2(1) in group A and 3(2) in group B with U-value 110.50 at baseline and 107.50 after 3 weeks of exercises. As, p-value was greater than 0.05 post intervention which revealed that there was no significant difference between both groups and both interventions were equally effective in the reduction of pain on NPRS in non-specific backache individuals (Table 3).

Table 3: Comparison between groups in the basis of NPRS

Intervals	Groups	MD (IQR)	U	p-value
At baseline	A	7(3)	110.50	0.93
	B	6(2)		
After 3 weeks	A	2(1)	107.50	0.82
	B	3(1)		

When comparison was made on the basis of health-related quality of- life in NSLBP participants it was found that there were improvement in both groups as median and IQR score reduced in all parameter of EQ-5D-5L questionnaire except in overall score where increase in score meant there is an improvement so, overall health score median and IQR improved in this parameter. But when analysis was made Man Whitney U test revealed that there was no significant difference between the both type of interventions because $p>0.05$. This showed that both interventions were found to be equally effective in the management of NSLBP sufferers. All median, interquartile ranges, U-values and p-values are depicted in table 4.

Table 4: Comparison between groups on the basis of EQ-5D-5L (QoL)

EQ-5D-5L (QoL)	Groups	MD (IQR)	U	p-value
Pre intervention Mobility	A	4(2)	90.00	0.36
	B	3(2)		
Pre intervention Selfcare	A	4(2)	101.0	0.65
	B	3(1)		
Pre intervention Usual activities	A	5(3)	84.00	0.25
	B	4(2)		
Pre intervention Pain/ Discomfort	A	4(3)	105.0	0.77
	B	4(2)		
Pre intervention Anxiety/ Depression	A	3(2)	103.5	0.71
	B	5(3)		
Post intervention Overall Health status	A	20(15)	74.00	0.10
	B	22(17)		
Post intervention Mobility	A	2(1)	83.50	0.23
	B	2(1)		
Post intervention Selfcare	A	2(0)	68.50	0.06
	B	1(0.5)		
Post intervention Usual activities	A	1(1)	101.50	0.65
	B	1(1)		
Post intervention Pain/ Discomfort	A	2(1)	92.50	0.41
	B	2(0)		
Post intervention Anxiety/ Depression	A	1(0.5)	99.20	0.59
	B	2(1)		
Post intervention Overall Health status	A	85(18)	85.00	0.26
	B	77(10)		

DISCUSSION

This study was conducted to evaluate the effectiveness of muscle energy technique and manipulation in the management of non-specific backache on the basis of pain and quality of life. Tools used for evaluation were NPRD and EQ-5D-5L. It was concluded from the results of this study that both MET and manipulation are equally effective for the management of non-specific backache sufferers. Dhinkara *et al.*, conducted an RCT in which they compared muscle energy technique with conventional strengthening exercises. They formulated two groups same as of our study (n=15 each group). They gave 6 sessions of exercises and evaluated on the basis of Visual analog scale (VAS) and ODI (Oswestry disability index). Post intervention results depicted that MET is somewhat more effective in reducing pain and enhancing functional outcome in backache patients as compared to conventional exercises. Our results of our study are in coherence with this study that MET is an effective intervention in NSLBP management. [16]. Fahmy *et al.*, conducted an RCT to compare the efficacy of MET and MEE (McKenzie extension exercises) in the management of non-specific back pain. They recruited 40 subjects in their study and divided them into two equal groups (n=20 each). Duration of study was of 3 weeks same as of current study and they gave total 12 sessions but, in our study, we gave 9 sessions in total. Their evaluation

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revealed that both interventions are equally effective in reduction of pain severity (VAS) and also function disability (ODI). Our results are positive supported by this study as well [17]. Ghasemi *et al.*, conducted RCT to compare the effectiveness of MET, CST (cranio sacral therapy) and SMT (Standard manual therapy). Tools used for evaluation were VAS & ODI. They gave total 10 session to each group at the rate of 2x/week for 5 weeks. Their results revealed that all interventions were effective in pain & depression reduction, improving the functional disability and in enhancing the quality of life. Our results are in coherence with this study [18]. An RCT was carried out by Patel *et al.*, to evaluate the effectiveness of MET and NTM (Neural tissue mobilization) in NSLBP sufferers. They included 20 patients in their study and divided them into two equal group (n-=10 each). Duration of their study was 2 weeks and they gave total 5 sessions to each group. Evaluation was done by the use of VAS and ODI scale. Results of their study depicted that both interventions are effective in management of LBP pain and improvement of functional outcome and ROM of hamstrings. Our results are positively supported by this study [19]. Sturion *et al.*, conducted a study to evaluate the efficacy of MET and manipulation (HVLA) in the management of backache. They formed two groups (n=5 in each group). They gave 3 sessions at the rate of 1 session/week for three weeks. Their results demonstrated that both interventions are equally effective in the pain reduction (NPRS, MPQ) & disability reduction (RMDQ). Current study used the same intervention as of this study with more treatment sessions than aforementioned study. Our results are in coherence with this study [20]. Licciardone *et al.*, conducted a narrative review to evaluate the efficacy of osteopathic manipulation (HVLA) in the management of NSLBP. Result of their review depicted that spinal manipulation is an effective technique in pain & disability reduction in LBP sufferers. Our results are in coherence with this review [21].,

CONCLUSIONS

It was concluded from the result of current study that both muscle energy technique and manipulation (HVLA) are equally effective in pain reduction and in improving the quality of life of NSLBP sufferers.

Authors Contribution

Conceptualization: SK
Methodology: MT, LM
Formal analysis: SK, SS
Writing-review and editing: SK, SS, MT, LM, AA, NK, MS

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Conflicts of Interest

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Original Article

Optimization and Development of an Efficient 13 X-STRs Multiplex PCR System for Paternity Testing

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ABSTRACT

X-chromosomal short tandem repeats (X-STRs) markers complement autosomal STR identification systems and valuable tools in complex kinship cases. **Objective:** To develop a multiplex PCR system that consists of 13 X-chromosome STR markers, including GATA172D05, DXS8378, DXS6801, DXS6793, DXS6810, DXS7132, GATA31E08, DXS9902, HPRTB, DXS6789, DXS7423, DXS8377, DXS981 and sex-determining locus Amelogenin. **Methods:** Primer sequences of all X-STR markers were acquired from the Genome databases, and the original sequences for HPRTB, DXS6789, DXS7423, DXS8377 and DXS981 were modified to eliminate primer-dimer formation and optimize melting temperatures to increase annealing efficiency. All primer pairs were labelled with fluorescent dyes to support amplification in a multiplex PCR, and the cycling conditions for multiplex PCR were optimized. Alleles for each locus were bi-directionally sequenced to determine the exact repeat size, and alleles generated in multiplex reactions were undistinguishable from alleles produced in a single marker PCR reaction. **Results:** The combined power of discrimination of 13 X-STRs was 2.96 x 10-13 and 2.58 x10^{-8} in females and males, respectively. **Conclusions:** In conclusion, we have developed a 14-plex PCR system that can potentially be used for parentage testing and forensic casework studies.

INTRODUCTION

X-chromosomal short tandem repeats (X-STRs) are an ideal complement to autosomal markers, particularly in cases of complex kinship analysis. This is especially true in cases where paternity is in question and the child in dispute is a girl. X-STRs can accurately determine sisterhood without needing the father's DNA and identify female DNA in mixed stains [1-3]. Many X-STRs have been evaluated for forensic use, and several X-STRs multiplex systems have been developed that can co-amplify three [4], four [5-7], five [8-9], six [10], seven [11], ten [12], 12 markers [13], 13 markers [14]. Multiplex with more markers has recently been developed to obtain a high degree of discrimination [15]. The approach of multiplex analysis of STR markers has proved worthwhile to minimize labor, genetic material and analysis time for casework in DNA testing laboratories [16]. One of the most critical parameters for the multiplex PCR reaction is the designing of primers. Primer pairs must have similar annealing temperatures to be amplified in a single reaction. Additionally, primers' interactions must be examined to avoid the primer-dimer formation that can be reduced by minimizing the excessive regions of complementarily between primers. The stringent initial

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primer selection reduces the costly optimization process of multiplex PCR [17]. Here, we describe developing a 14-plex PCR system with 13 X-chromosomal STR markers and sex-determining locus Amelogenin. Alleles for each locus were bi-directionally sequenced to determine the exact repeat size and repeat structure of the X-STRs. The estimated high combined power of discrimination for 13 X-STRs included in the multiplex strongly advocate for its potential to be used for parentage testing and forensic casework studies.

METHODS

Sequences of all primer-pairs, GATA172D05, DXS8378, DXS6801, DXS6793, DXS6810, DXS7132, GATA31E08, DXS9902, HPRTB, DXS6789, DXS7423, DXS8377 and DXS981 were obtained from the Genome Database (http://www.gdb.org). Primer sequences for GATA172D05, DXS8378, DXS6801, DXS6793, DXS6810, DXS7132, GATA31E08 and DXS9902 were used without modification. In contrast, primer sequences for HPRTB, DXS6789, DXS7423, DXS8377 and DXS981 were modified to avoid primer dimer formation and have similar melting temperatures for all markers included in the multiplex. *Taq* polymerase adds an extra Adenosine nucleotide to the 3′ end of each PCR product, and this PCR product is termed "plus A". In contrast, the PCR product without the additional adenosine is called "minus A" [18]. It has been shown that if the 5′-end of un-labelled primer is a guanosine nucleotide, it favors the plus A form of PCR product and reduces the split peaks that arise for two PCR products differing in length by one base pair [19]. GATA172D05, DXS6810, and DXS9902 sequences were modified by adding guanine to the 5′ end of either forward or reverse primer sequences. The fragment size of all markers labelled with the same fluorescent dye in a multiplex reaction must be sufficiently apart to eliminate overlaps that may lead to ambiguities in assigning the alleles, especially with the discovery of new allele(s). The fragment size for each newly designed primer pair was determined in *silico* PCR as previously described [20]. A multiplex layout schematic of 13 X-STRs and Amelogenin was prepared (Figure 1). All primer pairs were examined for the possible interaction with Autodimer software to avoid primer dimer formation in multiplex PCR as described [21]. Ten cc blood samples were collected from healthy, unrelated individuals of Pakistani descent and genomic DNA was extracted from white blood cells using the phenol-chloroform method described previously [22]. The genomic DNAs were quantified spectrophotometrically, and the multiplex PCR was performed in a 20 µl volume containing 10 ng of genomic DNA, 75 mM Tris HCl, 20 mM $(NH)_2$ SO_4, 2 mM $MgCl_2$, 6.25 µM Spermine Tetra-hydrochloride, 200 µM of each dNTP, and 1

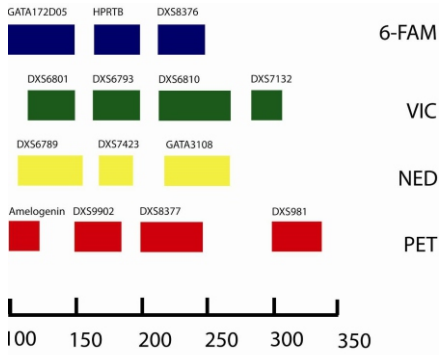

Figure 1: Multiplex layout schematics and dye labelling for 13 X-STRs and Amelogenin (14-plex PCR System)

The primer-pair sequences, their corresponding labelling dyes, fragment lengths and Tm values are shown in Table 1.

unit of *Taq* DNA polymerase. Primer concentrations, magnesium concentrations and annealing temperature were optimized for proper amplification. The optimized primer concentrations are shown in Table 1. The amplification program consisted of pre-amplification at 95 °C for 5 min, followed by 28 cycles of denaturation at 94 °C for 1 min, annealing at 57 °C for 1 min and 30 sec, and extension at 65 °C for 2 min. To terminate the "minus A" amplification sequence, a final extension for 60 min at 60 °C was added. DNA samples were genotyped in a 16-capillary ABI PRISM 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA). The loading mixture was prepared by mixing 1 µl of the multiplex PCR product with 15µl de-ionized Formamide (Applied Biosystems) and 0.2 µl GeneScan 500 LIZ size standard (Applied Biosystems). 9947 A DNA sample from Promega (Promega, Madison, WI) was used as a control [23]. GeneScan Analysis software 3.7 (Applied Biosystems) analyzed the resolved PCR products. Different alleles of all markers were sequenced on purified fragments using male genomic DNA to determine the allele size and the repeat sequence. Purified products were sequenced using the Big Dye Sequencing Kit from Applied Biosystems according to the manufacturer's instructions. The amplification process consisted of a pre-denaturation step at 96°C for 1 min, followed by 35 cycles of denaturation at 96°C for 20 sec, annealing at 50°C for 15 sec, extension at 60°C for 4 min and a final extension at 60 °C for 5 min. Sequencing products were separated on an ABI 3100 Genetic Analyzer (Applied Biosystems) and were assembled with Seq Scape software (Applied Biosystems). Sensitivity studies of 14-plex were performed using serial dilutions (20 ng, 10 ng, 5 ng, 2.5 ng, 1.25 ng, 0.625 ng, 0.312 ng) on female DNA samples to evaluate the minimum quantity required to obtain the complete DNA profile. The higher amount of template DNA (40-150 ng) was also tested for co-amplification of markers in the multiplex to observe if there were any non-specific products. The Gene Scan

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Table 1: Primer sequences, dye labels, fragment lengths, primer concentrations and physical characteristics of the 13 X-STR markers and sex-determining marker amelogenin

Marker	Primer labelled	Dye Labeling	Primer Sequences	Fragment Length	Multiplex PCR (Primer conc. µM)	Melting temperature (Tm) OC
GATA172D05	F	6-FAM	F-tagtggtgatggttgcacag	108-132	0.105	58.1
			R-ataattgaaagcccggattc			58
HPRTB	R	6-FAM	F-gtctctatttccatctctgtctcc	158-186	0.1	57.6
			R-ttctttctctcacccctgtct			58
DXS8378	F	6-FAM	F-cacaggaggtttgacctgtt	191-219	0.11	57.6
			R-aactgagatggtgccactga			59.3
DXS6801	F	VIC	F-agtcatttcctctaacaagtctcc	118-146	0.067	57.2
			R-tccagagagtcagaatcagtagg			57.7
DXS6793	F	VIC	F-acacacgtggtttagaccgt	178-199	0.125	58
			R-ccagagctacgggaatatga			57.8
DXS6810	F	VIC	F-acagaaaacctttgggacc	209-225	0.115	58
			R-cccagccctgaatattatca			57.5
DXS7132	F	VIC	F-agcccattttcataataaatcc	273-301	0.2	56.3
			R-aatcagtgctttctgtactattgg			56.8
DXS6789	F	NED	F-cctcgtgatcatgtaagttgg	121-161	0.06	58.09
			R-cagaaccaataggagatagatgg			56.9
DXS7423	F	NED	F-caacctgccctttatcacc	185-201	0.05	58
			R-ggcctttgtctccagtacc			57.1
GATA31E08	F	NED	F-aggggagaaggctagaatga	224-252	0.07	57.9
			R-cagctgacagagcacagaga			57.9
DXS9902	F	PET	F-tggagtctctgggtgaagag	160-176	0.07	57.9
			R-caggagtatgggatcaccag			57.9
DXS8377	F	PET	F-atctaccacttcatggcttacc	225-276	0.15	57.3
			R-gtgtatttttgctccttcgttc			57.9
DXS981	F	PET	F-cagattcatggttctccttgtg	299-331	0.16	59.6
			R-gaagtcaccaccatattgttcc			58.3
Amelogenin	F	PET	F-ccctgggctctgtaaagaata	ChrX=119 ChrY=125	0.042	58.3
			R-cttgaggccaaccatcag			57.6

Analysis threshold was set at 100 RFU (relative fluorescence units). The per cent stutter was calculated by dividing the peak height at the stutter position by the height of the true allele. We examined 432 DNA samples from five ethnic groups living in Pakistan and calculated the combined power of discrimination of all 13 markers [24]. We constructed an allelic ladder consisting of all variants identified in the Pakistani population. PCR amplification of all markers was performed in a single multiplex reaction, and the resulting peaks of alleles were balanced by mixing the markers in appropriate ratios. The amplification protocol included pre-denaturation at 95°C for 5 min, followed by 35 cycles of denaturing at 94°C for 1 min, annealing at 57°C for 1 min, and extension at 72°C for 1 min. The final extension was performed at 72 °C for 30 min. This mixture of all PCR products was concentrated at 30°C for about 30 min to obtain the locus-specific allelic ladder for all markers. This concentrated PCR product was diluted to a ratio of 1/100. PCR conditions were included using 1 ul of the diluted allelic mixture as a template to re-amplify all alleles. The process consisted of pre-denaturation at 96°C for 2 min, followed by 10 cycles of denaturing at 94°C for 1 min, annealing at 57°C for 1 min, and extension at 70° C for 1 min and 30 sec followed by 28 cycles of denaturing at 90°C for 1 min, annealing at 57°C for 1 min, and extension at 70°C for 1 min and 30 sec. The final extension was done at 60 °C for 30 min.

RESULTS

A multiplex PCR system was developed for paternity testing and complex kinship analyses with 13 X-STR markers and sex-determining locus amelogenin. The 14-plex PCR system included DXS7132, DXS6789, DXS9902, DXS8377, GATA172D05, DXS8378, DXS6810, DXS7423, GATA31E08, DXS981, DXS6793, HPRTB and DXS6801, and all of them were optimized to be amplified in a single multiplex reaction. These 13 X-STR markers were selected based on their genetic localization, high polymorphism and span of the X-chromosome representing all the 4-linkage groups categorized previously by Szibor R. and his co-workers [3].

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The markers used in this study were spaced sufficiently apart on the X chromosome to minimize linkage disequilibrium (LD). The analysis revealed no indication of LD between the 13 markers [24]. As a result, all markers investigated in this study have been identified as independent markers suitable for use in forensic practice. An example of a 14-plex assay showing the female DNA profile is in Figure 2.

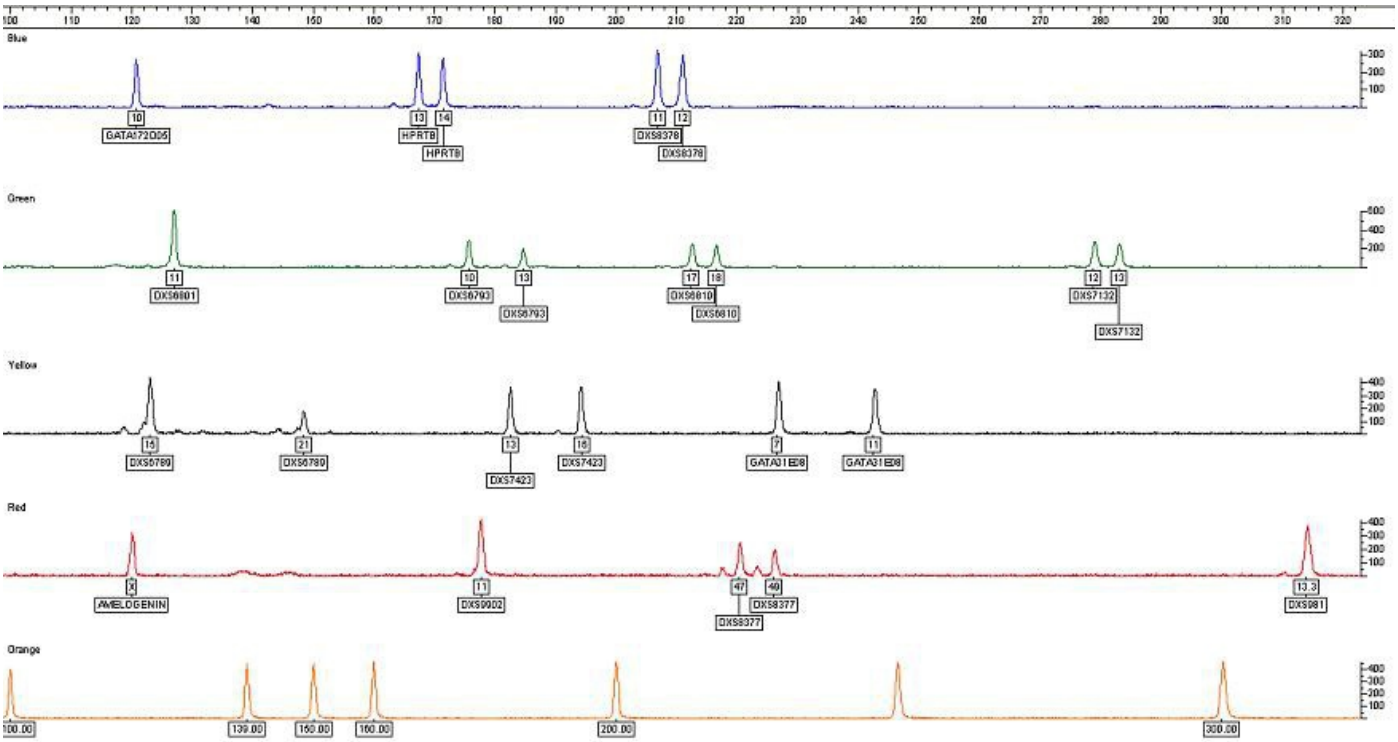

Figure 2: The DNA profile of a female generated using a 14 plex X-STR multiplex system developed during the course of this study

The formation of primer-dimer is a critical parameter, especially in multiplex amplification. All primer pairs were analysed by Auto-dimer software to eliminate primer dimers, and any primer pairs that exhibited an alignment score of 8 or greater were redesigned to obtain optimal primer pairs. Similarly, melting temperatures (Tm) is also another critical parameter for optimal amplification, and 5 X-STR markers HPRTB, DXS6789, DXS7423, DXS8377 and DXS981 were redesigned for Tm values in a small range (56.3-59.6°C). The primer (Tm) values and primer sequences are shown in Table 1. Finally, the primer annealing specificity to the target region is an equally important parameter. All primer pairs were examined with BLAST algorithms. Only those primer pairs were selected that showed specific binding to target regions. Smaller products provide more advantages than their larger counterparts for optimizing the analysis of degraded DNA [25]. Therefore, the total length of the amplified fragments in the multiplex was set at a maximum of 325 base pairs. We examined 432 DNA samples from five ethnic groups of the Pakistan population, and their profiles in multiplex reactions were similar to profiles obtained in PCR with single X-STR markers [24]. All markers' amplification was balanced by empirically varying the number of primers. DXS6801, DXS6789 and DXS9902 of multiplex PCR system showed preferential amplification due to their smaller product size, as reported previously [26]. Therefore, the concentration of primers of these three markers was reduced to approximately half to obtain balanced peaks in the DNA profile (Table 1). The markers labelled with NED dye (DXS7423, GATA31E08) also resulted in higher amplification and thus, the primers were used in low concentration to obtain a balanced DNA profile, as shown in Table 1. We examined a range of template DNA concentrations in our 14-plex system and obtained optimized results with 1-2 ng template DNA when used in 28 cycles of PCR. Amplification with 1-2 ng template DNA produced >100 RFU threshold, as mentioned in previous studies for the Y-STR "megaplex" system [27], whereas low input of template DNA amounts (< 1 ng) resulted in more variable results and partial profiles. Moreover, markers with considerable fragment lengths (DXS7132, DXS981) started dropping at a low amount of template DNA (< 1 ng), consistent with previous reports [28, 29]. On the other hand, nonspecific products were observed with a higher amount of template DNA (40-150 ng), particularly in the markers labelled with VIC and NED dyes, consistent with previous reports [27]. An allelic ladder is a laboratory-constructed model that

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contains the most frequent alleles for a particular short tandem repeat (STR) found in a human population [30]. It controls the size (migration) variations due to temperature fluctuations during electrophoresis [31]. We constructed an allelic ladder that includes all the common alleles of the 13 X-STRs identified in the Pakistani population, except for some rare alleles, as recommended in the literature [31]. In male subjects, the PCR product was sequenced to determine the exact size of the allele and to repeat the sequence. Ladder alleles were placed between rare alleles of adjacent markers with no overlapping. A minimum difference of 8 base pairs between two adjacent markers was also maintained (Table 1). However, there was an exception of difference between rare alleles of marker HPRTB and DXS8378 (5-bp) in the 6-FAM dye channel, but it was according to the recommendation of IFSH [32]. Therefore, overlapping between the multiplex markers was only observed in some populations even after discovering three new alleles in marker DXS6793 and two in marker DXS981 (Table 2) [24]. The Allelic ladder consisted of 102 alleles for 13 X-STRs alleles, as shown in Figure 3 and listed in Table 2.

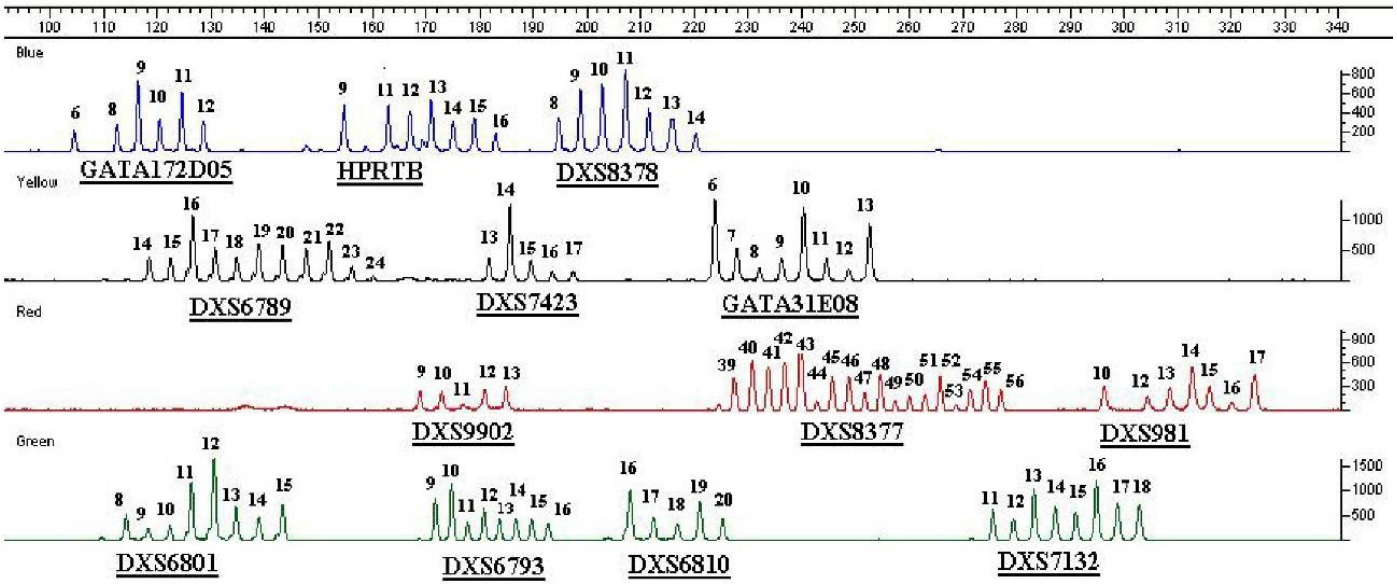

Figure 3: Allelic ladder with alleles from 13 X-STR markers. The development of the Allelic ladder is described in methods and materials.

Table 2: Alleles of all 13 X-STR markers combined to develop an Allelic ladder

Locus	Alleles included in allelic ladder
GATA172D05	6,8,9,10,11,12
HPRTB	9,11,12,13,14,15,16
DXS8378	8,9,10,11,12,13,14
DXS6801	8,9,10,11,12,13,14,15
DXS6793	9,10,11,12,13,14,15,16
DXS6810	16,17,18,19,20
DXS7132	11,12,13,14,15,16,17,18
DXS6789	14,15,16,17,18,19,20,21,22,23
DXS7423	13,14,15,16,17
GATA31E08	6,7,8,9,10,11,12,13
DXS9902	9,10,11,12,13
DXS8377	39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56
DXS981	10,12,13,14,15,16,17

Stutter for tetra-nucleotide repeat markers has been reported at approximately <10% of the central peak, and the amount of stutter observed for STR marker was inversely correlated with the length of the core repeat unit [33]. Therefore, the stutter is always higher with dinucleotide repeats but to a lesser extent with tri- and tetra-nucleotide repeat markers [34]. These results were further confirmed in our analyses as the stutter peaks for DXS7132 and DXS981 were negligible (<10%) [13, 35]. In contrast, the stutter products with tri-nucleotide repeat marker DXS8377 were intensive (up to 27%), consistent with previous reports [4, 36]. Another tri repeat marker, DXS6793, also produced up to 13% of stutter product, which was higher than stutter product (up to 10%) for tetra repeat markers (DXS7132 and DXS981). However, typing the samples was easy due to stutter peaks at all the markers, including DXS8377. This parameter should be considered during the mixture analysis because it has been proven essential to distinguish between stutter and true alleles [37].

DISCUSSION

Developing the 13 X-STR multiplex PCR system for paternity testing was a remarkable achievement in forensic genetics. Markers were selected based on their genetic localization, high polymorphism, and representation of all 4-linkage groups on the X-chromosome. Successful amplification of these markers in a single multiplex reaction further validated their suitability for paternity

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testing and complex kinship analyses. Primer design was essential to maximize amplification and minimize primer dimer formation. Autodimer software was used to analyses all primer and redesigned pairs with an alignment score of 8 or greater. The melting temperature (Tm) was carefully considered to achieve optimal amplification, and some primer pairs were redesigned to have Tm values in the smaller range. The specificity of primer annealing was also evaluated using the BLAST algorithm to ensure specific binding. These considerations increase the efficiency and reliability of multiplex PCR systems [25]. Quantitative optimization of primer pairs and template DNA concentration further improved the performance of the multiplex PCR system. Balancing the amplification of markers was achieved by adjusting primer concentrations for some markers, considering their product size and amplification characteristics. The optimal template DNA concentration was determined to be in the range of 1–2 ng. These improvements ensured consistent and reliable results for paternity testing. Designing and constructing an allelic ladder specific to the Pakistani population was another critical aspect of the multiplex PCR system. The allelic ladder is a size standard that allows accurate allele sizing and translocation variation during electrophoresis. The ladder was carefully constructed to include all common alleles of the 13 X-STR markers identified in the population and some rare alleles [31]. The allelic ladder consisted of 102 alleles, providing a comprehensive reference for allele identification in paternity testing. Stutter formation, a well-known phenomenon in STR analysis, was also investigated in the context of multiplex PCR systems. The extent of stutter formation was influenced by the length of the repeat unit of the markers, with tetranucleotide repeat markers exhibiting lower levels of stuttering than dinucleotide repeat markers. This excellent 13 X-STR multiplex PCR system offered a reliable and efficient tool for complex paternity testing and kinship analyses. Careful selection of markers, primer design, quantitative optimization, and consideration of perturbation formation contributed to the robustness and accuracy of the system. The International Society of Forensic Haemogenetics (ISFH) Commission guidelines were followed to assign the alleles of X-STR markers [32]. However, there are a few discrepancies in the reported nomenclature. In the case of GATA172D05, the repeat motif was first described as GATA [38] and later as the addition of an extra repeat of TAGA by Edelmann and colleagues [39, 40]. The flanking region of the TAGA repeat motif has a TATA sequence that added one repeat in nomenclature [41]. This research study used the nomenclature Edelmann *et al.*, 2002 concerning GATA172D05. The repeat motif (TCTA) of the coding strand was used by Hearne colleagues [42] for HPRTB. In contrast, Edwards and colleagues used the complementary strand resulting in an extra repeat motif AGAT [38], although it was according to the recommendation of ISFG [32]. Therefore, the AGAT repeat motif from the non-coding strand was used in allele calling in this study, which is very similar to Edwards *et al.*, [38]. A simple repeat motif (AGAT) has been described previously for marker GATA31E08 [43], followed by the marker's allele designation during this study. However, recently a change in nomenclature at this particular locus has been proposed with the inclusion of "AGGG" in the repeat motif [$(AGGG)_n(AGAT)_m$] [41]. Therefore, this nomenclature adds two extra repeats to the previously described nomenclature [43]. The alleles were designated according to the suggestion of Edelmann *et al.*, for marker DXS7132 and DXS8377 [40], Hering *et al.*, for marker DXS6789 [44], Edelmann *et al.*, for marker DXS9902 [39] and Edelman *et al.*, DXS6801 [45]. The allele designation of DXS8378, DXS6810, DXS7423 and DXS981 was according to Shin *et al.*, [43], whereas the allele designation of DXS6793 was according to Jia *et al.*, [46]. All 13 X-STR primer pairs showed high discriminatory powers ranging from 0.758-0.978 for females and 0.613-0.905 for males in our population [24]. The observed alleles, repeat size and motif structure of 13 X-STR markers are shown in Table 2. We examined DNA profiles generated with genomic DNAs of 432 individuals of Pakistani descent, and the combined power of discrimination of 13 X-STRs was determined to be 2.96×10^{-13} and 2.58×10^{-8} in females and males, respectively, which strongly advocates for their utility in complex kinship testing especially in deficiency paternity testing, grand-mother grand-daughter testing and analysis of mixed stains to identify the female DNA. Multiplex PCR-based STR analysis was the most effective technique for forensic DNA analysis. A recent study evaluated the efficacy of indirect multiplex kits for direct amplification of 103 saliva samples without pretreatment using thirteen non-direct multiplex kits, resulting in an 80% reduction in turnaround time. The developed protocol was cost-effective, time-efficient, and did not compromise the quality of the DNA profile. All tested samples produced complete DNA profiles matching the required quality parameters. That was the first report of direct DNA amplification with non-direct multiplex STR kits without pretreatment [47].

CONCLUSIONS

In conclusion, we have developed and optimized a 13 X-STR system with a combined power of discrimination $1\text{-}2.96 \times 10^{-13}$ and $1\text{-}2.58 \times 10^{-8}$ in females and males, respectively, due to its significant combined power of discrimination and sensitivity. This system can be efficiently used in parentage testing and forensic casework. To our

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knowledge, this was the first study that describes a combination of 13 X-STR markers in a single amplification system.

Authors Contribution

Conceptualization: MAT1
Methodology: MAT2
Formal analysis: MAT2
Writing-review and editing: MAT1, MAT2

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Association Studies of Common Variants of TCF4 Gene Conferring Risk of Schizophrenia in Pakistani Patients

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ABSTRACT

Schizophrenia is a psychiatric disorder and it is strongly inherited disease with a heritability of 80% or more. Rare genetic mutations are more frequent in schizophrenia patients. These genetic variations interfere with brain development and include hundreds of distinct genes. Transcription factor 4 (TCF4) has been emphasized as major players for disruption of brain development as well as function and consequently, the onset of schizophrenia. The dysregulation of TCF4 gene expression in brain affects the process of pre pulse inhibition (PPI) and consequently profound reduction in sensor motor gating that may results in to the onset of schizophrenia. **Objective:** To find out the genetic association of common variants of TCF4 gene conferring risk of schizophrenia. **Methods:** It was a case control study in which statistically significant number of blood samples of confirmed diagnosed schizophrenic patients as well as age matched healthy control subjects were analyzed to screen out selected Single Nucleotide Polymorphisms (rs9960767, rs4309482, rs12966547, and rs2958182) of TCF4 gene for their association with schizophrenia. **Results:** Out of these four SNPs rs9960767 and rs4309482 were significantly associated with schizophrenia. p-values for SNPs rs12966547 and rs2958182 were greater than 0.05 in both healthy controls and in patients. **Conclusions:** The results of this study offer compelling evidence for the link between particular TCF4 gene polymorphisms and schizophrenia. Two SNPs, rs9960767 and rs4309482, were found to have a strong correlation with schizophrenia in the research population, according to the analysis.

INTRODUCTION

Schizophrenia is a psychiatric disorder and it is strongly inherited disease with a heritability of 80% or more. It is a devastating mental illness that weakens social and mental functioning and often leads to the development of comorbid disease. The prevalence of schizophrenia is 1% worldwide and is equally common in men and women [1]. The morbidity rate of schizophrenia patients is high in young adulthood. The onset of schizophrenia varies between men and women with respect to age as males tend to have a younger onset. The peak incidence for males and females is in the decade 15–24 with an average reduction in lifespan of about 25 years [2]. There is a 10 percent lifetime chance of suicide in patients with schizophrenia. Both negative and positive symptoms have been observed in schizophrenic patients. Negative symptoms of schizophrenia allude to the lack of normal behaviors found in healthy individuals. Furthermore, Negative symptoms include poverty of speech, flat affect, loss of will or drive, loss of sense of pleasure and psychomotor retardation whereas positive symptoms include delusions,

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hallucinations and florid thought disorders [1]. Schizophrenia may cause by duplications or deletions of DNA sequences in genes that play role in brain development or neuronal signalization. Recent genome-wide association studies highlight schizophrenia as highly polygenic disorder and abnormal connection between different genes network can also leads to schizophrenia [3]. One of the most well-known schizophrenia risk genes is transcription factor 4 (TCF4). The TCF4 gene (Entrez Gene ID 6925; ensemble ENSG00000196628) is a basic helix-turn-helix (bHLH) Ephrussi-box (also known as "E-box" or "E-") protein transcription factor that is found on chromosome 18q21.2. TCF4 also goes by the names E2-2, ITF2, and bHLHb19. It is 437 kb long, has 41 exons, and has a human protein length of between 511 and 773 amino acids [4]. TCF4 has been actively expressed in brain, especially in thalamic neurons and plays important role in differentiation of glial cells, especially the maturation of oligodendrocyte progenitors [5]. The microRNAmir137, a regulator of neuronal development targets TCF4 and disrupts the tissue specific tuning of its expression that may leads to Schizophrenia [4]. Furthermore, SNPs in miR-137 and its target genes have shown association with risk of schizophrenia, as result of dysregulated neurodevelopment [6]. The cognitive impairments and deficits in pre-pulse inhibition has been reported in mice with over expressing TCF4 in the forebrain [7]. The significant mRNA over expression of TCF4has been reported in psychosis patients in comparison to controls as well as positive correlation with positive- and negative-symptom levels. Therefore, involvement of TCF4 variants in psychosis pathology especially abnormal neurodevelopment has been suggested in previous studies [8]. Furthermore, the increase in obstetric complications in children who later develop schizophrenia, cortical thickness reduction, enlargement of ventricles in the early phases of the disease, cognitive dysfunction, positive and negative symptoms support the neuro- developmental hypothesis for the onset of schizophrenia [8]. Most recent studies have found out the importance of common variants of TCF4 gene and their association with schizophrenia [9-11]. The significant association of SNP (rs9960767) of TCF4 gene has been observed with risk of schizophrenia in American and German populations [36]. Further evidence for the involvement of the same variant (rs9960767) for the risk of schizophrenia has been provided in British population [11]. Another SNP (rs2958182) of gene TCF4 appeared to be significantly associated with schizophrenia among Han Chinese population in recent studies [10]. The replication study of SNPs (rs4309482, rs12966547) showed their significant association with schizophrenia in Norwegian population [9]. The above-mentioned association studies motivated for testing of selected Single Nucleotide Polymorphisms rs9960767, rs4309482, rs12966547and rs2958182) of TCF4 gene for association with schizophrenia in Pakistani population. In this study, the genetic associations of common variants of TCF4 gene (rs9960767, rs4309482, rs12966547, and rs2958182) conferring risk of schizophrenia were carried out in case-control study pattern (case n=60, control n=60) in Pakistani population. The identification of disease susceptibility loci may lead to a better understanding of the biological mechanism of schizophrenia that will pave a way for the better diagnostic, prevention and treatment of schizophrenia.

METHODS

In k3 EDTA vials, blood samples from 60 Institute of Mental Health, Lahore confirmed diagnosed schizophrenia patients and 60 age-matched healthy control persons were taken. The preparation of these samples for molecular analysis. Following all ethical guidelines, blood samples were taken from patients, and clinical data were gathered from patient files. Blood samples were drawn by the knowledgeable paramedical staff. Using a DNA extraction by Thermofisher for purification of genomic DNA or by using the organic method of DNA isolation methodology outlined by *Maniatis et al.*, (1982), the DNA was isolated from the fresh blood samples [12]. Agarose gel electrophoresis was used to assess the DNA's quantity and quality. The quantity and purity of the DNA were evaluated using agarose gel electrophoresis. Using the Primer 3 program from the internet (https://primer3.ut.ee/), allele specific primers for allelic variations of TCF4 were created. For each marker, two universal primers and one allele-specific primer were created. Method of Hirotsu *et al.*, (2010) was followed for creating allele-specific primers, and the primer sequences and annealing temperatures are listed in Table 1 [13].

Table 1: Allele specific primer sequences for TCF4 alleles and their annealing temperatures.

TCF4 SNPs	Name of Primer	Sequences of primers	Annealing Temperature (ºC)
rs9960767	T Reverse	5'-AGGGGTAATA ATTTGTGAAT-3'	51
	G Reverse	5'-AGGGGTAATAA TTTGTGAAG-3'	51
	Universal Forward	5'-CAAGAGATT CCATTGTATGC-3'	51
rs4309482	A Forward	5'-ATGCTAAGTG ACAGGAGTCA-3'	56
	G Forward	5'-ATGCTAAGT GACAGGAGTCG-3'	56
	Universal Reverse	5'-GATGTGTGT AGAGTTGGGCA-3'	56
	A Forward	5'-CCTATGTCC TTCCAAGAATA -3'	52

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rs2958182	T Forward	5'-CCTATGTCC TTCCAAGAATT -3'	52
	Universal Reverse	5'- CAGCTCTTT CTAAACCCATA-3'	52
rs12966547	Universal Forward	'5'- AGACTGAGA GAATTTAGAGT-3'	52
	T Reverse	5'-TCCACTCTG ACTTACTATT-3'	52
	C reverse	5'-TCCACTCTG ACTTACTATC -3'	52

Genomic DNA (10 ng), oligonucleotide primers (0.4 ρM each), dNTPs (200 µM), 1X PCR Buffer, Taq Polymerase (1U) and MgCl (2 mM) were all used in the PCR. The following PCR cycling circumstances were used: With varying annealing temperatures listed in table 1 for 30 seconds each, one cycle was performed at 95°C for 5 minutes, followed by 32 cycles at 95°C for 30 seconds, and one cycle was performed at 72°C for 5 minutes. Products from amplified SNPs were separated by gel electrophoresis and staining was performed with Ethidium Bromide (EtBr) and then seen under an Ultra Violet light source. The genotyping of the allelic variations of TCF4 was done using a gel-based approach. Sanger sequencing of purified PCR products from chosen samples was carried out to confirm the various allelic variants of TCF4 in order to validate the gel-based approach of SNP identification. BigDye Sequencing Kit was used to sequence the purified products using universal primers in accordance with the manufacturer's instructions (Applied Biosystems). Sanger sequencing was done at the business facilities. Chi-square, odds ratios (ORs), and 95% confidence intervals (CIs) were performed to estimate the association of genetic variations of TCF4 with schizophrenia. A 0.05 p-value was regarded as statistically significant. The haplotypes association with the risk of schizophrenia was assessed using Fisher's exact test. SHEsis, an online statistical analysis tool, was used for all statistical analysis.

RESULTS

This study comprised of Pakistani Schizophrenia patients (n=60) and age-matched normal healthy control subjects (n=60). DNA isolation was performed from fresh blood samples, and four variants of TCF4 gene containing (rs9960767, rs2958182, rs12966547&rs4309482) were genotyped. The allele specific extension method was exploited to amplify the variant regions of TCF4 gene and amplified products were analyzed by agarose gel electrophoresis. The amplified PCR product for all four SNPs of TCF4 (two possible variants of each genetic marker) are shown in gel image (Figure 1).

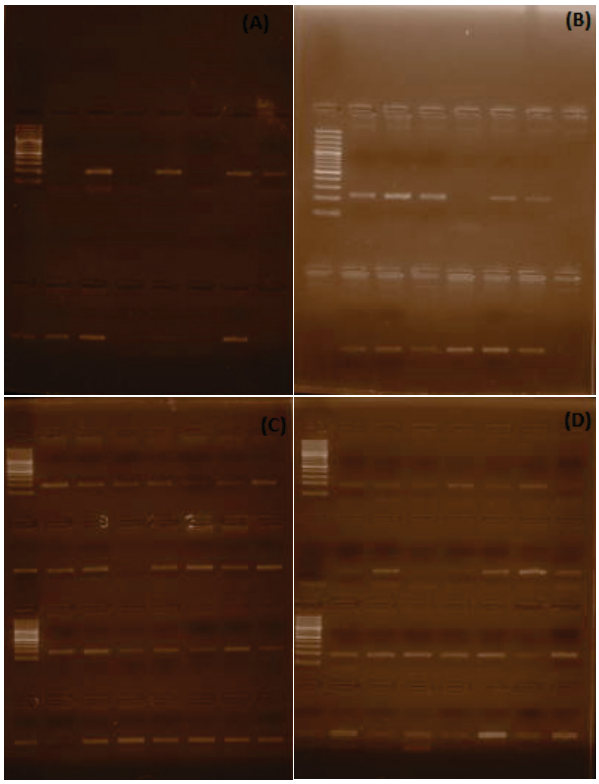

Figure 1: Gel images of four SNPs of TCF4 (A) rs2958182 (B) rs4309482 (C) rs9960767(D) rs12966547

Four SNPs of TCF4 were genotyped in 60 Pakistani schizophrenic patients and in normal healthy individuals. Chi square analysis was performed for all four SNPs genotyped in schizophrenia patients and in controls. Table 2 shows p-values for each SNP and its association with schizophrenia risk in both case and control individuals. By considering p-values, two SNPs i.e. rs9960767 and rs4309482 of TCF4 showed significant association (<0.05) with risk of schizophrenia in Pakistani population p=7.47e-007 and p=0.000537 respectively). However, other two SNPs rs2958182 and rs12966547 were not significantly associated with risk of schizophrenia in this population. The strongest association with the schizophrenia was observed for rs9960767(p=7.47e-007) in Pakistani schizophrenia patients.

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Table 2: The association of TCF4 (rs9960767, rs4309482, rs2958182, rs12966547) with Schizophrenia in Pakistani patients

Gene	Marker ID	Odds Ratio	%95 CI	Fisher's p- value	Pearson's p- value
TCF4	rs9960767	7.666667	[4.131957~14.225168]	7.47e-007*	7.17e-007
	rs4309482	1.115533	[0.657053~1.893930]	0.000537 *	0.000537
	rs12966547	1.105820	[0.665594~1.837213]	0.925377	0.925376
	rs2958182	1.115533	[0.657053~1.893930]	0.245469	0.245373

TCF4=transcription factor4. *Marker showed significant association with Schizophrenia ($p<0.05$)

The study further focused on haplotyping of all variants to check whether patients carrying more risk alleles are at greater risk of schizophrenia. Table 3 shows haplotypes of four SNPs of TCF4. In the four TCF4 SNPs, the haplotype analysis found 15 common haplotypes with frequencies greater than 0.03; 11 of these haplotypes were significantly associated with the risk of schizophrenia, demonstrating that patients carrying more risk alleles have a higher risk of developing schizophrenia.

Table 3: The association of TCF4 haplotypes with Schizophrenia

Gene	Marker	Haplotype	Case frequency	Control frequency	p-value	Odds Ratio [95%CI]
TCF4	rs99660767 rs2958182 rs12966547 rs4309482	G A C A*	7.57(0.063)	1.46(0.012)	0.037423	5.821 [0.884~38.316]
		G A T A*	8.34(0.069)	0.11(0.001)	0.00617	2.083 [0.820~5.294]
		G A T G*	6.76(0.056)	1.09(0.009)	0.03866	5.186 [1.458~18.455]
		G T C A*	7.16(0.060)	1.30(0.011)	0.03950	6.759 [0.977~46.751]
		G T C G	14.16(0.118)	7.30(0.061)	0.11660	5.821 [0.884~38.316]
		G T T A*	14.10(0.117)	3.03(0.025)	0.00523	2.083 [0.820~5.294]
		G T T G*	7.68(0.064)	1.21(0.010)	0.02639	5.186 [1.458~18.455]
		T A C A*	7.67(0.064)	17.89(0.149)	0.03368	6.759 [0.977~46.751]
		T A C G	6.58(0.055)	2.78(0.023)	0.20176	0.391 [0.161~0.952]
		T A T A*	0.00(0.000)	12.05(0.10)	0.00034	2.462 [0.592~10.243]
		T A T G	4.85(0.040)	4.12(0.034)	0.79831	1.191 [0.312~4.542]
		T T C A	10.68(0.08)	11.78(0.09)	0.81978	0.904 [0.378~2.159]
		T T C G*	7.94(0.066)	19.99(0.16)	0.01593	0.356 [0.150~0.847]
		T TT A*	6.49(0.054)	17.37(0.14)	0.01958	0.339 [0.132~0.869]
		T TT G*	6.79(0.057)	16.01(0.13)	0.04386	0.392 [0.153~1.000]

DISCUSSION

TCF4 is considered as a most susceptible gene that cause schizophrenia. This study comprised of Pakistani Schizophrenia patients (n=60) and age-matched normal healthy control subjects (n=60).

Four variants of TCF4 gene containing (rs9960767, rs2958182, rs12966547, rs4309482) were genotyped. In this study of patients of schizophrenia, significant association was seen between two SNPs of TCF4 [rs9960767, rs4309482 with p=7.47e-007 and p=0.000537 respectively] and Schizophrenia. These results are similar with the study of Stefansson et al., which showed that rs9960767, an SNP found in an intron of TCF4 (P.4.1_10_9), was one of seven single nucleotide polymorphisms (SNPs) that were reported as being related with schizophrenia at a genome-wide level, which included data from different GWAS [14]. This association was replicated in a study of Han Chinese patients using a different SNP (rs2958182, in high linkage disequilibrium (LD) with rs9960767). Another significant GWAS found rs4309482, which is intergenically located upstream of CCDC68 and downstream of TCF4 [15]. Finally, two novel TCF4 SNPs (rs17512836, which is located in intron 3 of TCF4, and rs12966547, which is in high LD with rs4309482) were discovered and supported TCF4 as a disease gene for schizophrenia in recent meta-analyses. mRNA levels and TCF4 sequence variations are related to neurodevelopmental traits in psychotic illnesses. TCF4 and schizophrenia were first linked by the SNP rs9960767 in intron 3 of the gene (P. 4.1_ 10_9; OR 1.23 [1.15, 1.32]) [14]. Our findings also indicated a substantial link between the SNP rs4309482 and schizophrenia. These outcomes are consistent with those of several research. In a subsequent analysis (P147.8109; 1.09 [1.06, 1.12]), Steinberg et al., discovered that the mutation (rs4309482) downstream the TCF4 gene had achieved a genome-wide significance level [16]. In a GWAS mega study from the psychiatric GWAS collaboration, a second variation (rs12966547) was significantly linked to schizophrenia (P142.601010; OR 1.09 [1.06-1.12]). [17]. From the PGC schizophrenia analysis, a third variant, rs17512836, has also been linked to schizophrenia (P142.35108); upon follow-up, this resulted in a total p-value of 1.05106 (OR 1.23 [1.14-1.31]) [17]. Physically (within 1.5 kb) in LD (r21–41), rs12966547 and rs4309482 are practically identical markers. In the Caucasian population, rs4309482 and rs12966547 are in extremely weak LD with rs9960767 (D0140.05, r2140), indicating that they are

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producing independent association signals with schizophrenia. Similar to rs4309482 and rs12966547, rs17512836 is in very low LD with both, but is in moderate LD with rs9960767 (D0141, r2140.52), indicating that the association signal there is not independent [18]. Another study by Wirgines et al., revealed a positive correlation between rs4309482 and SCZ. The two associated rs12966547 and rs4309482 are linked to less effective verbal fluency, which is a gauge of cognitive function, according to an analysis of known TCF4 risk variants for schizophrenia [19]. The identical risk variations, rs12966547 and rs4309482, were connected to a higher ventricular capacity even though this did not endure correction for multiple testing. One of the most common symptoms of schizophrenia is an increased ventricular volume[20].

CONCLUSIONS

In conclusion, the goal of this study was to determine how Pakistani patients' vulnerability to schizophrenia may be influenced by the TCF4 gene. The results of this study offer compelling evidence for the link between particular TCF4 gene polymorphisms and schizophrenia. Two SNPs, rs9960767 and rs4309482, were found to have a strong correlation with schizophrenia in the research population, according to the analysis. Overall, this research adds to the growing body of data that TCF4 is a schizophrenia susceptibility gene.

Authors Contribution

Conceptualization: FI, MAT
Methodology: NG
Formal analysis: FI, AM
Writing-review and editing: FI, MKAK, MAT

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Girls' Attitude towards Menstrual Hygiene among Nursing Students at College of Nursing, AIMC, J/H, Lahore, Pakistan

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ABSTRACT

Menstruation has a higher impact on educational quality than other aspects of puberty because it combines a learning component with features influenced by the school environment and infrastructure. **Objective:** To analyze the females' attitudes toward menstrual hygiene among Nursing students at AIMC, J/H, Lahore. **Methods:** This descriptive cross-sectional study took place between July 1st to June 30, 2022. A total of 80 study populations were selected with a purposive sampling technique. The questionnaire of this study was adopted by Doctor Funmito Omolola Fehintola. **Results:** More than half of the participants (52.5%) knew about menstruation before menarche, while the majority of the study population (90.2% and 96.5%, respectively) has strong knowledge and practice about menstruation. While, the majority of participants' reactions to their menarche were uncomfortable (51.2%) and emotionally distressing (41.3%). The education of parents has a significant impact on their children's conduct because they adapt to what they observe. Overall, more than two-thirds (76.8%) of the participants come from educated homes, which results in higher outcomes in our study findings. **Conclusions:** According to the study findings, the majority of the respondents practice good menstrual hygiene and have good knowledge about menstruation. Efforts must be made to ensure that teenagers are thoroughly educated on menstruation and the requirement of suitable hygiene practices at school and home.

INTRODUCTION

The term adolescence is derived from the Latin word "Adolescere," which means "to grow up." Adolescence is a period of transition from childhood to adulthood. It is a vital phase with physical, sexual, and mental consequences [1, 2]. Adolescents are defined by the as anyone aged 10 to 19 [3, 4]. To ensure their development into healthy adults, this age group requires good nutrition, education, counselling, and guidance [5-7]. Menstruation is defined as the "periodic discharge of blood from the uterus occurring more or less at regular monthly intervals throughout the active reproductive life of a female" [8, 9]. While menarche is a natural event in a girl's life, it also marks the start of physical and social development [10]. Even though regular menstruation is evidence of a female's excellent reproductive health, menstruation itself is misunderstood and adulterated in many societies [11]. Furthermore, in some societies, discussing menstruation and related issues is prohibited. As a result, a natural biological process that elevates women and girls becomes a source of embarrassment and annoyance. Such social taboos and

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myths make postpubescent females more vulnerable to unsanitary practices [12-14]. Moreover, pubertal development and sexual maturation are finished during this time due to hormonal changes. First menstruation is the most significant of all developmental milestones. Menarche is the critical point at which menstruation begins. Menstruation is a qualitative event that has a significant impact on a woman's life [15, 16]. Good hygiene is essential for young women's health during menstruation. Today's healthy young women will be tomorrow's healthy mothers. Menstruation is a normal physiological process, and communities must be made aware of this fact. A girl in her reproductive age menstruates 3-5 days each month on average or more. [17, 18]. Furthermore, the uterine medullary is exposed during vaginal bleeding, bacteria from the vagina can enter the uterus body and fallopian tube, resulting in infection. Young girls are vulnerable for reproductive system infections due to a lack of health awareness, social immaturity, and physical status. A lack of accurate or sufficient menstrual cycle information in developing countries has resulted in negative outcomes such as unhealthy behavior, negative body image, susceptibility to reproductive tract infections and pelvic inflammatory diseases, infertility, anxiety, and low self-esteem. There is a risk of infection during vaginal bleeding because the uterine osseous is open and allows bacteria from the vagina to enter the uterus body and fallopian tube, resulting in infection. Because of their lack of health information, social immaturity, and physical status, young girls are a vulnerable group for reproductive system infections. In developing countries, a lack of accurate or sufficient information about the menstrual cycle has resulted in negative outcomes such as unhealthy Behavior, negative body image, susceptibility to reproductive tract infections (RTI) and pelvic inflammatory diseases (PID), infertility, anxiety, and low self-esteem [17, 18].These consequences are worsening by physical, psychological changes and menstrual hygiene [18, 19]. The use of hygienic sanitary protection, for example, reduces the incidence of reproductive tract infections. Knowledge of menstruation and menstrual hygiene is essential for reproductive health. Menstrual behaviors are influenced by a variety of factors, the most important of which is household economic status [20]. Depending on the information they acquire, young girls can or cannot follow an appropriate menstrual period hygiene practice. The internet, media, relatives and friends, particularly mothers, can all play an important role in providing accurate information about menstruation. It has been estimated that about 50% of adolescent girls worldwide suffer from menstrual irregularities and their negative consequences. All of this is due to the psychosocial stress and emotional changes that occur at that age [21, 22]. Menstrual hygiene is often poor because menstruation is considered a "culture of shame" for girls and women, resulting in a lack of support from their partners and families. Menstruation and related issues are surrounded by a culture of silence in less developed countries. Menstruating girls' isolation, as well as restrictions imposed by their cultural values and beliefs, have reinforced a negative attitude towards this phenomenon. Even after menarche, adolescence is given very little information in such cultures. Young girls who have higher menstrual hygiene knowledge are less likely to have unsuitable health effects [23-25]. In the most extreme case, menstruation and menstrual hygiene remain mired in customs ethnic and social restrictions, myths, and misinformation, which result in girls being embarrassed, preventing them from seeking information, and even hiding their menstruation because they must be separated from the others during menstruation; demonstrating the importance of culture in menstruation [26, 27]. Onset of menstruation is one of the most important changes occurring during adolescence. Menstruation is a milestone event in a girl's life and the beginning of reproductive life. There are several cultural traditions, myths and misconceptions related to menstruation, which make them vulnerable to genital tract infections [28]. Lack of menstrual hygiene in adolescent girls can make them susceptible to various morbidities, for example, reproductive tract infection, urinary tract infection and their long-term consequences i.e., cervical cancer, infertility, and ectopic pregnancy [29]. The purpose of this cross-sectional descriptive study was to assess adolescent girls' attitudes, gaps in knowledge, beliefs, and hygienic practices regarding menstruation while they were being treated at a tertiary care teaching hospital for their various medical problems. Good hygiene is essential for young women's health during menstruation. Today's healthy young women will be tomorrow's healthy mothers. This study will be raised community awareness about menstrual hygiene practices. The study's findings can be used to improve hygiene practices in accordance with community standards. It can also be used to prevent and control reproductive tract infections and other reproductive disorders caused by poor hygiene.

METHODS

It was descriptive cross-sectional study by using purposive sampling method. This study was conducted between 1st, July 2021 to 30th June 2022. The population of the study were the Nursing students at the College of Nursing, Allama Iqbal Medical College, Jinnah Hospital, Lahore. A purposive nonprobability sampling technique was utilized for in this study. This technique was used purposefully and

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conveniently approaching the subjects. Data were collected by using a questionnaire. Inclusion Criteria: Nursing Students in College of Nursing, AIMC, J/H, Lahore. Exclusion Criteria: It includes students from other institutes, menopausal women, girls before menarche and mentally sick girls of same age group. Moreover, the students who were on medical leave and the participants who were unwilling to participate in the study.

The Sample size was selected using following formula:

Sample size n=[DEFF*Np(1-p)]/[(d^2/$Z^2$1-α/2*(N-1)+P*(1-P)]

Where DEFF= Design Effect, N= Sample Size, P= Population size, Z=1.96, CI=5%

Sample size: 80

Data were collected by using a questionnaire equipped by Doctor Funmito Omolola Fehintola. It was mainly divided into four parts, demographic profile of the participants, Part II consisting of Questions on knowledge towards menstrual process, Part III Questions about Attitudes towards Menstruation and Part IV Questions Based on Practice during Menstruation. A standardized tool was used for data collection. It was accessible to all participants through an introductory conversation. The contributors were helped during questionnaire fulfillment too. The data were collected conveniently and co-operatively. Written permission was obtained from the Principal of the Concern Organization. The study participants provided written consent outlining the purpose and benefits of the study. There was no request for personal information or contact with any of the participants. The participants' privacy and confidentiality were respected. The information gathered was solely for research purposes. Any danger to the participant was avoided. Data were analyzed by using SPSS version 25.0. The demographic and other variables are presented in the form of Frequencies, Percentages, and Graphs. Bar char or pie chart were made. The quantitative variables were presented by mean, median, and standard deviation.

RESULTS

This section contains the data in four parts. The first part includes demographic characteristics of population containing age groups, class, marital status, qualification, father's level of education, mother's level of education, and religion. The second part contains question assessing the knowledge of the participants regarding menstruation. The third part contains questions about attitudes of participants towards menstruation. The last part includes questions related to hygienic practices during menstruation. Table 1 shows the demographic profile of the participants. Nearly three fourth of the participants are lying in age group range from 18-25 years. This is because of selection of title i.e., girls' attitude towards menstrual hygiene. Above half of the participants (52.5%) belong to Generic Nursing as they are readily available to provide data with co-operation and convenience. Parents' education plays vital role in their children behavior as they adapt what they observe. Overall, above two third (76.8%) of the participants belong to educated families. Majority (92.5%) of the participants are Muslims as the study conducted in an Islamic Country. Above three fourth of the participants are single in our study population (Table 1).

Table 1: Demographic profile of the participants

Demographic profile of the participants	Variables	Frequency (%)
Age	18-25 years	59 (73.8)
	26-35 years	17 (21.3)
	Above 35 years	4 (5)
Class	Post RN	20 (25)
	Generic Nursing	42 (52.5)
	Diploma Nursing	18 (22.5)
Marital status	Married	17 (21.3)
	Single	63 (78.8)
	Others	0 (0)
Father's level of education	None	4 (5)
	Primary	15 (18.8)
	Secondary	43 (53.8)
	Tertiary	18 (22.5)
Mother's level of education	None	17 (21.3)
	Primary	16 (20)
	Secondary	38 (47.5)
	Tertiary	9 (11.3)
Qualification	Post RN	20 (25.0)
	Generic Nursing	42 (52.5)
	Diploma Nursing	18 (22.5)
Religion	Muslim	74 (92.5)
	Christian	6 (7.5)

Table 2 shows the knowledge of respondents regarding menstruation. Overall, above two third (75.6%) of the study population have satisfactory knowledge about menstruation as the study is conducted among medical students. Most of the participants (87.5%) know that menses is a normal physical process having considerable significance in a woman's life. It is observed from data analysis that each cause of menstruation according to participants is concerning to this phenomenon to some extent but the most important one that observes in greater frequency is hormonal fluctuations (65%). More than half of the participants (52.5%) are already heard about menstruation prior to menarche as they belong to literate family. The main source of information is found to be mothers (75%), others may include friends, teacher etc. Overall, 90.2% of the respondents have good knowledge on menstruation but the only 9.8% have poor knowledge (Table 2).

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Table 2: Knowledge of respondents about menstruation

Variables	Frequency (%)
What is menstruation?	
Physiological process	70 (87.5)
Pathological process	3 (3.8)
Both	7 (8.8)
Cause of menstruation	
Hormonal changes	52 (65)
It's a sign of virginity	3 (3.8)
Purification of blood	2 (2.5)
Both a & b	23 (28.7)
Sources of menstrual blood	
Uterus	69 (86.3)
Vaginal	9 (11.3)
Bladder	2 (2.5)
Abdomen	0 (0)
Normal cycle length	
21-35 days	76 (95)
>35 days	4 (5)
Ever heard about menstruation before menarche	
Yes	42 (52.5)
No	38 (47.5)
Sources of information	
Mother	60 (75)
Teacher	3 (3.8)
Friends	17 (21.3)
Books	0 (0)
Media (TV, Radio)	0 (0)

DISCUSSION

Menstruation is an important pubertal development in the life of a female. There are many misconceptions about this normal physiological process, such as a lack of knowledge about menstruation and poor hygienic practices during menstruation. The current study sheds light on the higher percentage of menstruation process awareness and reveals that mothers are the primary source of information for their female children prior to menarche. The current study's findings are similar to those of a study conducted to assess the knowledge, attitude, and practice of Secondary School girls [29], but they are contradictory to those of a study conducted in India among school-aged girls at the Urban Health Training Centre IGIMS, Patna [30]. The reason for the current studies' findings in the variable that exists in this study is the mother's level of education. The majority are tertiary educated (11.3%), secondary educated (47.5%), and primary educated (20%). The current study's findings are similar to those of a study conducted in Karachi, Pakistan [31]. Cultural considerations also influence the current study's findings. In the current study, more than half of the participants had satisfactory knowledge about menstruation and good hygienic practices, which was similar to a study conducted in Bengaluru Urban District, South India, which found that females (72.3%) had higher awareness levels than males (29.6%). Menstrual hygiene practices were deemed acceptable [32]. The current study's findings differed from those of a previous study conducted in the Marh block of Jammu district among adolescent school girls in the Govt. Higher Secondary School, which revealed that only 49.24% of respondents were aware of menstruation before menarche. It could be due to the fact that the study divided understanding into good and poor [33] In the current study, the majority of participants (51.2%) were either uncomfortable or emotionally disturbed (41.3%). These findings were comparable to those of Tiwari's study in India [34]. Hygiene practices are important in confirming the absence of disorders in girls. The use of materials repeatedly during menstruation increases the likelihood of infection due to improper cleaning and washing. The current study's findings show that the vast majority of participants (93.8%) use sanitary pads during menstruation. This was similar to the findings of a study conducted in rural settings among adolescent school girls in Jammu district These findings could be attributed to the high poverty level in this area, as a number of participants' parents or guardians were underemployed [35]. In this study, the majority of participants discarded used materials by wrapping them in plastic bags (61.3%) and paper (36.3%) and throwing them away (98.8%). These findings are similar to those of a study conducted in a tertiary care hospital in India on the knowledge, attitude, and socio-cultural beliefs of adolescent girls about menstruation [36]. This was in contrast to the findings that majority of their respondents burned and disposed of the absorbent materials used during menstruation and disposed of it in the same manner as solid waste. The practice of disposing of used material without wrapping during menstruation should be discouraged because it can create a breeding ground for insects and increasing the risk of various infections or illnesses [37]. Overall, the hygiene practices during menstruation among Nursing Students at the College of Nursing in Lahore are satisfactory, with the majority of respondents demonstrating good hygiene practices. This study's findings were similar to another study which revealed that all participants who were knowledgeable about menstruation and used menstrual hygiene products when necessary. In the current study, there was a positive relationship between parents' educational level and good knowledge of menstruation and its hygiene practices. When compared to uneducated mothers, educated mothers are more likely to discuss menstruation with their children in a friendly manner [38].

CONCLUSIONS

This study findings revealed the majority of the

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respondents practice good menstrual hygiene and have good knowledge about menstruation. Efforts must be made to ensure that teenagers are thoroughly educated on menstruation and the requirement of suitable hygiene practices at school and home.

Authors Contribution

Conceptualization: SA
Methodology: SA, IR, RS, SA, ADA
Formal analysis: SA, RS
Writing-review and editing: IR, SR, SA, ADA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Frequency and Outcome of Hyponatremia among Elderly Patients

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ABSTRACT

It is widely recognized that eight physiological alterations make elderly people more susceptible to contracting hyponatremia. The frequency and outcome of this condition however, seldom studied and thus merits exploration. **Objective:** To study the frequency and outcome of hyponatremia among elderly patients. **Methods:** The present descriptive case series was conducted from on a group of 207 consented elderly individuals of both sexes at Liaquat university hospital. A survey contains questions about biographical information, socio-demographics, the existence and degree of hyponatremia. The chi-square test was used to examine the relationship between hyponatremia and outcome. The data were analyzed with SPSS version-21.0. **Results:** Males made up 61.8% of the sample, while females made up the remaining 38.2%. The average length of hospitalization was five days (±3 SD). Hyponatremia was present among 59 (28.5%) of the inpatients (43 males and 16 females), out of which a majority (45) recovered and 11 died while the chronic liver disease and diabetes mellitus were common comorbid observed in relation to hyponatremia among elderly population. **Conclusions:** Hyponatremia exists in a substantial proportion of geriatric patients, as determined by meticulous examination and the condition may lead to adverse outcomes.

INTRODUCTION

The aging process frequently results in maladaptation in the organ systems and physiological functions, making the geriatric more prone to imbalances in electrolytes [1-3]. Contributing to these changes are eight physiologic changes, including decreased body water amount, glomerular filtration rate, the urinary concentrating capacity, raised anti-diuretic hormone quantity, atrial natriuretic peptide level, declining aldosterone quantity, decreased thirst central nervous system sensitivity, and decreased free water clearances [4-6]. In addition, diminished intrarenal prostaglandin production may impact elderly people's capacity to excrete water. Additionally, the elderly may be more sensitive to osmotic stimuli, contributing to hyponatremia. However, the majority of elderly individuals retain the ability to dilute their urine, and hyponatremia only arises in the context of rise in water intake and triggering factors [7-9]. In addition to a low-salt diet, elderly individuals with hypertension or heart failure can additionally decrease the amount of protein they consume, which may impair their water

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excretion. Hyponatremia is periodic and varies with the seasons due to diminished renal function, increased sodium losses, decreased consumption of salt, and higher fluid intake. Among all the other electrolyte imbalances, hyponatremia is the commonest in the elderly, and even more so among those who are hospitalized [10]. Hyponatremia is when the amount of sodium in the blood is less than 135 mEq/L (135 mmol/L). It is thought that about 7% of healthy older people have blood sodium levels of 135 mEq per L or less. The prevalence among in-patients may only be higher [11]. Despite the high prevalence, there is little awareness regarding the serious implications and clinical consequences of hyponatremia. The clinical presentation of patients with hyponatremia varies from mild symptoms like lethargy (22.5%) to vomiting (314%) and neurological manifestations such as seizures and altered sensorium (10.4%) [12, 13]. Hyponatremia has been linked to bad things happening to older people. A study of 4,123 elderly people found that 16% of those diagnosed with hyponatremia died in the hospital, while only 8% of individuals with the illness did [14]. The magnitude of this problem is immense and an end to it is nowhere in sight. With a greater proportion of population reaching the age of 60 years and most living longer (due to advanced healthcare facilities), a greater number of individuals are likely to encounter hyponatremia and face its associated morbidity and mortality. There was a scarcity of recent published evidence pertaining to this important matter and research is therefore necessary to explore the matter in depth and assess the frequency and outcome of hyponatremia in the elderly so that we might understand the situation better. This research hopes to fill this knowledge gap. Thus, the objective of the study was to determine the frequency and outcome of hyponatremia in elderly patients admitted at Liaquat University Hospital, Hyderabad.

METHODS

The sample size for this descriptive case series was determined using the WHO formula and was 207 elderly in-patients who were treated at the Department of Medicine at the Liaquat University of Medical and Health Sciences in Jamshoro between the months of August 2019 and February 2020 on individuals who were over 60 years, patients from both sexes, and a history of fatigue, vomiting, or convulsions were among the eligibility requirements for the study. The criteria for exclusion for the study were those who did not agree to take part in the trial, as well as patients who had pseudo-hyponatremia. The informed permission of each and every elderly in-patient was obtained prior to the recruitment process, and the non-probability consecutive sampling method was utilized. A venous blood sample measuring 2 cc was drawn into a syringe with a capacity of 5 cc, and it was then delivered for analysis of the serum electrolyte (sodium) level. After doing an examination on the specimen, a senior pathologist who has more than five years of relevant work experience was given the responsibility of writing the final pathology report. Hyponatremia, a blood sodium level of below 135 mEq/L, mild = 130-134 mmol/L, moderate = 125-129 mmol/L, and severe beneath 129 mmol/L, an elderly person as 60 to 80 years while the recovered (improved) outcome as normalization of blood sodium level (above 135 mEq/L) within 7 days of hospitalization whereas the death outcome as demise of the individual (no sign of existence, both pupils fixed and dilated, no heartbeat or breathing, no blood pressure readings recorded). The information was gathered through the use of pre-structured surveys, which had questions concerning fundamental biodata, sociodemographic particulars, and inferences drawn from history taking, clinical examination, and laboratory tests. The researcher was responsible for covering any and all costs associated with laboratory investigations that were pertinent to this study. During the course of the research project, strict confidentiality was upheld, and informed consent was collected in languages that were either nationally or regionally prevalent (depending on the circumstances). All of the procedures were carried out in accordance with medical ethics. SPSS version-20.0 was used to do the analysis on all of the patients' data. When it came to qualitative data, we computed both the frequency and the percentage (%), but when it came to quantitative variables like age, we computed the mean and the standard deviation (SD). The stratification process was carried out while the post-stratification chi-square test was carried out on the variables that were categorical and a p-value of less than ≤0.05 was regarded as being significant in statistical terms.

RESULTS

The average age of the group was 69.00 ± 5.00 while 61.8% of the group was made up of men and 38.2% was made up of women. The mean duration of hospitalization was 5 days (±3 SD). Hyponatremia was present among 59 (28.5%) of the inpatients (43 males and 16 females), out of which a majority (45) recovered. A majority (61.8%) of the sample comprised of males i.e., 128 patients, while females constituted a minority (38.2%) i.e., 79 patients. A greater proportion (nearly 3/4th) of the study participants hailed from urban areas (78.3%). Hyponatremia was present among a considerable proportion i.e., 28.5% of the patients. Among the patients with hyponatremia, the severity was categorized most commonly as moderate, followed by severe and lastly mild. Recovery (in 7 days) was achieved in less than a quarter of the sample. Adverse outcome (mortality) was noted in 18% of the patients. The severity of

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hyponatremia increased with increasing age and more common among males. The results are presented in Table 1-6.

Table 1: Prevalence of hyponatremia V/S age

Age (Years)	Hyponatremia (n = 59)		p-value
	Yes	No	
Up to 65 (n = 51)	08 (15.7%)	43 (84.3)	<0.05*
66 – 70 (n = 79)	18 (22.8%)	61 (77.2%)	
71 – 75 (n = 62)	24 (38.7%)	38 (61.3%)	
76 – 80 (n = 15)	09 (60%)	06 (40%)	
Total (207)	59 (28.5%)	148 (71.5%)	

Table 2: Severity of hyponatremia V/S age

Age (Years)	Severity of Hyponatremia		
	Mild	Moderate	Severe
Up to 65 (n = 08)	04 (50%)	03 (37.5%)	01 (12.5%)
66 – 70 (n = 18)	02 (6.1%)	11 (61.1%)	05 (27.8%)
71 – 75 (n = 24)	04 (16.7%)	12 (50%)	08 (33.3%)
76 – 80 (n = 09)	01 (11.1%)	02 (22.2%)	06 (66.7%)
Total (59)	11 (18.6%)	28 (47.5%)	20 (33.9%)

Table 3: Prevalence of hyponatremia V/S gender

Gender	Hyponatremia		p-value
	Yes	No	
Male (n = 128)	43 (33.6%)	85 (66.4%)	> 0.05
Female (n = 79)	16 (20.3%)	63 (79.7%)	

Table 4: Severity of hyponatremia V/S gender

Gender	Severity of Hyponatremia		
	Mild (n = 11)	Moderate (n = 28)	Severe (n = 20)
Male (n = 43)	08 (18.6%)	21 (48.8%)	14 (32.6%)
Female (n = 16)	03 (18.7%)	07 (43.8%)	06 (37.5%)

Table 5: Outcome (recovery Vs mortality) among study population

Variables	Frequency (%)
Recovery	
Achieved	45 (76.30%)
Not Achieved	14 (23.70%)
Mortality	
Yes	11 (18.60%)
No	48 (81.40%)

Table 6: Prevalence of hyponatremia V/S spectrum of comorbidity

Comorbidity		Hyponatremia	p-value
Pulmonary Tuberculosis (n = 18)	Yes	02 (11.1%)	< 0.05
	No	16 (88.9%)	
Chronic Liver Disease (n = 41)	Yes	15 (36.6%)	> 0.05
	No	26 (63.4%)	
Congestive Cardiac Failure (n = 13)	Yes	07 (53.8%)	> 0.05
	No	06 (46.2%)	
Acute Cerebrovascular Accident (n = 28)	Yes	03 (10.7%)	< 0.05
	No	25 (89.3%)	
Obstructive Airway Disease (n = 21)	Yes	02 (9.5%)	< 0.05
	No	19 (90.5%)	
Hypertension (n = 77)	Yes	17 (22%)	> 0.05
	No	60 (78%)	
Diabetes Mellitus (n = 64)	Yes	14 (21.9%)	> 0.05
	No	50 (78.1%)	
SIADH (n = 34)	Yes	09 (26.5)	> 0.05
	No	25 (73.5%)	

DISCUSSION

Hyponatremia is a common and serious entity among the elderly in-patients. In parallel with increased prevalence of people reaching the age of 60 years, the prevalence of hyponatremia is also believed to be increasing, worldwide. This descriptive study was performed to evaluate the frequency and outcome of hyponatremia among elderly patients [15]. Hyponatremia may affect people of all ages. However, published evidence states that the elderly individuals are most affected by the condition [16]. This research observes a similar trend. The average age of the people in the sample was 69.00 ± 5.00 years. Looking into the gender paradigm, it is revealed that there was a predisposition towards the male gender with 61.8% of the sample comprising of males while the remaining 38.2% being comprised of females. Literature review reveals that there is conflicting evidence on the matter with some suggesting that the condition is more common in females than in males, while others reporting that more elderly females are admitted for hospital care around the world [17, 18]. Additionally, a greater proportion of the male patients were found to be suffering from hyponatremia than the female patients even when weighed against their individual frequencies, suggesting that males may be more at risk of developing hyponatremia than their female counterparts. Literature too reports synonymous findings [19]. In this research, 78.3% of the study participants belonged to urban areas, while the remaining 21.7% hailed from rural background. Several studies on the prevalence of individuals admitted for hospital care have demonstrated the importance of residence on the likelihood of needing hospital care [20, 21]. Our findings, backed by research, show that the incidence of hyponatremia rises with age and sex [22]. These results corroborate other published research linking hyponatremia to an elevated disease burden risk [23, 24]. Our study found people who had medical issues that require them to take drugs that have been linked to hyponatremia. Our findings corroborate previous research linking the use of thiazides, ACE inhibitors/ARBs, SSRIs, TCAs, carbamazepine, and lamotrigine to hyponatremia. This, though a unique approach is supported by the findings of studies that take a more in-depth approach [25, 26]. It had been difficult to determine if hyponatremia is only a sign of illness progression or whether hyponatremia is actually detrimental to hospitalized patients, despite the fact that both hyponatremia and its implications have been linked to negative outcomes. Hyponatremia has been shown to be a

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proxy for root pathology instead of an independent harmful condition, according to recent evaluations of small inpatient populations with hyponatremia. Although we do not investigate the root causes of the undesirable results we observe, we do aim to find some sort of correlation in our study [27-29]. We also show that those with hyponatremia with no other known medical problems have a higher mortality rate than those with the same demographics with normonatremia. Hyponatremia has been associated with a significantly higher likelihood of mortality in all participants, even after taking into account age, sex, comorbidities, and other factors which may affect death rates. This suggests that there is an adverse effect of a chronic hypotonic state above that of the underlying illness. Similar findings have been seen in other studies [30, 31]. Smaller studies conducted recently on older individuals in community settings have found similar links between hyponatremia and all-cause death. Our research is one of very few to show that hyponatremia is clinically significant and increases the risk of death in a large in-patient group of the elderly [32, 33]. Our findings add to the increasing amount of proof that mild hyponatremia is not benign, and they call attention to the need for more research into the association among chronic hyponatremia and adverse outcomes, as well as the possibility that increased monitoring for hyponatremia in ambulatory healthcare environment as well as therapy of these individuals may improve outcomes [34, 35]. The hyponatremia was observed as 11.1%, 24.7% and 51% in the study by Jastaniah *et al.*, [36], Zhang *et al.*, [37] and Jain *et al.*, [26] whereas the mortality was observed as 11.7%, 17.4% and 19% in the study by Zhang *et al.* [37], Ioannou *et al.*, [38] and Shapiro *et al.*, [39]. In the study by Dash *et al.*, the most prevalent comorbidity was hypertension (63%), and the presence of multiple comorbidities was associated with hyponatremia (p=0.001) [40]. Even though the longer hospital stays (p=0.001) and a greater death rate was not possible to demonstrate (p=0.699). Using a public hospital provided us with many benefits, one of which was an extensive group that was generally representative of the population. However, our study was limited by time and only measured serum sodium once, so the results do not reflect shifts in clinical practice. Because blood osmolality was not monitored, pseudo-hyponatremia and dilutional hyponatremia had to be detected by indirect means. The general prevalence of hyponatremia was reduced by excluding participants with pseudohyponatremia and dilutional hyponatremia from the subset of individuals with hyponatremia. However, this did not substantially alter the general statistics.

CONCLUSIONS

It is possible, after giving the matter significant thought, to reach the conclusion that hyponatremia affects a sizeable percentage of older persons and the condition may lead to adverse outcomes.

Authors Contribution

Conceptualization: HA, IK
Methodology: HA, MKS, SJ
Formal Analysis: HA, MAL, IK, MKS
Writing-review and editing: HA, MAL, MKS, SJ, SR, SZAS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Nurses' Knowledge Regarding Nursing Process and Barriers in its Application

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ABSTRACT

Nursing process increases patients' satisfaction and enhances the quality of care provided to patients according to their needs. **Objective:** To determine the level of knowledge of nurses regarding nursing process and barriers in its application. **Methods:** The current study used cross-sectional study design for this research project. A self-administered questionnaire to be used to record responses of 80 nurses working in three different teachings hospitals in Peshawar through convenient sampling technique. Frequencies and percentages mean and standard deviation were analyzed through SPSS-20.0 as descriptive statistics. The study was approved by institutional review board while informed consent was taken from each participant. **Results:** Eighty staff nurses (N=80) completed the survey, where female were in majority (72.5%) In knowledge section, 70% participants answered it as a five-step process which is correct. Of the total, 73.75% answered true by considering the assessment as the data collection part of the nursing process. Moreover, 68.75% participants have a satisfactory knowledge who answered correctly to consider the goals as a part of Planning. 82.50% replied they have access to equipment's for provision of nursing care while 17.50% has no access to equipment were the barriers in the implementation of nursing process. **Conclusions:** The study concluded that nursing process is a tool that are implemented for quality care, and most of the participants of the study have knowledge about the nursing process, while lack of facilities for smooth implementation of nursing process was barrier faced by the respondents.

INTRODUCTION

The Nursing Process represents the quality of care which provided by nurses to the patients according to their needs. It consists of planning of nursing actions, performing those actions, recording them and evaluating patient's condition upon the bases of care delivery. The nursing profession requires a systematic high level of critical thinking with actions which is linked to nursing process; a tool for problem solving [1]. It is an important element both in professional nursing practice and nursing education curriculum [2]. Nursing process is a tool for systematic thinking which helps to assess and identify patients need, help to select appropriate interventions and evaluate the situation either the same care action should keep continued or need some new action plane [3]. The nursing process has been used by nurses to provide quality care by systematizing their thoughts and actions and delegate them effective and efficiently to the nursing team. It is a useful problem-solving method which identifies the actual and potential needs of the patients. It is included both physical and mental health [4]. The patient's individual physiological, psychological, sociological, and spiritual requirements are the subject of the nursing assessment. A

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patient's successful evaluation begins with this first step. This process necessitates the collection of both subjective and objective data. Using an age- or condition-appropriate pain scale, vital signs like temperature, respiratory rate, heart rate, blood pressure, and pain level are taken as part of the assessment. By allowing the formation of a nursing diagnosis, the assessment identifies the patient's current and future care requirements. The nurse helps to prioritize interventions and care by recognizing both normal and abnormal patient physiology [5, 6]. The purpose of the initial nursing assessment is to determine the parameters of the assessment and the responsibilities necessary to plan and provide the patient with appropriate, individualized care [7-9]. To provide care to patient the nurses are responsible for their care by assessment, investigation of problems, and to take required steps for the patient like other health professionals [10]. Therefore, nursing process needs both physical resources and materials for each organization to enables its implementation with the aim to enhance health outcome of the patients [11]. There is a need to integrate the nursing process into clinical care in every hospital, healthcare facility, and in the community at large. However, none of the procedures are actually carried out in a systematic manner because it is always thought to be difficult and time-consuming. The nursing process enables nurses to priorities the requirements of specific patients and treats them as such, rather than based on a medical diagnosis [12]. The nursing process always takes the perspective of the patient, guarantees high-quality, personalized care, and encourages patients to get involved at all stages of the procedure. Similar to doctors, nurses also benefit from increased job satisfaction and professional advancement. The nursing process establishes the parameters of nursing practice and adds to the profession's autonomy [13, 14]. Every day, there is a growing need for high-quality nursing care. The nursing process, which is the most important tool for putting nursing knowledge into practice, will be the solution to this demand. The study was conducted with the aim to determine the level of knowledge of nurses regarding nursing process and barriers in its application.

METHODS

The current study design was Cross-sectional, Descriptive, which was conducted three tertiary care hospitals of Peshawar (North-west general Hospital, Rehman medical institute, and Hayatabad medical complex). The study was conducted from June 2022 to August 2022. The study population was nurses working in these three Tertiary Care Hospitals of Peshawar, so considering all the nurses as population using 95% confidence level, having 5% margin of error, and 80% prevalence the total sample size was 88, so due to incomplete data of the 8 respondents the sample size that was consider for statistical analysis was 80 using convenient sampling technique. Nurses who education is diploma and graduation and working on clinical site, supervisor and head nurse/team lead was the inclusion criteria, while nurses who work on director or manager post or having less than one-year experiences was excluded from the study. To initiate the process of data collection, the study was approved by institutional review board, and then permission for data collection from all the three studies setting was granted. As a primary investigator I visited these hospitals in morning, evening and night shifts to have the data collected. For data collection a pre-test questionnaire was used that contain two parts: Part A Contains: Demographic variables included details about the Age, Gender, Education Level, Professional experience of participants. Part B Contains: It had 12 items with a different response option about the knowledge regarding the nursing process and perceived barriers faced by the nurses while applying the nursing process. Frequencies and percentages were calculated for categorical variables, while mean and standard deviation was calculated for continuous variables as descriptive statistics through SPSS-20. The study was approved by institutional review board, for each participant, proper information was given regarding the aim and objectives of the study and their informed consents were taken. Then the self-administered questionnaires were given to them for filling. We made sure that their inputs are kept confidential and anonymous. They were assured that their participation is voluntary and they could withdraw from the study anytime.

RESULTS

In the present study the total number of students was n=80. The Table 1 shows that the number of female respondents was higher (72.5%) compare to male participant (27.5%). The majority of participants was single (60%), graduate (47.5%) in education, diploma nurses (78.8%) in professional education, and private sector nurses (63.8%) among institutional status. The first question from the participant was asked that who the founder of the nursing process concept was. Majority of the participants (68.75%) answer that Florence nightingale, which was wrong. Only 25% answer correctly that Lydia Hall was the founder who gave the concept of nursing process.

Table 1: Demographic Data of the Participants

Categories		Frequency (%) n=80
Gender	Male	22 (27.5%)
	Female	58 (72.5%)
Marital status	Married	32 (40%)
	Single	48 (60%)
Education	Matric	20 (25%)
	Intermediate	22 (27.5%)

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	Graduation and above	38 (47.5%)
Professional education	4 years BSN	17 (21.2%)
	Diploma in nursing	63 (78.8%)
Institutional status	Public sector	29 (36.2%)
	Private sector	51 (63.8%)
Nursing school	Government nursing school	40 (50%)
	Private nursing school	40 (50%)
Working unit/ Wards	Surgical	21 (26.2%)
	ICU/CCU/NICU	22 (27.5%)
	Medical	37 (46.2%)
Current position	Supervisor	6 (7.5%)
	Head nurse / Team leader	17 (21.2%)
	Charge nurse	57 (71.2%)
What is nursing process?	Critical thinking technique	8 (10%)
	Systematic problem-solving method	30 (37.5%)
	Help nurses to develop patient care	39 (48.8%)
	Others	3 (3.8%)

Table 2 demonstrates the knowledge of the participant regarding operationalize nursing process. 93.7% answer that intervention play important role in nursing process, 90% were assured regarding the application of nursing process, 67.5% respond positively that we document as we implement nursing process, 82.5% answer that they utilize the equipment required for nursing process, 75% answered that they apply steps in a timely manner, 78.7% answered that their organization support nursing process, and 83.7% responded that Hugh number affect the implementation of nursing process.

Table 2: Knowledge about Nursing Process

Question	Yes	No
Intervention is an important part of nursing process?	93.7%	6.3%
Do you have any confidence to apply nursing process?	90%	10%
Do you document when apply nursing intervention?	67.5%	32.5%
Do you access to equipment's required for nursing care?	82.5%	17.5%
Are you managing your time to apply all the steps of nursing process?	75%	25%
Does your institution support in applying nursing process?	78.7%	21.3%
Does the maximum number of patients affect the application of nursing process?	83.7%	16.3%

Another question was asked where the majority of the participant (75%) learn nursing process during their college training, followed by learn in clinical setup (17.5%), while (6.25%) answer that they learn in seminar and only 1.25% answered that they learn from other sources. As shown in Table 3, three items were asked to identify the knowledge of the responded regarding the steps of nursing process. 1st question was regarding that data collection belong to what step, majority of the nurses (73.75%) answer that it belongs to assessment. In next item it was asked that problem identification belong to which step, majority of the nurses (45%) answer correctly. In last item it was asked about the step that contain short- and long-term goal, majority of the nurses answer correctly (68.75%).

Table 3: Knowledge of nurses regarding the steps of nursing process

Variable	Assessment	Diagnosis	Planning	Intervention	Evaluation
Data collection is considered in which step of nursing process?	73.75%	20%	0	6.25%	0
Patient problem is identified in which step of the nursing process?	42.50%	45%	0	5%	7.5%
Short term and long-term goals are the part of which step in nursing process?	15%	8.75%	68.75%	0	7.5%

DISCUSSION

Research by various scientists in nursing community has proved that the systematic approach of nursing process enhances clients' satisfaction and the quality of care provided. Indeed, nursing process ensures that every patient gets the best care through application of the best practices in an integrated way [15]. To implement nursing process in this holistic approach, one needs to understand the importance and introduction of this concept [4]. When asked about the definition and basic concept of nursing process, only 37.75% respondents in our study agreed that the systematic problem-solving method. Broad majority of the participants answered that it helps in patients care but didn't agree to the point that it is a systematic approach. They also got their answer wrong about the pioneer of nursing process. Only 25% of our study participants knew that it was Lydia Hall who introduced the concept of nursing process back in 1955. Although, the nursing profession is an established systematic high level of critical thinking; a tool for problem solving, many in our study participants don't utilize this process to improve their level of critical thinking [1]. According to 66.25% participants they were not applying nursing process due to several reasons. 15.00% were not applying due to no proper format, 13.75% have time constraints, while 5.00% replied they have no supervision to documentation. If the nursing process is not properly considered and applied, patients may not get the quality care they need. Researchers have argued that the understanding and application is not only important to maximize patients benefit, it is also important to improve the outcome of nursing education [2, 12]. Quality nursing care is provided by Nursing process is a tool for systematic thinking which helps to assess and identify patients need, help to select appropriate interventions and evaluate the situation either the same care action should keep continued or need some new action plane [3]., In the current study very few (6.25%) in our respondents have

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known about the six processes. Many (23.75%) had misconception as NP having four steps. Majority participants (70%) answered it as a five-step process which is satisfactory. It is encouraging that 75.00% participants were able to manage their time to follow steps of nursing process and 25.00% are unable to do. It is much better than a study done elsewhere which establishes the fact that knowledge about the nursing process and its performance varies from place to place. In a study it was stated that among 200 participants 90.5% reported that they have only heard about nursing process and 61% are unable to follow N.P. Response of our study participants with regards to carrying out the right steps of nursing process is much significant than the study quoted here [4]. There could be many factors influencing nurses' adherence to the practice of nursing process. Personal interest and discipline as well as organizational environment have a role to play in the practice of nursing process [16]. A study conducted in Ethiopia reveals that 90% of the respondents had poor knowledge about nursing process [3], while a study in north Ethiopia report that 88.7% of the respondents were knowledgeable [17]. Other studies report that in Psychiatric hospital the most (92%) of the respondent's possessed good knowledge [18]. Another study illustrates that half of the nurses working in critical care didn't learn about nursing process before positing [19]. Our study shows that 78.75% participants replied that their organization supports them in application of nursing process which shows a positive result. 21.25% responded that organization has no contribution in application of nursing process. This trend in organizational support shows a similar trend in the practice of nursing process. Better knowledge leads to improved practices. A study reported that insufficient knowledge affects 24.0% to fully carryout the nursing process. That study shows that learning of nursing process should continue from nursing colleges to entire professional journey i.e. on training and on-site learning of the nursing process [20]. This is not the case in our study participants. Majority of our study participants learnt nursing process from their training institute (75%) while 17% learnt from their clinical setups. Only 6.25% had learnt from seminar/workshop which is much less and can be improved through organization training sessions on site in forms of seminars and workshops for on job nurses. Also, if frequent exposures are not provided for onsite learning and continued on job training, professionals' attitude to nursing process declines with time [17]. Accessibility to equipment has very important role in provision of quality and standardized nursing care. Among our study participants 82.50% replied they have access to equipment's for provision of nursing care while 17.50% has no access to equipment. Resource barriers were reported by 67.6% nurses in another study [15]. Very economical resources like stationaries, linens and record maintenance arrangements can have a very significant effect on provision of quality care, through affecting the smooth implementation of the nursing process [15]. Nurses who have sufficient knowledge regarding nursing process practice put more impact on the health of nurses compare to those nurses who have not satisfactory knowledge [21]. High number of patients affects the ability of nurses to apply nursing process. In our study, we came to conclusion that 83.75% participants had faced workload as barriers to implementation of nursing process. A similar trend is shown by another study which shows that the highest perceived barriers with regards to implementation of NP was work load, which was reported by 81.1% of the study participants [15]. 27.50% participants in our study replied that they are attending more than 20 patients per shift, while 17.50% reported; attending 10-20 patients per shift. This number understandably affects their capacity to fully follow implementing all the steps of NP. Similarly, our study participants also hinted towards lack of time and administrative difficulties as reason for poor implementation of nursing process. Similar reports are made in another study, which showed that 68.2% nurses face lack of time as a barrier in implementation of NP while and 62.8% reported about administrative barriers when it comes to implementation of NP [15].

CONCLUSIONS

Based on the findings, the study established that the majority of the nurse's knowledge regarding the founder of the nursing process was average. Regarding the steps of the nursing process, the knowledge was satisfactory, while the majority of the participants didn't know the number and sequence of steps involved in the nursing process. The study also concluded that departmental workload, lack of facilities, and required physical resources are barriers to the implementation of the nursing process.

Authors Contribution

Conceptualization: ZJ
Methodology: GS
Formal Analysis: AS
Writing-review and editing: ZJ, GS, NB, JI, AS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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Original Article

Stone Clearance Rate Between Extracorporeal Shock Lithotripsy (ESWL) V/S Retrograde Intrarenal Surgery (RIRS) in Patients with Lower Calycx

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ABSTRACT

One of the techniques used most frequently to treat urolithiasis is shockwave lithotripsy (SWL). Extracorporeal shock wave lithotripsy (ESWL) and retrograde intra-renal surgery (RIRS) are recommended treatments for inferior calyceal (IC) calculi measuring 1-2cm. **Objective:** To compare the rate of stone clearance between extracorporeal shock wave lithotripsy (ESWL) and Retrograde Intrarenal Surgery (RIRS) in patients with lower calycx calculi. **Methods:** The randomized control trial of six months was conducted at LUH Jamshoro. Informed consent was gained when the procedure, risks, and advantages of the study were explained. The patients were divided into one of two groups at random: group A (ESWL) or group two (RIRS). A week later, the patient underwent a contrast-enhanced computed tomography (CT) scan, and the kidney stone was noted as having been removed. **Results:** The group A's mean age (SD) was 46.50 ± 14.73 whereas group B's mean age (SD) was 42.37 ± 16.07. The stone clearance was observed in 13 (43.3%) of group A's cases compared to 1 (3.3%) of group B's, with a highly significant p-value of (p=0.0001). **Conclusions:** In terms of stone removal among patients with lower calycx, a significantly significant difference among the use of extracorporeal shock wave lithotripsy and retrograde intrarenal lithotripsy was seen.

INTRODUCTION

The third most frequent condition affecting the urinary tract is urolithiasis. Open stone surgery is no longer as common due to the development of lithotripsy using shock waves and minimally invasive techniques like endoscopic surgery [1]. Among urologic patients, urinary stones are a significant cause of illness and distress. The first-line therapeutic techniques for the therapy of ureteral stones now considered by many are ureteroscopy and shock-wave lithotripsy, although the precise function of laparoscopic ureterolithotomy is still unclear [2]. The pain that urolithiasis patients experience, together with job loss and morbidity, have serious socioeconomic repercussions [3]. With the potential for problems, interventional nephron-lithotripsy (PCNL) is regarded as the gold standard for treating big and/or difficult kidney stones [4]. Retrograde intrarenal surgery (RIRS), also known for its adaptable uretero-reno scopy (fURS), is not as invasive, has fewer side effects, and is particularly helpful in patients with complex kidney anatomy, those taking anticoagulants, and those who have bleeding diathesis [4, 5]. The two major least-invasive therapeutic stone removal methods available today for kidney stones between 1 and 2 cm in diameter are the use of extracorporeal shock wave lithotripsy (ESWL) or retrograde intrarenal surgery (RIRS). The therapy cycle and

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reduced calyceal calculi in the kidney are longer with ESWL, despite the fact that its effectiveness is still unknown. With the introduction of holmium laser lithotripsy, contemporary flexible ureteroscopes, and its inherent orifice transluminal endoscopic surgical origin, RIRS has been gaining favor among urologists and becoming a commonly accepted alternative to ESWL in the therapy of renal stones. However, it's still uncertain which modality is better, and the debate rages on [6]. The study of Vilches *et al.*, reported the stone clearance rate between ESWL & RIRS as (0% v/s 42.3%) [7]. whereas Kumar *et al.*, found as 73.80% vs 86% [8]. Bas *et al.*, reported 86.5% vs 91.5% stone clearance rate [9] while another study documented the stone clearance rate to be 67.7% vs 86.5% in ESWL & RIRS groups [10]. Two different studies noted the stone clearance rates between ESWL and RIRS groups to be 76% vs 73.68% and 48.5% vs 83% respectively [11, 12]. Extracorporeal lithotripsy with shock waves (ESWL), which achieves average stone-free rates (SFR) of about 80% [13], is generally agreed to be the preferred treatment for kidney stones smaller than 2 cm. However, considering the limited effectiveness of ESWL when removing stones in such a position, with an SFR of 40-62% [14], Lower-pole kidney stone treatment is a disputed area in endourology. In contrast, percutaneous nephrolithotomy (PCNL), with a rate of 90–100% in this patient population, results in an improved SFR in treating lower-pole stones. Unfortunately, the adoption of this approach in these situations is constrained by its higher risk of complications, perioperative morbidity, hospital days, anesthetic requirements, and expense [14, 15]. In this setting, flexible ureteroscopy (URS) has been steadily gaining ground over the past fifteen years for the management of renal calculi thanks to technological advancements that have led to improved visualization devices (digital camera), larger the distal deflecting angles, the efficient intracorporeal laser lithotripsy, and different techniques for the elimination of stones with a smaller diameter [16]. Retrograde intrarenal surgery (RIRS), which is a substitute for the management of lower-pole renal stones, has an SFR that is equal to or better than ESWL, according to comparative studies against other techniques, in prospective research on calculi less than 1 cm and retrospective research on calculi among 10 and 20 mm being available [17, 18]. Although studies have compared the extracorporeal shock wave lithotripsy (ESWL) versus retrograde intrarenal surgery (RIRS) for the treatment of lower calycx. Consequently, it is crucial to contrast these two methods. The goal of this study was to provide an efficient and pragmatic surgical technique for surgical decision making to reduce the complications. Therefore, this study was designed to assess statistically significant difference between these two techniques to generate local data and further strategies could be made to improve the outcome in such patients by adopting the superior approach as first choice of treatment in future Thus, the objective was to compare the stone clearance rate between extracorporeal shock wave lithotripsy (ESWL) v/s retrograde intrarenal surgery (RIRS) in patients with lower calycx.

METHODS

The randomized control trial of six months (from June 14, 2022 to December 13, 2022) was conducted at Department of Urology, LUMHS, Jamshoro. By using W.H.O sample size calculator using stone clearance rate (0% v/s 42.3%) 7 RIRS versus ESWL, Power of Test (1-β) = 90%, level of significance (1-α) 5% then the estimated sample size came out to be n=15 in each group. But we took n = 30 patients in each group in order to meet the statistical assumption of normality thru non-probability, consecutive sampling. The inclusion criteria of the study were patients between age group 20-60 years, both gender and the patients with stone size ≤ 1 cm and the patients presented with lower calycx and underwent surgery while the exclusion criteria were culture positive (urine c/s > 10% c/c), patients with abnormal coagulopathy state (increased PT & PTT), patients recently using NSAIDs, lactating or pregnant women, upper urinary tract anatomy such as horseshoe kidney, ectopic kidney and pelvi-ureteric junction obstruction and axial skeletal abnormality such as scoliosis and kyphosis. Prior to taking part in the trial, all subjects who met the inclusion criteria and presented themselves to the Department of Urology at LUMHS, Jamshoro, gave their consent. After describing the potential benefits and hazards of the surgery to each patient and close relative in advance, everyone received a written consent. Predesigned proforma recorded age, gender, contact number, and admission date. Before operation, a comprehensive history and physical exam were done. Patients were blinded and randomised to group A (ESWL) or group B (RIRS) using computer-generated sequential numbers in sealed envelopes. Electromagnetism powered ESWL. Fluoroscopy targeted the stone and 3000 shock waves were transmitted at 60–90 per minute. Shock wave energy was increased until patients were comfortable with stone fragmentation. To optimize ESWL, all patients were properly hydrated. Fluoroscopy was used occasionally during the treatment to check stone cleavage and retarget. Nursery was used. All patients received weight-based analgesia in supine posture. All patients were discharged with an oral painkiller and specific alpha-1 D adrenergic blocker to promote stone clearance. After preventive antibiotics, RIRS patients had general Anaesthesia lithotomy. Aseptic cystoscopy and hydrophilic guide wire 0.038 inch coiled in kidney. Fluoroscopy was used to pass C

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arm ureteral access sheath through guide wire to pelvis and perform retrograde pyelogram to assess anatomy. Start irrigation with flexible scope (6.5Fr tip and 7.5Fr base). DJS passed after holmium laser 30W laser fibre vaporized the stone. Contrast CT after 1 week showed renal stone removal. A custom proforma captured the data. The study was relevant, targeted, and employed suitable exclusion criteria to control bias and confounders. SPSS version 26.0 input and analyzed the data. Qualitative variables were computed using frequency and percentage, whereas numerical variables were calculated using mean ± standard deviation. ESWL and RIRS stone removal rates were compared using chi-square test. The two groups were contrasted by age, gender, and residential status using suitable Chi-square / Fisher's exact test to evaluate how this affected outcome with $p \leq 0.05$ was consideration for significance.

RESULTS

In order to contrast the stone clearing rate among extracorporeal shock wave lithotripsy (ESWL) vs. retrograde intrarenal surgery (RIRS) for individuals with lower calycx, a total of 60 patients 30 in both groups as group A (ESWL) and group B (RIRS) were included in this randomized control trial. Group A's mean age (SD) was 46.50 ± 14.73 whereas group B's mean age (SD) was 42.37 ± 16.07. The age, gender, and residence status were broken down in order to assess the statistical difference in significance between the two groups (Table 1-4).

Table 1: Comparison of stone clearance between groups n=60

Group	Stone Clearance		p-value
	Yes	No	
Group A (N=30)	13(43.3%)	17(56.7%)	0.0001
Group B (N=30)	1(3.3%)	29(96.7%)	

Applied Chi-square test

Table 2: Stratification of age group with stone clearance between groups n=60

Age Group [In Years]		Stone Clearance		p-value
		Yes	No	
20 – 40 (N=26)	Group A	1(9.1%)	10(90.9%)	0.423
	Group B	0(0.0%)	15(100.0%)	
>40 (N=34)	Group A	12(63.2%)	7(36.8%)	0.001
	Group B	1(6.7%)	14(93.3%)	

Applied Fisher's exact test

Table 3: Stratification of gender with stone clearance between groups n=60

Gender		Stone Clearance		p-value
		Yes	No	
Male (N=36)	Group A	9(52.9%)	8(47.1%)	0.002
	Group B	1(5.3%)	18(94.7%)	
Female (N=24)	Group A	4(30.8%)	9(69.2%)	0.067
	Group B	0(0.0%)	11(100.0%)	

Applied Fisher's exact test

Table 4: Stratification of residential status with stone clearance between groups n=60

Residential Status		Stone Clearance		p-value
		Yes	No	
Urban (N=33)	Group A	8(42.1%)	11(57.9%)	0.005
	Group B	0(0.0%)	14(100.0%)	
Rural (N=27)	Group A	5(45.5%)	6(54.5%)	0.027
	Group B	1(6.3%)	15(93.8%)	

Applied Fisher's exact test

DISCUSSION

The third most frequent condition affecting the urinary tract is urolithiasis. Open stone surgery has lost some of its utility due to minimally invasive treatments like endoscopic surgery and the development of lithotripsy using shock waves. Among urologic patients, urinary stones are a significant reason for morbidity and distress. The first-line therapeutic techniques for the therapy of ureteral stones now considered by many are ureteroscopy and shock-wave lithotripsy, although the precise function of laparoscopic ureterolithotomy is still unclear. In the case of a failed ureteroscopy and ureteric stones where open surgery is being considered, laparoscopic ureterolithotomy is predominantly appropriate. Laparoscopic ureterolithotomy has been proven in numerous trials [19-21] to be a safe and successful choice for treating ureteral stones, either as a main procedure for big impacted crystals or as a salvage procedure when shock wave lithotripsy or ureteroscopy failed. One of the most painful diseases, urolithiasis has an average lifetime incidence of 10%, albeit this varies depending on demographic shifts [22]. Although the kidney is the most common site, the entire urinary tract can host it. Among the treatment options are extracorporeal lithotripsy with shock waves (SWL), interventional nephrolithotomy (PNL), mini-PNL, flexible ureterorenoscopy (F-URS), laparoscopy, and open surgery. Medical attention and observation are further options. Due to advancements in endourologic technology, open surgery is currently only used to treat 1-2 percent of kidney stones [23]. Kidney stones are among the most common disorders seen in urology practices. In recent years, urological practices have tended to be minimally invasive, with one of the milestones of minimally invasive treatments being percutaneous nephrolithotomy (PCNL). Open surgery still has an option in the form of shock wave lithotripsy. Despite the fact that PCNL has the best success rate of first-line therapies, its comparatively higher invasion and rate of complications have led to a quest for alternate treatments [24]. It quickly came into the spotlight when retrograde intrarenal surgery was introduced. The results of our investigation are comparable to those of several studies carried out globally.

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In our study, mean age in group A (ESWL) was 46.50 ± 14.73 and group B (RIRS) was 42.37 ± 16.07 years. Another study noted mean age as 33.1 ±1.3 and 33.4 ± 1.4 years [8]. In the study of Bas *et al.*, the mean age of the patients was 46.4 ± 15.1 and 47.2 ± 14.2 years [9]. Ozturk *et al.*, noted as 44.2 years in SWL and 52 years in RIRS [11]. The mean age in the study of Singh *et al.*, was 34.5 ± 13.07 (SWL) and 37.65 ± 11.8 years (RIRS) [12]. In this study, 17 (56.7%) males and 13 (43.3%) females were included in group A while 19 (63.3%) males and 11 (36.7%) females were included in group B respectively. Kumar *et al.*, reported to have 50% males in SWL group and 46.5% males in RIRS group [8]. As per the study of Bas O, *et al.*, there was 53.84% males in group I and 63.82% males in group II [9]. The study of Ozturk *et al.*, recorded to have 123 (55.65%) males and 98 (44.35%) females in SWL group while 22 (57.89%) males and 16 (42.11%) females in RIRS group [11]. There were 57.14% males and 42.86% females in SWL while 22 (62.85%) males and 13 (37.15%) females in RIRS [12]. In present study, in comparison of both groups, stone clearance was noted in 13 (43.3%) in group A whereas 1 (3.3%) in group B having highly significant p-value i.e. (p=0.0001). The study of Vilches *et al.*, reported the stone clearance rate between ESWL & RIRS as (0% v/s 42.3%) [7], Whereas Kumar *et al.*, found as 73.80% vs 86% [8]. Bas *et al.*, reported 86.5% vs 91.5% stone clearance rate [9] while another study documented the stone clearance rate to be 67.7% vs 86.5% in ESWL & RIRS groups [10]. Two different studies noted the stone clearance rates between ESWL and RIRS groups to be 76% vs 73.68% and 48.5% vs 83% respectively [11, 12]. In the study by Saygın *et al.*, the stone-free clearance for the lower calyx stones in ESWL and RIRS was 33.3% and 83.3% respectively [25] while in the study by Rasheed *et al.*, [26] the post ESWL, 99 (68%) patients were found to be stone free and 47 (32%) patients remain suffered with residual stones whereas in the study by Rehman *et al.*, [27] the stone clearance rate after RIRS was found to be 78.67% and on the other hand by contrast it is observed as 96.88% with less effective ESWL for lower pole renal stones identified by Sabnis *et al.*, [28] although the findings of the former study by Saleem *et al.*, [29] shown the success rate for stone clearance in ESWL was 65.5% and is consistent with the current study.

CONCLUSIONS

In terms of stone removal among patients with lower calycx, a significantly significant difference comparing the use of extracorporeal shock wave lithotripsy and retrograde intrarenal lithotripsy was seen.

Authors Contribution

Conceptualization: ZHR, KQS
Methodology: ZHR, SM, SAS
Formal Analysis: ZHR, KQS
Writing-review and editing: A, SM, SAS, FQS, SZAS

All authors have read and agreed to the published version of the manuscript.

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Original Article

Navigating the Research Landscape: An In-Depth Analysis of Challenges Encountered by Public and Private Medical and Dental Undergraduate Students

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ABSTRACT

Understanding the challenges experienced by undergraduate students in different educational environments is crucial for navigating the evolving research landscape effectively. **Objective:** To review the challenges faced by undergraduate students enrolled in public and private sector dental and medical colleges in Khyber Pakhtunkhwa, Pakistan's. **Methods:** The study used a cross-sectional design and a tailored questionnaire that was distributed to undergraduate students in both sectors to gather data. Time limits, knowledge and research abilities, the availability of mentoring and training, institutional support, and language difficulties were covered by the questionnaire. The chi-square test and descriptive statistics were used to analyse the data. **Results:** Key findings include research engagement is low, particularly in the private sector. Time restrictions are a significant barrier that are particularly severe in the private sector. Significant barriers include a lack of research abilities and information, as well as inadequate mentoring and training programs. Particularly in the public sector, there is a dearth of institutional support. Language obstacles are typically not very severe. The chi-square test confirms a significant difference in challenges between public and private sector students. **Conclusions:** Both public and private sectors have low levels of research engagement, with the private sector having a larger non-participation rate. Both students in the public and private sectors encounter significant challenges, with private sector students identifying time restraints and a lack of information and research skills as the most significant barriers. Lack of readily available mentorship and training programs, as well as institutional support, is a significant barrier for students in both sectors.

INTRODUCTION

Globally, there have been significant pedagogical transformations utilized in the medical and the dental profession educational systems [1-4]. In order to foster an in-depth comprehension of the medical and dental sciences, integrated curricula have been employed at the educational institutions to bridge the gap between basic and clinical sciences. Along with the adjustment, problem-based learning strategies have become more widely used, emphasizing the application of knowledge in real-world situations and fosters students' critical thinking skills [5]. Understanding the challenges experienced by undergraduate students in different educational environments is crucial for navigating the evolving research landscape effectively. This study focuses on specific challenges encountered by undergraduate students enrolled in medical and dental colleges in public and private sector in the Khyber Pakhtunkhwa Pakistan. The policymakers and medical education experts can employ the findings to establish tailored interventions and support systems to enhance the learning experience once they have an in-depth understanding of the distinctive challenges that students in multiple fields encounter. There isn't a lot of research available concerning the challenges encountered by medical and dental students in

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KP or the comparison between public and private institutions there. However, certain studies provide useful information. In a regional study (2021) conduced in Saudi Arabia on the challenges and obstacles experienced by medical and dental students, found that the majority of students displayed a favourable attitude toward and moderate behaviour of research. This finding further suggests that training and support services be organized to overcome the difficulties and barriers in conducting research [6]. Another study by Aziz *et al.*, (2020) investigated the challenges faced by medical students in Pakistan, including factors such as examination stress, high workload, and family related problems, highlighted the need for better support systems and mentorship programs [7]. In the context of KP, a study conducted by Waheed *et al.*, (2021) examined the challenges faced by undergraduate students in the province, published in The Professional Medical Journal, their research focused on factors such as knowledge, attitude, inadequate faculty support, and difficulty in conducting research because of inadequate capacities. These findings underscore the need for targeted interventions to address the challenges specific to undergraduate students in KP. It is crucial to compare the challenges faced by students at public and private colleges in the context of KP. Public institutions deal with a lack of resources, poor facilities, lack of competent and experienced staff, lack of opportunities for research, and inadequate interaction between staff and students [8-10]. On the other hand, private institutions may experience difficulties such as high tuition fees, financial constraints, and access to clinical training opportunities [11]. Policymakers and educators gained a thorough understanding of the diverse experiences that students have at both private and public colleges through analysing these issues, allowing them to develop tailored plans of action to fulfil their needs. This study intends to add value to the existing body of knowledge by undertaking an in-depth review of the difficulties faced by undergraduate medical and the dental students in KP. The policymakers, educators, and institutions can use the findings as a valuable resource for developing targeted measures that address the specific issues that students at both public and private universities experience, eventually enhancing undergraduate medical and dental education in KP, which aid in the development of a skilled and adaptable healthcare staff, boosting healthcare outcomes for the people of the province.

METHODS

The cross-sectional study was conducted from April to June 2023 to document the difficulties encountered by undergraduate students enrolled in the public and private sector colleges in Khyber Pakhtunkhwa, Pakistan. Convenience sampling was used as the sample method since it was appropriate to including all easily accessible participants within the intended audience. All academic years' undergraduate students at KP's public and private sector colleges enrolled in medical and dental colleges were considered eligible for the study. No particular requirements existed for exclusion. A customized questionnaire was developed to collect data regarding the challenges faced by undergraduate medical and dental students when conducting research. The questionnaire covered various aspects related to research and publication, including the availability of research resources, mentorship and guidance, time constraints, research skills, and publication barriers. A senior faculty member was selected from each of Khyber Pakhtunkhwa's public and private medical and dental colleges in order to ensure extensive engagement. The faculty members were included in a WhatsApp group that was used for communication during the research. The questionnaire was uploaded on Google Forms, and the faculty members were given access to it by way of a WhatsApp group. The questionnaire was distributed out to the undergraduate students by the faculty members. They either visited each class in every academic year in person or distributed the link to the survey through relevant WhatsApp groups for students. Before completing the survey, the respondents gave their informed consent, and their identities were kept confidential. The intended use of the data was made very clear. To encourage participation, two reminders were sent to the students through the faculty members. The reminders emphasized the voluntary nature of participation and the importance of their contribution to the study. It was made explicit that the information will be used for publication, group data presentations, and policy decisions aimed at enhancing the research environment in undergraduate medical and dental institutions. Descriptive statistics were used to summarize the responses. To analyse the significance of differences in challenges between different groups, the Chi-square test employed.

RESULTS

In total, 58 men and 138 women participated in the study. The public sector had a very balanced gender distribution in terms of sector representation, with 43 males and 52 females. With 15 males and 87 females participating in the study from the private sector, there was a substantial gender disparity. When assessing the gender distribution within the particular programs, there were 11 male and 28 female students enrolled in the study from public sector Bachelor of Dental Surgery (BDS) programs. In the private sector, there are 15 males and 80 females enrolled in the study from the BDS program. Regarding Bachelor of Medicine, Bachelor of Surgery (MBBS), 32 males were

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enrolled in the study from the public sector, compared to 7 females and 0 males from the private sector. The study found that 32% of students in the public sector engaged in research projects throughout their academic careers, as opposed to 68% of those who did not. 63% of our participants from the private sector had not participated in research activities, compared to 37% of them. Regarding the challenges that medical and dental students face when conducting research, the study revealed a number of significant findings. Time constraints were found to hinder 29% of medical and dental students in the public sector with major obstacles, 35% with moderate challenges, and 36% with small challenges. In contrast, data from the private sector showed that more students (50%) viewed time restrictions as severe obstacles, 31% as moderate challenges, and 19% as minor challenges. A sizable portion of students from both sectors struggled with their lack of knowledge and research skills. 46% of respondents said it was a major hurdle in the public sector, 16% thought it was a moderate challenge, and 38% thought it was a minor challenge. Similar to how the public sector perceived it, 47% of the private sector saw it as a significant issue, 22% as a moderate challenge, and 31% as a minor challenge. The study also considered how readily available mentoring and training are, both of which are crucial for conducting research. In the lack of mentorship and training, 52% of students perceived a major problem, 33% a moderate problem, and 15% a minor obstacle in the public sector. In the private sector, 44% believed it was a minor obstacle and 6% thought it was significant. Another significant obstacle cited by students was the lack of institutional support for research efforts. 64% of respondents said it was a significant obstacle in the public sector, 14% thought it was a moderate challenge, and 22% thought it was a minor challenge. It was considered as a significant issue in the private sector by 42%, a moderate challenge by 25%, and a minor challenge by 12%.

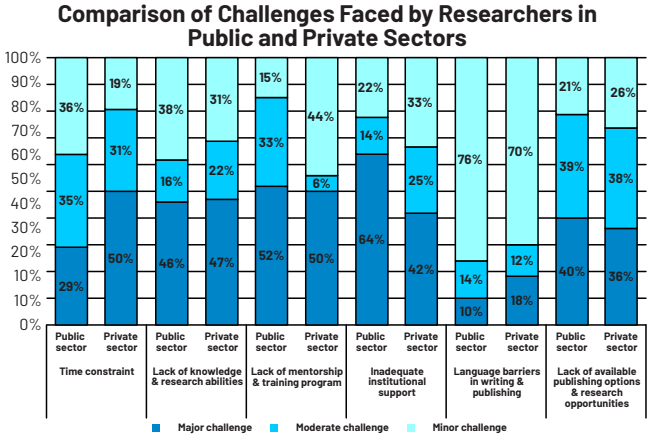

Figure 1: Comparison of Challenges Faced by Researchers in Public and Private Sectors

Language barriers were discovered to be generally minor obstacles when it came to writing and publishing research papers. Only 10% of students thought it was a huge challenge in the public sector, 14% thought it was a moderate challenge, and 76% thought it was a small challenge. Similar to how the public sector felt, the private sector saw it as a small difficulty for 70%, a moderate challenge for 12%, and a major challenge for 18%. The data analysis was conducted using Microsoft Excel. The chi-square test was conducted to compare challenges of public vs private sector undergraduate students, yielding a chi-square test statistic of 79.966. Given that the computed p-value was less than 0.001, the result was considered to be highly significant. In conclusion, the chi-square test results showed a significant difference in the challenges faced by undergraduate students in institutions in the public and private sectors (p 0.001), indicating that there is a variation in the challenges faced by students between these two sectors.

DISCUSSIONS

The study found that 32% of students in the public sector and 37% of students in the private sector had engaged in research projects throughout their academic careers. Low levels of student involvement in research, is a reflection of the challenges involved in fostering a research culture in undergraduate medical and dental programs. The study found that 32% of students in the public sector engaged in research projects throughout their academic careers, as opposed to 68% of those who did not. In the private sector, 63% of participants had not participated in research activities, compared to 37% who had. The low research engagement among students, particularly in the private sector, reflects a significant challenge in fostering a research culture in medical and dental undergraduate education. Study conducted by Nadeem (2018), found a similarly low level of research engagement among medical students in Pakistan and recommended measures be taken to promote research opportunities and enhance student awareness [12]. For both students in the public and private sectors, time constraints were identified as an important obstacle. Only 29% of students in the public sector agreed, compared to 50% of students in the private sector who thought it was a significant challenge. These results underline the need of flexible involvement in research on the part of undergraduate students, as well as the need for efficient time-management strategies. Due to a research-focused academic environment, funding availability, experienced faculty, significant research prospects, and the perceived competitive advantage of research experience, private sector students—who typically have a demanding academic schedule, lots of

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work, and little time for flexible scheduling—have a greater propensity for conducting research [13]. These findings highlight the need for effective time management strategies and flexibility in research involvement for undergraduate students. Similar findings were observed and time constraints including other factors have been identified as a major barrier to dental students' participation in research [14, 15]. The findings highlight the need for considering and incorporating set apart time for research activities into the curriculum to help students balance their research obligations with their academic responsibilities. Inadequate knowledge and research skills viewed as a significant impediment by 46% of respondents in the public sector and 47% of respondents in the private sector. These findings emphasize the importance of including research mentoring and training programs in undergraduate curricula [16-18]. Regional studies have also emphasized the challenges that dental students face in developing their research abilities [12, 16, 18]. The study also found that students in both sectors struggled since mentoring and training programs were not readily available. In the public sector, students thought it to be an important concern (52%), whereas in the private sector, they thought it to be a minor problem (44%). The undergraduate institutions ought to consider about establishing mentorship programs, seminars on scientific writing, and innovative techniques to enhance students' abilities to conduct research and provide them with the resources to promote research culture [15]. Students from the public and private sectors concurred that the lack of institutional support was a significant barrier. It was cited as a major problem by 42% of respondents in the private sector and a significant barrier by 64% of respondents in the public sector. These results highlight the importance of institutional support for research initiatives at educational institutions. Studies emphasise on how crucial institutional support and resources are for students who want to participate in research [12, 15, 19, 20]. Institutions should set aside funds to create specialized research divisions or departments that support research. Institutions should set aside funds to create specialized research divisions or departments that support research.

CONCLUSIONS

The impact of time constraints is felt in both the public and private sectors, yet students within the private sector experience more pronounced challenges. Inadequate knowledge and research skills hinder students' engagement in research endeavours, limiting their participation. Both sectors struggle to provide accessible mentorship and training opportunities, with the public sector facing particularly notable obstacles in this regard. Institutional support for students is lacking in both sectors, though it's perceived as a more significant hindrance in the public sector. Research involvement among undergraduate students remains modest in both sectors, with the private sector exhibiting a higher percentage of non-participation compared to the public sector.

Authors Contribution

Conceptualization: WQ, AN
Methodology: WQ, AN
Formal Analysis: WQ, AN
Writing-review and editing: WQ, AN

All authors have read and agreed to the published version of the manuscript.

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Original Article

Assessment of Quality of Nurses' Work Life in Tertiary Care Hospitals of Peshawar, Khyber Pakhtunkhwa, Pakistan

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ABSTRACT

Nurses have been considered the backbone of health care delivery system, but regretfully saying that very limited attention has been paid to the development of nursing throughout the world. **Objective:** To assess the Quality of Nurses Work Life (QNWL) in Tertiary Care Hospitals of Peshawar Pakistan. **Methods:** Descriptive cross-sectional approach was applied to assess the QNWL in Lady Reading Hospital and Hayatabad Medical Complex Peshawar. Sample consisted of 240 participants via selection of multistage random sampling technique. Brook QNWL questionnaire was adopted for data collection and then validated and pre-tested it. **Results:** The sample data consisted of 79.20% female 20.80% male participants, out of which 46.02% were married and 53.98% un-married. The sample consisted of 94.25% Charge Nurses, 4.42% Head Nurses and 1.33% Nursing Managers in the study. The mean score of QNWL in this study was 162.24 ± 21.16. Furthermore, 3.98% nurses reported Low QNWL, 92.48% Moderate QNWL and 3.54% High QNWL in the sample. There was found an association between employment type with home life and work load subscales of QNWL whereas, home life has also an association with gender, marital status and salaries. **Conclusions:** It was concluded from the study findings that majority (92.48%) nurses have moderate QNWL in selected hospitals. Nurses home life and work load subscale of QNWL is affected by some demographics. Therefore, the study findings suggest recommendations in home life and work load management for policy makers in order to enhance QNWL in Tertiary Care Hospitals of Peshawar Pakistan.

INTRODUCTION

Nurses have been considered the backbone of health care delivery system [1]. American Nurses Association in 2014 reported that there are three mostly repeated debate of nurses that are relating to manpower, overtime and workplace protection [2]. A decade before, nursing development has been evolved in health care system in many western countries due to role diffusion, stressed working environment, aging and low workforce [3, 4]. Therefore, QNWL is a key indicator for an organization to hold on brilliant staff to ensure standardized care [5]. Nurses were more prone to psychological and physical stress in contrast to other health profession due to longer period of work [6]. It has been reported that 63.25% nurses in China and 46% of Canadian new nurses feels mild to moderate level of employment related burnout [7]. According to a report, nearly 20% of nurses give resignation annually [8]. A survey in 11 countries has shown that 2-5 out of 10 nurses leave their job in a year or in five years [9]. Some of the mentioned factors like high work burden, low support, career development, poor governing, incentives and work safety has an impact on QNWL [10]. Furthermore, 50% of nurses were not satisfied from their

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employment because of poor QNWL due to scarcity and huge resignation, which is a global burning issue [11]. Additionally, employee work in rotation for continuity of care has negative impacts on health care personnel and is associated with various disorder [12]. QWL is an important component of human health and its concept has been rooted in multidimensional phenomenon [13]. A study by Morsy and Sabra in Egypt analyzed that nurses QNWL was not satisfactory due to demographic variables like gender, age, educational level and salary [14]. Another study by Borhani *et al.*, that in Iran that nurses were more productive when their QWL was conducive for their work and hence contributed to the good quality of health care delivery system [15]. A study by Sadat *et al.*, in Iran predicted that 56.70% nurses had good QWL, and 43.30% low QWL [16]. A study by Kelbiso *et al.*, in Ethiopia determined that 67% dissatisfaction in QWL and was greatly affected by different factors like educational level, working department, salary [10]. Similarly, a study in India analyzed that QWL of private hospital nurses was interconnected with the health of nurses, pleasure at work, work context and work environment [17]. A study by Lee *et al.*, in Thailand reported that 56.1% might leave their job, 2.5% resigned one year later and this resignation was due to having no self-respect, self-reliance and low QWL [18]. A study by Kowitlawkul *et al.*, in Singapore explored that support of family, friend and having soundness was very necessary for good QOL [19]. A study by Suleiman *et al.*, in Jordan concluded that the average score for QWL was 140.15 ± 28.34. A study by Esteban in Spain concluded that health care setting, marital status, working in shift and locality of the center had impact on Compassion satisfaction [20]. A study by Ibrahim Alzamel *et al.*, in Malaysia analyzed negative partial effect between QNWL and turnover intention due to organizational commitment [21].

METHODS

Descriptive cross-sectional study was conducted in tertiary care hospitals of Peshawar. The OpenEpi software for sample calculation was used. Using 95% confidence interval, 5% margin of error, 25% hypothesized prevalence and a population of 1400 registered nursing staffs working at the mentioned above tertiary care hospitals. The calculated sample size was 240 register nurses working in these tertiary care hospitals. The study was completed in a one-year period starting from June 2020 to May 2021. Approval was obtained from Khyber Medical University Advance studies and Research Board, and from medical director of each hospital. Written informed consent was administered to the participants prior to data collection. The primary data were collected through structured questionnaire from 240 nurses through multistage random sampling technique in Lady Reading Hospital and Hayatabad Medical Complex Peshawar Khyber Pakhtunkhwa. Those nurses whose experience was less than 3 months or not willing to participate and or working at higher management level excluded in the study.

RESULTS

SPSS Version-22.0 was used for analysis of the data. In descriptive statistics, mean and standard deviation was calculated for continuous variables and frequency and percentage calculated for categorical variables. The inferential statistics include the use of t-test and one-way ANOVA between dependent variable (QNWL) and independent variables (Selected demographics). All the result was considered statistically significant when the p-value < 0.05 at 95% confidence interval. The mean age of the participants was 31.80 ± 3.49 years. There were 53.98% married and 46.02% un-married participants in the study. Furthermore, 64.16% participants have general nursing diploma education, followed by 29.20% Bachelor of Subject in Nursing, 2.21% Master of Subject in Nursing and 4.42% have highest education other than nursing. Figure 1 described that 79.20% female and 20.80% male participated in the current study.

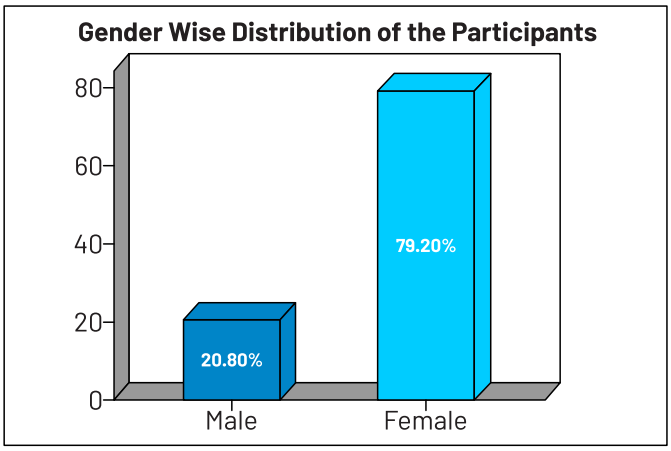

Figure 1: Gender of the Participants

Furthermore, the study consisted of 49.12% civil servants (Permanent), and 50.88% Medical Teaching Institution job (Contractual) employees participated. It was analyzed that 84.51% participants were responsible for the care of their elderly parents'/family members and 15.49% responded that they were not responsible for it. Moreover, 94.25% participants responded that their duty were in shift rotation and 5.75% not rotated in shift. Similarly, 18.58% nurses participated from Medical Surgical wards, followed by 18.14% from Critical Care Units, 15.93% from Emergency department, 13.28% from Pediatrics wards, and 8.41% from Obstetric /Gynae department and the remaining 25.66% staffs from rest of the departments. The above graph showed that 94.25% were Charge Nurses, 4.42% Head Nurses and 1.33% Nursing Manager participated in the

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study. Study findings revealed that 85.84% participants responded that there was mandatory shift rotation and 14.16% rotation in shift on voluntary basis. There was no incentive for shift rotation. It was analyzed that 34.07% participants have salary below 50,000 PKR, 46.90% salary in between 51,000-70,000 PKR, and 19.03% salary above 70,000 PKR. The mean score of QNWL was 162.24 ± 21.16. In this graph, 3.98% participants responded that they have low QNWL, 92.48% moderate QNWL, and 3.54% high QNWL as shown in the Figure 2. In this stage, the t-test and one-way ANOVA was applied for an association between the score of quality of nurses' work life its sub scales score and selected demographics.

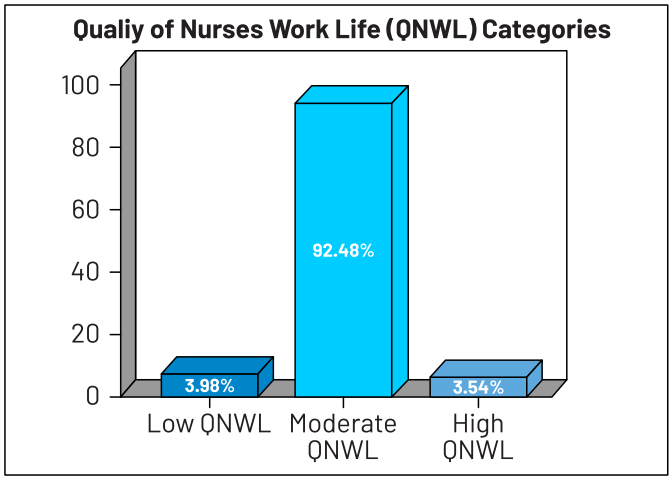

Figure 2: QNWL Categories

T-test was applied in the Table 1 for an association between QNWL total score, score of its subscales and demographics variables. It was analyzed that there not an association found between QNWL total score and gender of the participants, however, a statistically significant (p-value < 0.002) association was found between QNWL subscale of home life dimension and gender. Similarly, the QNWL subscale of home life dimension was statistically significant (p-value < 0.000) with respect to marital status as shown in the above table-1. In the next step, employment status was putted for an association with QNWL total score as well as its sub scales. There was not an association found between QNWL total score, however, an association found between QNWL sub scale of home life dimension (p-value < 0.001) and work load dimension with respect to an employment status as described in the above table-01. Finally, there was not found an association between QNWL total score and its sub scales with respect to shift rotation.

Table 1: t-test for an association between quality of nurses' work life, its subscales and demographic variables

Variable	N (%)	Home Life	Work Design	Work Context	Work Load	Total Score
Gender						
Male	47(20.79)	29.57±5.03	38.42±6.74	78.89±10.68	17.72±3.41	164.61±22.88
Female	179(79.20)	27.19±4.53	38.25±6.30	77.81±10.22	18.36±3.28	164.62±20.71
T	-	3.126	.166	.621	-1.151	.813
p	-	.002*	.868	.536	.254	.419
Marital Status						
Un-Married	104(46.01)	28.94±4.86	38.13±6.05	77.89±10.51	17.79±3.21	162.76±21.21
Married	122(53.98)	26.62±4.35	38.41±6.67	78.16±10.16	18.59±3.36	161.80±21.19
T	-	3.74	-.332	-.195	-1.81	.341
p	-	.000*	.740	.845	.070	.733
Employment Types						
Permanent	111(49.11)	26.65±4.59	38.13±6.47	77.47±10.69	19.09±3.13	161.36±21.80
Contractual	115(50.88)	28.68±4.66	38.43±6.32	78.58±9.92	17.40±3.28	163.10±20.59
T	-	-3.29	-.352	-.805	3.95	-.618
p	-	.001*	.725	.421	.000*	.537
Shift Rotation						
Voluntary	32(14.15)	26.78±4.00	37.81±6.44	80.18±9.77	17.34±2.96	162.12±19.09
Mandatory	194(85.84)	27.84±4.83	38.36±6.38	77.68±10.37	18.37±3.35	162.26±21.53
T	-	-1.174	-.451	1.27	-1.63	-.035
p	-	.224	.654	.204	.103	.972
***p<0.05 Significance Level and at 95% Confidence Interval**						

The above table 2 was plotted for an association between QNWL total score, score of its subscales and demographic variables. One-way ANOVA was used between dependent variable i.e. QNWL and independent variables i.e. selected demographics. Sequentially, in the first phase and second phase, an educational level and current nursing position were putted for an association with QNWL total score and its subscales score. There was neither QNWL total score nor its subscales score correlated with an educational level and current nursing position respectively as described in the above table 2. Finally, current salary status was putted for an association between QNWL total score and its subscales score. There was an association (p-value < 0.000) found between only home life dimension and current salary status as shown in the above table-02.

Table 2: One-way ANOVA between quality of nurses' work life, its sub scales and demographic variables

Variable	N (%)	Home Life	Work Design	Work Context	Work Load	Total Score
Educational Level						
Diploma in Nursing	145(64.15)	27.80±4.49	38.55±6.20	78.15±9.93	18.38±3.35	162.89± 20.47
Bachelor Degree in Nursing	66(29.20)	27.25±5.48	37.28±7.01	77.25±11.99	17.77±3.22	159.57± 24.41
Master Degree in Nursing	05(2.21)	27.60±2.40	39.20±3.76	79.60±3.28	18.40±4.82	164.80± 7.72
Others	10(4.42)	29.00±3.71	40.60±5.16	80.70±4.21	18.90±2.64	169.20±6.77
F	-	.462	1.095	.390	.664	.777
p	-	.709	.352	.760	.575	.508
Current Position						
Charge Nurse	213(94.24)	27.79±4.81	38.36±6.53	77.72±10.49	18.22±3.39	162.10±2.176
Head Nurse	10(04.42)	26.60±2.59	37.20±3.04	83.50±3.83	18.501.58	165.80±5.00
Nursing Manager	03(01.32)	23.66±1.52	36.66±3.51	82.33±3.21	17.66±1.52	160.33±3.05
F	-	1.41	.254	1.77	.076	.157
p	-	.246	.776	.172	.927	.855
Current Salary Range						
Below 50,000 PKR	77(34.07)	29.10±4.50	38.48±6.67	79.03±10.65	17.90±3.80	164.53± 22.16

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51,000-70,000 PKR	106(46.90)	27.57±4.62	38.61±6.22	77.84±9.92	18.53±2.96	162.57± 20.25
Above 70,000 PKR	43(19.02)	25.44±4.56	37.13±6.26	76.72±10.66	18.04±3.19	157.34± 21.23
F	-	8.902	.867	.731	.883	1.62
p	-	.000*	.422	.483	.415	.200
*p<0.05 Significance Level and at 95% Confidence Interval						

DISCUSSIONS

In the current study, the mean score of total QNWL was 162.24 ± 21.16. The current study used Brooks Quality of Nurses Work Life Survey (BQNWL) tool for data collection. Similar findings were reported by a study conducted by Suleiman *et al.*, in Jordan having mean score of total QNWL was 140.15 ± 28.34 while using BQNWLS [22]. Similar to the current study result, a study had total mean score of QNWL was 146.56±37.02 and was considered moderate level of QNWL [23]. A study by Macairan *et al.*, findings showed that the quality of nurse's work life in public school of Philippine was high [24]. Furthermore, it was high due to constitutionalism at work, opportunities at work, social integration at work and working condition. A study by Sirisub *et al.*, also concluded that there was overall moderate level of quality of work life among Thai nurses [25]. Furthermore, quality of work life was observed good in work environment, collaborative communication and nurse perception. The result of the Karaaslan and Aslan study was similar to the current study as there was observed moderate level of QNWL among Turkish Prisoner nurses [26]. Kelbiso *et al.*, study result was similar in total score of QNWL as it was moderate level and was strongly affected by educational status, working environment, working unit and monthly income [27]. The quality of work life subscales in current study showed that it was greatly affected in home life subscale by gender (p-value= 0.003), marital status (p-value= 0.0001), and employment status (p-value= 0.005). Similar result was also derived from the study conducted by Anon [7] on Chinese nurses and their quality of work life was greatly affected by gender, marital status, number of children, educational level, monthly income, shift work, professional title, patient to nurse ratio and finally working experience. In connection to this, a study by Lee *et al.*, showed that QWL was predicted more by intention to leave profession, intention to leave organization than intention to leave the unit [8]. Furthermore, a study by Morsy and Sabra also reported that QNWL was not satisfactory in 66.7% of the participants and there was found statistical significance between QNWL and selected demographics such as age, marital status, educational qualification, and income. Moreover, there was observed high mean score for work context subscale of QNWL. Furthermore, the result of current study was similar to Morsy and Sabra as there was highest mean score for work context sub scale of QNWL [14]. A study by Thakre *et al.*, analyzed the dimensions of quality of QNWL [28]. There was observed least mean score for work world dimension followed by work context, work home life/ work life and final for work world dimension. However, this result was contradictory to the current study as there was observed least mean score for work load followed by work design, work home life/ work life and then finally for work design.

CONCLUSIONS

It was concluded from the current study findings that 3.98% had low level of QNWL, 92.48% nurses had moderate level of QNWL and only 3.54% had high level of QNWL. Furthermore, the QNWL was greatly affected by age, income and employment status. Hence, the ultimate goal of it would be to improve the standard of care provided to the patients.

Authors Contribution

Conceptualization: TR, NS
Methodology: AA, BAS
Formal Analysis: EAK
Writing-review and editing: TR, AA, BAS, EAK, NS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Outcome of Suprachoroidal Triamcinolone Acetonide in Resistant Diabetic Macular Edema

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ABSTRACT

One of the most frequent cause of central vision deterioration in people with retinopathy due to diabetes is diabetic macular edema. Suprachoroidal injections offer a novel way of delivery for the administration of corticosteroids that may have various benefits. **Objective:** To observe outcome of triamcinolone acetonide given by suprachoroidal route for the treatment of resistant diabetic macular edema. **Methods:** A descriptive case series study which was carried out at Department of Ophthalmology, Layton Rahmatullah Benevolant Trust Hospital Multan Road Lahore from July 14, 2021 till Jan 14, 2022. A total of 60 cases meeting selection criteria was taken after taking approval from hospital ethical committee. All injections were given by a single surgeon to avoid any related bias. 30-gauge 1cc insulin syringe was used in all cases. **Results:** The study included patients aged between 30 and 70 years, and the average age was 52.73 ± 10.99 years. There were 39(65%) male with 21(35%) female cases. The average central subfield thickness before and after one month was 593.62 ± 116.87 µm and 303.55 ± 31.29 µm with statistically significantly less mean central subfield thickness after 1 month, p-value less than 0.001. The mean visual acuity after correction before and after one month was 0.81 ± 0.16 and 0.45 ± 0.03 respectively, with statistically significantly less mean optimally corrected visual acuity after 1 month, p-value less than 0.001. **Conclusions:** It was found that suprachoroidal triamcinolone acetonide is useful in managing the central subfield and optimally corrected visual acuity in resistant diabetic macular edema.

INTRODUCTION

In recent decades, there has been a gradual rise in the prevalence of diabetes, which is expected to reach 430 million by 2030 [1]. Almost all the countries in the world have shown such large increase in DM prevalence. Diabetes causes numerous macrovascular and microvascular complications, which include diabetic retinopathy (DR) [2]. Macular edema is a major consequence of numerous inflammatory and vascular retinal disorders [3]. The risk of developing macular edema in diabetic patients is very high [4]. and the most prevalent reason of central vision deterioration in diabetic retinopathy patients is Diabetes-related macular edema [5, 6]. "Resistant diabetic macular edema is defined as if patient has at least three-monthly treatment of anti-vascular endothelial growth factor injections one month apart and still have central foveal thickness ≥ 300 µm on spectral-domain optical coherence tomography" [7]. VEGF and a number of inflammatory mediators are increased in diabetic macular edema-

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affected eyes [8]. This is one of the major reasons that an effective approach is essential in management of diabetic macular edema to avoid irreversible harm to visual function [9]. Inhibitors of vascular endothelial growth factor and corticosteroids have all proved effective in treating diabetic macular edoema [8]. Dexamethasone intravitreal implant, triamcinolone acetonide, and fluocinolone acetonide intravitreal implant are the three corticosteroids that are currently on the market; nevertheless, the effectiveness of each treatment option varies considerably [8]. Administration of corticosteroids through suprachoroidal injection has provided a new route of delivery which has proved quite advantageous [10]. As a result, there has been an increase in interest in exploring suprachoroidal space for drug administration. This has also been done in order to reduce the adverse effects of intravitreal steroids, despite all this, investigators have weighed the risk-benefit ratio of using the suprachoroidal delivery method for steroids to the posterior portion [5]. Furthermore, due to the reported adverse-effects of corticosteroids such as cataract progression and glaucoma they are still regarded as the second-line of treatment, especially in diabetic macular edema cases refractory to anti-VEGF agents [11]. If a patient with diabetic macular edema does not respond well to repeated injections of intravitreal bevacizumab, the doctor can try alternative anti-VEGFs, corticosteroids, or a macular laser. However, other reasons of macular edema like those of vitreomacular traction may be evaluated via optical coherence tomography, this may suggest surgical treatment. Focal areas of leakage from microaneurysms can be adjunctively identified via fluorescein angiogram, which might be responsive to laser treatment. To date, only a few smaller published uncontrolled studies can provide some insight to compare treatment regimens for refractory diabetic macular edema and no large randomized prospective clinical trials have been done so far [12]. In individuals with residual macular edema, (CSFT >300μm) shifting from bevacizumab to three monthly injections of 0.5 mg ranibizumab has been shown to be beneficial in a 12-month prospective non-randomized trial of 43 patients) [13]. An additional investigation revealed similar outcomes [5]. In order to treat refractory DME, Shoeibi *et al.*, evaluated the effects of combining 2 mg of triamcinolone acetonide with intravitreal bevacizumab. Adding triamcinolone acetonide had no additional benefits, he concluded, despite the fact that intravitreal bevacizumab injections are effective for treating refractory DME [14]. Therefore, the goal of this study was to evaluate how well resistant macular edema in the local population is treated by triamcinolone acetonide given by suprachoroidal route.

METHODS

A descriptive case series study was done at Department of Ophthalmology, Layton Rahmatulla Benevolant Trust Hospital Multan road Lahore after approval from hospital ethical committee. The study duration was 6 months from July 14, 2021 till Jan 14, 2022. We used non-probability consecutive sampling. A total of 60 cases are estimated using mean post injection optimally corrected visual acuity at one month as 0.47 ± 0.3^{4} at 95% confidence level and as absolute precision (d) = 0. Inclusion criteria was patients having age 18-70 years, either gender reported as having resistant diabetic macular edema. Exclusion criteria was patients with macular ischemia, diagnosis of retinal vasculopathies besides diabetic retinopathy, glaucoma or ocular hypertension, vitreomacular traction, history of vitreoretinal surgery, intraocular surgery within the last 6 months, focal laser or pan-retinal treatments within the last 3 months. A total of 60 cases meeting selection criteria was collected form department of Ophthalmology, LRBT Multan road Lahore after taking an informed consent from patients. Their demographic details such as name, age, gender and contact details were taken. All injections were given by a single surgeon to avoid any related bias. 30-gauge 1cc insulin syringe was used in all cases. Additional commodities included injectable triamcinolone acetonide (TA) 40mg/ml and 24gauge intravenous branula. Before administering Supra-Choroidal Triamcinolone Acetonide, all patients were dilated, and an indirect ophthalmoscope was used for fundus examination. Only 1000 um of the insulin syringe remained visible at the branula's edge after the needle was removed from it and the branula was cut. The syringe was filled up to 0.1 ml point with Triamcinolone Acetonide. The eye was rinsed using a solution consisting of 10% povidone iodine. 5% of the solution was then applied to the fornices and left there for 30 seconds. An intraocular procedure-like drape was used to cover the eye. A point was marked in the supratemporal quadrant at 3.5mm from the limbus. After labelling, 0.1 ml of a 4 mg triamcinolone acetonide solution was instilled into the suprachoroidal region at a distance of 3.5 mm from the limbus in the aforementioned quadrant. The needle was placed at 90 degree to the sclera and with the bevel pointing backwards. To ensure minimal reflux, the needle was slowly removed, and the injection site was covered with an applicator with a cotton tip. The central artery of retina was immediately examined using indirect ophthalmoscopy, and any drug spillage in the vitreous cavity were noted. A 15-degree phacoemulsification incision knife was used to perform an anterior chamber paracentesis if the central artery of retinal was found to be occluded. One drop of a commonly used antibiotic was administered into the eye after the surgery. Premeasurement and Outcome i.e. central

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subfield thickness on OCT and BCVA on ETDRS chart was measured at one-month post injection as per operational definition. All data were collected by myself on attached Proforma. For data entry and analysis, SPSS version 25.0 was used. Mean ± S.D was calculated for age, duration of disease, before and after central subfield thickness and best corrected visual acuity. Frequency and % was calculated for categorical data like gender. Data were stratified for gender, age, duration of disease and HbA1C (controlled <7 and uncontrolled diabetes ≥ mellitus). The post-stratified paired sample t-test was used, with p-values of 0.05 or below considered notable.

RESULTS

The average age of patients was 52.73 ± 10.99 years with minimum and maximum 30 and 70 years. There were 24(40%) cases who were 30-50 years old and 36(60%) case were 51-70 years old. There were 39(65%) males and 21(35%) females. The mean duration of 5.12 ± 1.40 years, with minim 4 and 10 years. There were 46(76.7%) case who had duration of disease since ≤ 5 years and 14(23.3%) cases had duration since > 5 years. A total of 38(63.3%) patients had controlled and 22(36.7%) patients had uncontrolled diabetes. The mean central subfield thickness before and after one month was 593.62 ± 116.87 µm and 303.55 ± 31.29 µm with statistically significantly less mean central subfield thickness after 1 month, p-value < 0.001. (Table 1).

Table 1: Central subfield thickness (pre and after 1 month)

Central subfield thickness		
	Pre	At 1 month
Mean ± SD	593.62 ± 116.87	303.55 ± 31.29
Range	392.00	99.00
Minimum	407.00	251.00
Maximum	799.00	350.00

t-test = 18.962, p-value < 0.001

The average optimally corrected visual acuity before and after one month was 0.81 ± 0.16 and 0.45 ± 0.03 respectively, with statistically significantly less mean best corrected visual acuity after 1 month, p-value less than 0.001 (Table - 2).

Table 2: Best corrected visual acuity (pre and after 1 month)

Best corrected visual acuity		
	Pre	At 1 month
Mean ± SD	0.81 ± 0.16	0.45 ± 0.03
Range	0.51	0.10
Minimum	0.58	0.40
Maximum	1.09	0.50

t-test = 16.22, p-value < 0.001

When data were clustered for age, gender, duration and HbA1c, mean central subfield thickness and optimally corrected visual acuity after one month was statistically reduced in each stratum, p-value < 0.001 (Table 3 to 6).

Table 3: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to age groups (years)

Age groups (years)	Central subfield thickness	Mean ± SD	t-test	p-value
30-50	Pre	599.42 ± 131.38	10.768	<0.001**
	1 month	308.54 ± 32.39		
51-70	Pre	589.75 ± 107.91	15.753	<0.001**
	1 month	300.22 ± 30.54		
Best corrected visual acuity				
30-50	Pre	0.79 ± 0.16	9.471	<0.001**
	1 month	0.46 ± 0.03		
51-70	Pre	0.82 ± 0.16	13.211	<0.001**
	1 month	0.45 ± 0.03		

**Highly Significant

Table 4: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to gender

Gender	Central subfield thickness	Mean ± SD	t-test	p-value
Male	Pre	585.13 ± 105.38	16.717	<0.001**
	At 1 month	304.38 ± 29.70		
Female	Pre	609.38 ± 137.10	9.951	<0.001**
	At 1 month	302.00 ± 34.77		
Best corrected visual acuity				
Male	Pre	0.80 ± 0.16	12.605	<0.001**
	At 1 month	0.45 ± 0.03		
Female	Pre	0.82 ± 0.16	10.075	<0.001**
	At 1 month	0.45 ± 0.03		

**Highly Significant

Table 5: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to duration (years)

Duration (years)	Central subfield thickness	Mean ± SD	t-test	p-value
≤ equal 5 years	Pre	599.63 ± 116.06	17.152	<0.001**
	At 1 month	301.17 ± 31.27		
>5 years	Pre	573.86 ± 121.74	8.173	<0.001**
	At 1 month	311.36 ± 31.21		
Duration (years)	**Best corrected visual acuity**	**Mean ± SD**	**t-test**	**p-value**
≤ equal 5 years	Pre	0.81 ± 0.15	14.794	<0.001**
	At 1 month	0.45 ± 0.03		
>5 years	Pre	0.81 ± 0.18	6.785	<0.001**
	At 1 month	0.45 ± 0.03		

**Highly Significant

Table 6: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to HbA1c

HbA1c	Central subfield thickness	Mean ± SD	t-test	p-value
Controlled	Pre	598.84 ± 115.84	15.153	<0.001**
	At 1 month	305.84 ± 33.35		
Uncontrolled	Pre	584.59 ± 120.82	11.150	<0.001**
	At 1 month	299.59 ± 27.66		

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HbA1c	Best corrected visual acuity	Mean ± SD	t-test	p-value
Controlled	Pre	0.80 ± 0.16	11.596	<0.001**
	At 1 month	0.45 ± 0.03		
Uncontrolled	Pre	0.83 ± 0.15	12.027	<0.001**
	At 1 month	0.45 ± 0.03		

**Highly Significant

DISCUSSION

Several researches have looked into various techniques to treating diabetic macular edema (DME), a disorder that affects the retina in diabetics. Ahmadieh *et al.*, investigated the long-term outcomes of intravitreal bevacizumab, with or without triamcinolone, for refractory DME [14]. Al Rashaed and Arevalo explored the potential of combination therapy for DME, taking into account the utilization of multiple therapeutic modalities to successfully address the condition [15]. Patel *et al.*, investigated suprachoroidal drug administration using hollow microneedles, proposing a novel method for delivering drugs to the back of the eye [16]. We investigated diabetic macular edema (DME) as one of the primary reasons contributing to patients' deteriorating vision who have diabetes mellitus (DM). Diabetic macular edema (DME) is commonly associated with visual impairment in persons with diabetic retinopathy (DR). Laser photocoagulation is one way for treating people with DME. It can retain or increase visual acuity but can potentially reduce contrast sensitivity, color vision, and range of vision. The suprachoroidal region has attracted interest as a possible route for ocular medication administration. Emami-Naeini and Yiu examined different medical and surgical applications for the suprachoroidal area, emphasizing its potential for drug delivery to the posterior portion of the eye [17]. Specific investigations looked into the efficacy of suprachoroidal medication administration in the treatment of DME. Jahangir *et al.*, investigated the effect of suprachoroidal triamcinolone injection on refractory DME, whereas Yousef *et al.*, investigated the use of triamcinolone acetonide injection in cases of DME [18, 19]. Rai *et al.*, went on to highlight the suprachoroidal channel as a new medication delivery route to the back of the eye, highlighting its potential benefits for treating disorders such as DME [20]. The intravitreal injection of steroids has been demonstrated to reduce macular edema caused by various eye disorders. Lastly, Seiler *et al.*, conducted an ex-vivo study to investigate the effect and distribution of contrast medium after injection into the anterior suprachoroidal space. This work shed light on the anatomical characteristics of this drug delivery method [21]. In summary, several studies have been conducted to investigate the possibility of intravitreal and suprachoroidal medication administration for the treatment of DME. While some research looked at the long-term effects of certain treatments, others focused on the suprachoroidal space's potential as a unique drug delivery channel. The findings emphasize the importance of more research to completely comprehend the efficacy and safety of these therapy approaches for diabetic macular edema. Diabetic macular edema (DME) is one of the major causes of failing eyesight in people with diabetes mellitus (DM). Diabetic macular edema (DME) is commonly associated with visual impairment in persons with diabetic retinopathy (DR). Laser photocoagulation is one way for treating people with DME. It can retain or increase visual acuity but can potentially reduce contrast sensitivity, color vision, and range of vision. Steroid injections intravitreally have been shown to alleviate macular edema caused by a variety of eye conditions.

CONCLUSIONS

It is concluded that suprachoroidal triamcinolone acetonide in resistant diabetic macular edema is useful to manage the central subfield and best corrected visual acuity. Hence it can be used to improve patient's visual conditions and to improve their quality of life.

Authors Contribution

Conceptualization: MHJ, AA
Methodology: AK
Formal Analysis: BA, MBA
Writing-review and editing: MHJ, AA, AK, BA, MBA, FS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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