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ORIGINAL ARTICLE

Gender based differences in in-hospital complications in patients with acute coronary syndrome.

Kashif Ijaz[1], Abbad Ur Rehman[2], Muhammad Akram Asi[3], Farhan Umair[4], Naeem Asghar[5], Hafiz Rana Faiq Ilyas[6]

ABSTRACT… Objective: To determine the frequency of in-hospital complications in patients being admitted with acute coronary syndrome and also to compare the prevalence of in-hospital complications between male and female patients presenting with acute coronary syndrome. **Study Design:** Cross-sectional study. **Setting:** Faisalabad Institute of Cardiology, Faisalabad. **Period:** 01-01-2022 to 30-06-2022. **Methods:** objective of the present study was to determine the frequency of in-hospital complications in patients being admitted with acute coronary syndrome and also to compare the prevalence of in-hospital complications between male and female patients presenting with acute coronary syndrome. **Results:** Among 965 ACS patients (mean age 58.4 ± 11.5 years, range 26–92), most were over 55 years (56.7%), and males constituted 66.6%. STEMI was the most prevalent ACS type (58.1%), followed by NSTEMI (35.9%) and unstable angina (6.0%). STEMI was more common in males (60.7%) compared to females (53.1%), while NSTEMI was more prevalent in females (41.9% vs. 32.8%). **Conclusion:** This study highlights significant patterns in the presentation, complications, and gender differences among patients with acute coronary syndrome (ACS). These findings underscore the importance of gender-specific approaches in ACS management.

Key words: Acute Coronary Syndrome, Complication, Gender, In-hospital.

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INTRODUCTION

Ischemic heart disease has become the major cause of disease burden worldwide and increased incidences has been reported in low- and middle-income nations, including Pakistan.[1] Acute coronary syndrome (ACS) is defined by reduced myocardial perfusion, which encompasses unstable angina and myocardial infarction.[2] Delays in diagnosis and treatment are linked to higher morbidity and death.[2]

Gender variances in the presentation and management of acute coronary syndrome (ACS) are well known internationally.[3] Recent advancements in cardiovascular treatment have led to a decrease in cardiovascular death rates. However, some studies suggest gender differences in ACS therapy and outcomes.[4,5] While effective treatments for ACS have been developed, it is unclear how widely these tactics are employed in clinical practice.[6]

Women often live longer than males, and as the prevalence of cardiovascular disease rises with age, it is likely that preventing CVD among older women will be a significant public health concern.[7] There is speculation that increased complications in the hospital in females with acute coronary syndrome, which leads to increased mortality, are caused by their unusual symptoms and the delay in therapy.[8] A research found that in-hospital consequences in individuals presenting with acute coronary syndrome included: Left ventricular failure occurs in 5.7% of men and 9.1% of women. Cardiogenic shock occurred in 2.8% of men and 3.1% of women. Cardiac arrest is 1.7% in males and 1.7% in females.[8]

The impact of gender on mortality in acute coronary syndrome patients is unclear, and there is less data on its significance as an independent predictor of disease progression. Therefore, the objective of the present study was to determine the frequency of in-hospital complications in patients being admitted with acute coronary syndrome and also to compare the prevalence of in-hospital complications between male and female patients presenting with acute coronary syndrome.

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The gender-based difference in complications and mortality will highlights the importance of conducting more local gender-based studies that may provide useful evidence for the diagnosis and management of acute coronary syndrome.

METHODS

This cross-sectional study has been conducted in Faisalabad Institute of Cardiology, Faisalabad for the duration of six months from 01-01-2022 to 30-06-2022. Prior approval was obtained from Institutional Ethical Review Committee (letter no. 25-2019/DME/FIC/FSD, dated November 09, 2019). The sample size for the study was calculated using WHO sample size calculator keeping P=1.7%, Confidence level=95% and absolute precision=1%, the calculated sample size is 645.

All male and female patients presenting with acute coronary syndrome for the first time were recruited in the study. However, patients with prior LV dysfunction, history of any kind of arrhythmia before this hospital admission, and history of any structural heart disease were excluded from the study.

Non probability consecutive sampling was applied to recruit patients. After taking approval from hospital ethical committee, patients coming through the emergency fulfilling the inclusion criteria were enrolled and informed consent was taken. Patients were treated as per protocol of acute coronary syndrome by primary PCI/fibrinolysis or anticoagulation. Standard management was done. Complications at the time of presentation or during the hospital stay were assessed, managed and documented. All the information was collected on a specially designed proforma.

Data was entered and analyzed with the help of SPSS version 21.0. Frequency and percentages was calculated for qualitative variable. A p-value of <0.05 has been implied as significant.

RESULTS

Total 965 patients were included. The mean age of the patients was 58.4 + 11.5 years with minimum and maximum value of 26.0 to 92.0. Majority of the patients being over 55 years old 56.7% compared 43.3% were from age between 25 to 55 years. There were 66.6% male and 33.4% female. Among the type of acute coronary syndrome, (ACS), STEMI was the most common affecting 58.1% of patients, followed by NSTEMI as 35.9% and unstable angina at only 6.0% (Table-I).

TABLE-I

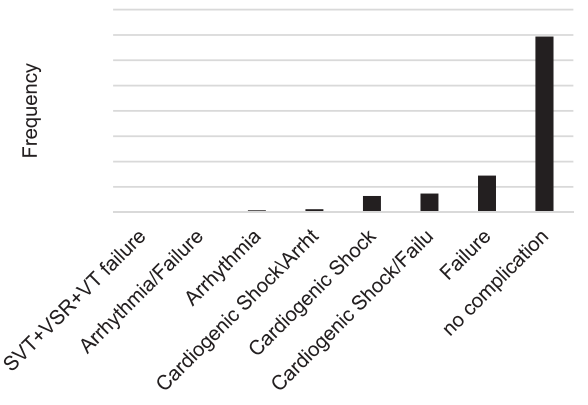
Descriptive of age, gender and type of ACS

Age	Mean (+ SD)
	58.4 + 11.5
Age Group	**N (%)**
25 to 55 years	418(43.3%)
>55 year	547(56.7%)
Gender	
Male	643(66.6%)
Female	322(33.4%)
Type of ACS	
STEMI	561(58.1%)
NSTEMI	346(35.9%)
Unstable Angina	58(6.0%)

Out of 965 patients, the majority 69.3% had no complications. Among those with complications, the most frequent was failure, occurring in 14.4% of cases, followed by cardiogenic shock/failure 7.4% and cardiogenic shock alone 6.4%. Less common complications included cardiogenic shock with arrhythmia 1.1%, arrhythmia alone 0.7%, and arrhythmia with failure 0.3%. Rare complications such as cardiogenic shock with VT, SVT, VSR, and VT failure each accounted for only 0.1% of cases (Figure-1).

FIGURE-I

Complication



Among patients aged 25 to 55 years, males had a slightly higher frequency 43.7% compared to female 42.5%, while in >55 years' age group, females were most common (57.5%) compared to males 56.3%. Although the difference between genders was not statistically significant (p=0.73). As type of acute coronary syndrome, STEMI was significantly more common in male 60.7% than in females 53.1% (p=0.01). NSTEMI was observed in a higher percentage of females 41.9% compared to males 32.8%. Unstable angina occurred slightly more common in males 6.5% than in females 5.0%. Overall, Males show a higher frequency in STEMI and unstable angina, while females have higher percentage in NSTEMI and older age group (Table-II).

Among 965 patients, males 70.9% had a higher frequency of no complications compared to females 66.1%. Failure was more common in females 15.8% than males 13.7%. Cardiogenic shock combined with failure occurred more frequently in females 9.3% compared to males 6.4%. Arrhythmia was slightly more common in males 0.9% than in females 0.3% and the remaining one as shown in table: 3 Overall, males experienced more cases with no complications, while females had slightly high number of severe complications like failure and cardiogenic shock with failure. There was no significant relationship of complications between gender (P<0.05) (Table-III).

DISCUSSION

This cross-sectional study was conducted to determine the frequency of in-hospital complications in patients being admitted with acute coronary syndrome and also to compare the prevalence of in-hospital complications between male and female patients presenting with acute coronary syndrome. Among 965 ACS patients (mean age 58.4 ± 11.5 years, range 26–92), most were over 55 years (56.7%), and males constituted 66.6%. STEMI was the most prevalent ACS type (58.1%), followed by NSTEMI (35.9%) and unstable angina (6.0%).

TABLE-II

Comparison of age group and type of ACS with gender

	Group	Male	Female	Total	P-Value
Age group	25 to 55	281(43.7%)	137(42.5%)	418(43.3%)	0.11(0.73)
	>55	362(56.3%)	185(57.5%)	547(56.7%)	
Type of ACS	STEMI	390(60.7%)	171(53.1%)	561(58.1%)	7.94(0.01)
	NSTEMI	211(32.8%)	135(41.9%)	346(35.9%)	
	Unstable Angia	42(6.5%)	16(5.0%)	58(6.0%)	

TABLE-III

Comparison of complication with gender

Complication	Gender		Total	P value
	Male	Female		
Arrhythmia	6(0.9%)	1(0.3%)	7(0.7%)	10.11(0.43)
Arrhythmia/Failure	1(0.2%)	2(0.6%)	3(0.3%)	
Cardiogenic Shock	41(6.4%)	20(6.2%)	61(6.3%)	
Cardiogenic Shock VT	1(0.2%)	0	1(0.1%)	
Cardiogenic Shock/Failu	41(6.4%)	30(9.3%)	71(7.4%)	
Cardiogenic Shock\Arrht	7(1.1%)	4(1.2%)	11(1.1%)	
Failure	88(13.7%)	51(15.8%)	139(14.4%)	
No complication	456(70.9%)	213(66.1%)	669(69.3%)	
SVT	1(0.2%)	0	1(0.1%)	
VSR	0	1(0.3%)	1(0.1%)	
VT Failure	1(0.2%)	0	1(0.1%)	

Complications were absent in 69.3% of patients. Heart Failure was the most frequent complication (14.4%), followed by cardiogenic shock with failure (7.4%) and cardiogenic shock alone (6.4%). STEMI was more common in males (60.7%) compared to females (53.1%), while NSTEMI was more prevalent in females (41.9% vs. 32.8%). Males had a higher frequency of no complications (70.9%), whereas females showed a slightly higher incidence of severe complications like failure (15.8% vs. 13.7%) and cardiogenic shock with failure (9.3% vs. 6.4%). Although there were gender differences in ACS types and complication patterns, no significant relationship between gender and complications was observed ($p<0.05$).

STEMI patients were much more likely to be male.[9] Patients with NSTEMI were more likely to be female, with a little significant difference in the prevalence of unstable angina.[10] In our study Females who were suffering from ischamic heart disease were older than males and had more comorbidities. A USA study of 78,254 AMI patients (2001–2006) found women were older and had more comorbidities. More recent USA data from 413,500 STEMI hospitalizations confirmed higher comorbidity rates in women, except for smoking and prior sternotomy. Studies from Switzerland, Germany, and the Netherlands also exhibited that ACS women were significantly older and possessed greater rates of hypertension and diabetes.[11,12,13,14,15]

Evidence-based medicine showed no significant difference in medication use between the two groups during admission. In-hospital treatment such as aspirin, ACE inhibitors, lipid-lowering agents, LMWH and PCI were consistent between female and male patients with ACS.[16] Female NSTE-ACS patients had a greater incidence of in-hospital congestive heart failure, leading to reduced administration of βblockers compared to male patients.[17]

Hao et al. found that women hospitalized for ACS had a higher unadjusted in-hospital death rate than males.[8] This difference was especially significant in patients with STEMI.[8] After adjusting for age and other clinical factors, the risk of death in women with STEMI was significantly reduced. In-hospital death rates were greater among women aged 55-64, 65-74, and ≥75 years compared to males. After adjusting for clinical profiles and acute therapies, there were no significant interactions between age categories and sex in terms of in-hospital mortality risk. Inconsistent results in subgroup and sex-age interaction analyses may be due to varying in-hospital mortality rates, age categories, and variables utilized in various research.[8]

Other variables, such as delayed hospital presentation and acute therapies, may also contribute to the reported gender disparity in STEMI fatality rates. A research found that women arrived at hospitals for STEMI treatment 1.4 hours later than males.[8] Delays in presenting with STEMI have been linked to higher risk of mortality and recurring episodes.[18] Female patients may take longer to make it to the hospital than males due to symptom misunderstanding, lack of knowledge, and impediments to treatment access.[19] Women received less acute therapies, such as DAPT and reperfusion therapy, than males. Disparities in acute care led to the higher death rate among males compared to women. A meta-analysis indicated that women's higher death rates during primary PCI were likely due to differences in baseline cardiovascular risk factors and clinical characteristics.[20]

Although, this study also has some limitations. Firstly, this is a single center study which may limit the generalizability of the findings. The patient population may not fully represent the diverse demographics and clinical characteristics seen in different regions or healthcare settings, potentially affecting the applicability of the results to broader populations. Secondly, the study did not provide long-term follow-up data to examine the evolution of complications or outcomes, which may have provided further information about the prognosis and effectiveness of therapies for ACS patients.

CONCLUSION

This study identifies significant trends in presentation, complications, and gender differences in individuals with acute coronary syndrome (ACS). STEMI appeared as the most prevalent kind, mostly affecting men, whereas NSTEMI was more common in women. The majority of patients reported no issues, however females had a greater rate of

serious consequences such as cardiogenic shock with failure. These findings highlight the necessity of gender-specific methods in ACS management. The study also emphasizes the need of early diagnosis and personalized therapy to reduce consequences. Further studies with varied demographics and longitudinal follow-ups are needed to better knowledge and outcomes for ACS patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Kashif Ijaz:** Manuscript writing.
2	**Abbad Ur Rehman:** Study design, synopsis.
3	**Muhammad Akram Asi:** Data analysis.
4	**Farhan Umair:** Results, references.
5	**Naeem Asghar:** Proof reading.
6	**Hafiz Rana Faiq Ilyas:** Finalize.

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ORIGINAL ARTICLE

Frequency, types and causes of anaemia in ischemic stroke patients admitted to medical wards of Khyber Teaching Hospital.

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ABSTRACT… Objective: To determine the frequency, types and causes of anaemia in ischemic stroke patients admitted to medical wards of Khyber Teaching Hospital Peshawar. **Study Design:** Cross-sectional study. **Setting:** Department of Medicine, Khyber Teaching Hospital, Peshawar. **Period:** 5th December 2023 till 4th June 2024. **Methods:** Convenient sample technique was used. A total 368 patients presenting with stroke were enrolled. The patients were evaluated for the type and cause of anemia. Hb <12.0gm/dl was considered the cut off for anemia. Data was analysed using SPSS version 24. **Results:** Mean age of the patients was 53.34 ± 13.29 years. Male to female ratio was nearly 1: 1. Hypertension was the most common comorbidity observed in 86 patients (23.4%). Normochromic normocytic anemia was the common type observed in 150 patients (40.7%). **Conclusion:** Normochromic normocytic anemia is the most common type of anemia in patients with ischemic stroke. Elderly female patients with underlying chronic disease like disease and prolonged illness are more likely having anemia.

Key words: Anemia Types, Hypertension, Ischemic Stroke.

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INTRODUCTION

Stroke is the second most common cause of mortality worldwide.[1] Any rapidly increasing deficit of one or both sides of the body that lasts more than twenty-four hours is referred to be a stroke. Either an ischemic or hemorrhagic stroke causes the brain's supply of blood and nutrients to be reduced in that area. It is estimated that each year, about 15 million people worldwide suffer from strokes. Of these 15 million individuals, two thirds will die and a third will become disabled. Stroke is the third leading cause of death in developing nations, after cancer and coronary heart disease, respectively. 87% of stroke cases are ischemic strokes, which are the most frequent type of stroke.[2,3]

Stroke is the primary cause of both chronic neurologic impairment and severe functional impairment globally. Slurred speech, abrupt weakening of one side (arm, face, or leg), obscured vision in one or both eyes, problems walking suddenly, and a sudden, intense headache are common clinical signs of stroke.[4] A number of possible risk factors for stroke include alcohol intake, smoking, dyslipidemia, hypertension, and—most importantly—diabetes mellitus (DM).[5]

According to Jo YJ et al.'s study, among patients who had an ischemic stroke, the most prevalent risk factor was found to be hypertension, smoking, ischemic heart disease, diabetes mellitus, hyperlipidemia, atrial fibrillation, carotid artery stenosis, obesity, and a history of stroke in the family in all age group whereas as per Safeer M et al., common risk factors in the younger group were obesity, smoking, and hypertension, and the older group's most common risk factors were diabetes mellitus, and hypertension.[6,7]

Limited research has been done on risk factors in stroke patients due to cerebral infarction in Pakistan, therefore, the current study aims to assess the prevalence of risk factors among ischemic stroke. It will help in prevention of this disease by providing awareness about the risk factors of ischemic stroke in general population. It will help physicians in better management of stroke and decrease chances of its recurrence.

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The aim of this study was to determine the frequency, types and causes of anaemia in admitted ischemic stroke patients.

METHODS

A Cross sectional study conducted at Department of Medicine, KTH, Peshawar, from 5th December 2023 till 4th June 2024. The Sampling Technique was Non – probability Consecutive technique. The WHO sample size calculator was used to determine the sample size. Previously reported prevalence of anaemia in ischemic stroke patients= 39.6%.[8] The Margin of Error: d=5%, 95 % confidence level. Expected sample size was 368. All those patients with age 40 to 70 years, both genders and patients presenting with ischemic stroke were included in study. Exclusion criteria included Ischemic stroke patients having recent blood transfusions, hemorrhagic stroke and space occupying brain lesion.

Patients were enrolled from the medical units after receiving approval from the hospital ethics board (286/DME/KMC-11/5/2022). An informed consent was obtained from each patient. Age, gender, educational attainment, monthly income, diabetes, hypertension, smoking, and obesity were among the demographic data that were recorded. Both a physical examination and a thorough history were obtained. A complete blood count, a renal function test, a liver function test, serum electrolytes, a chest x-ray, a routine examination of the stool, and a routine examination of the urine were all performed as baseline investigations (BLIs). On specially created proforma, the causes, forms, and duration of ischemic stroke were recorded.

SPSS version 23 was used to examine the data that was obtained. For quantitative characteristics like age, hemoglobin level, length of ischemic stroke, and monthly income, mean +/- SD was computed. For categorical factors such as gender, medicines used, status of BLIs, types and causes of anemia, and background medical illnesses such as diabetes, hypertension, and obesity, frequency and percentages were determined. Data stratification was used to address effect modifiers such as age, gender, length of disease, diabetes, hypertension, smoking, and obesity. A p-value < 0.05 was deemed statistically significant.

RESULTS

The mean age of our study population was 53.34 ± 13.29 years with ranged of 30 to 80 years. The mean BMI was 24.05 ± 2.6 Kg/m^2 [Table-I].

TABLE-I

Demographic characteristics of study participants

Parameters		Frequency	Percent
Gender	Male	189	51.4
	Female	179	48.6
Age in years	≤55	183	49.7
	>55	185	50.3
Diabetes	Yes	29	7.9
	No	339	92.1
Hypertension	Yes	86	23.4
	No	282	76.6
Smoking	Yes	54	14.7
	No	314	85.3
Obesity	Yes	147	39.9
	No	221	60.1
Disease duration (in months)	≤3	217	59.0
	>3	151	41.0
Anemia Type	Microcytic	144	39.1
	Normocytic	150	40.8
	Macrocytic	74	20.1
Causes Of Anemia	Iron Deficiency	157	42.7
	Sickel Cell Disease	52	14.1
	Folate/B12 Deficiency	159	43.2

Type of anemia on basis of cell size and cause of anemia with age and gender as shown in Table-II. No significant association of gender and age with types and causes of anemia.

Stratification of type of anemia and cause of anemia with obesity and duration of stroke as shown in Table-III. There is significant association of causes of anemia compared obesity and duration of stroke (P 0.000).

TABLE-II

Cross tabulation of patients` gender and age with types and causes of anemia

Risk Factors		Gender			Age (Years)		
		Male	Female	P value	≤55	>55	P-Value
Types of anemia	Microcytic	70 (48.6%)	74 (51.4%)	0.564	66 (45.8%)	78 (54.2%)	0.154
	Normocytic	82(54.7%)	68 (45.3%)		73 (48.7%)	77 (51.3%)	
	Macrocytic	37 (50.0%)	37 (50.0%)		44 (59.5%)	30 (40.5%)	
Causes	Iron Deficiency	89 (56.7%)	68 (43.3%)	0.206	77 (49.0%)	80 (51.0%)	0.974
	Sickle Cell Disease	24 (46.2%)	28 (53.8%)		26 (50.0%)	26 (50.0%)	
	B12/folate deficiency	76 (47.8%)	83 (52.2%)		80 (50.3%)	79 (49.7%)	

TABLE-III

Cross tabulation of obesity and stroke duration with types and causes of anemia

Risk Factors		Disease Duration (Months)			Obesity		
		3 or Below	More Than 3	P-Value	Yes	No	P-Value
Types of anemia	Microcytic	81 (56.3%)	63 (43.8%)	0.336	51 (35.4%)	93 (64.6%)	0.292
	Normocytic	95 (63.3%)	55 (36.7%)		62 (41.3%)	88 (58.7%)	
	Macrocytic	41 (55.4%)	33 (44.6%)		34 (45.9%)	40 (54.1%)	
Causes	Iron Deficiency	72 (45.9%)	85 (54.1%)	0.000	65 (41.4%)	92 (58.6%)	0.000
	Sickle Cell Disease	37 (71.2%)	15 (28.8%)		38 (73.1%)	14 (26.9%)	
	B12/folate deficiency	108 (67.9%)	51 (32.1%)		44 (27.7%)	115 (72.3%)	

TABLE-IV

Stratification of anemia types and causes with comorbidities (Diabetes and Hypertension)

Risk Factors		Diabetes			Hypertension		
		Yes	No	P value	Yes	No	P-Value
Types of anemia	Microcytic	19 (13.2%)	125 (86.8%)	0.000	49 (34.0%)	95 (66.0%)	0.000
	Normocytic	0 (0.0%)	150 (100.0%)		17 (11.3%)	133 (88.7%)	
	Macrocytic	10 (13.5%)	64 (86.5%)		20 (27.0%)	54 (73.0%)	
Causes	Iron Deficiency	9 (5.7%)	148 (94.3%)	0.419	32 (20.4%)	125 (79.6%)	0.135
	Sickle Cell Disease	5 (9.6%)	47 (90.4%)		9 (17.3%)	43 (82.7%)	
	B12/folate deficiency	15 (9.4%)	144 (90.6%)		45 (28.3%)	114 (71.7%)	

Cross tabulation between type of anemia, causes of anemia with obesity and duration of stroke as shown in Table-III. There is significant association of types of anemia compared obesity and duration of stroke (P 0.000), whereas no significant association compared to causes of anemia.

DISCUSSION

The most prevalent morphological kind of anemia was normocytic normochromic (40.8%) blood image, which was followed by microcytic hypochromic anemia. In contrast, the study's macrocytic normochromic anemia was the least morphologically significant kind of anemia. This study's normocytic normochromic blood picture of anemia is not surprising because it has been documented in several earlier studies conducted in Benin, Pakistan, India, and other countries.[9-11]

Additionally, compared to those of normal weight, hospitalized obese patients had a twofold increased risk of developing anemia. The outcome was consistent with research done in Austria, Pakistan, Iran, and the United States of America.[12-14]

Low-grade systemic inflammation, seen in obese individuals, is the main mechanism tying obesity and anemia together.[15] Patients with obesity have significantly higher serum levels of hepcidin and interleukin-6, which lowers their iron intake since their liver and splenic macrophages sequester iron and they absorb less of it.[15] Malnourished patients had a 2.59-fold higher incidence of anemia than normal admitted patients. The outcome was consistent with research from India and the Netherlands.[11,16] Malnutrition is associated with poor treatment tolerance, reduced quality of life, higher healthcare expenses, poverty, and medical conditions like intestinal obstruction and malabsorption syndrome.[11,17]

Patients with diabetes mellitus at the time of admission were 3.20 times more likely to have anemia. The following causes could be the cause of this: Anemia is frequently caused by bleeding, especially in the gastrointestinal tract in patients with cirrhosis and chronic liver disease.[18] A chronic liver disease may result in anemia from bleeding because of thrombocytopenia, decreased platelet activity, or a deficiency in liver produced clotting factors.[19] Additionally, hepcidin, the main regulator of iron homeostasis, is secreted by the liver making iron deficiency prevalent in individuals with advanced chronic liver disease (CLD).[20]

Compared to COPD patients, admitted patients with hypertension had an 11.2-fold increased risk of anemia. This may be because individuals with chronic kidney disease (CKD) are more likely to experience anemia due to the fact that their failing kidneys generate less erythropoietin.[11,22] Nearly half of individuals with CKD have normocytic normochromic anemia, which is caused by peritubular fibroblasts in the kidneys producing less erythropoietin than usual.[22]

Anemia was more common in patients with longer illness durations than in COPD patients who were hospitalized. The primary causes of anemia due malaria are rapid hemolysis of parasitized red blood cells.[23] This may be the result of infections raising hepcidin levels, which also exacerbate anemia. The prevalence of anemia in HIV-positive people rises as the illness progresses, leading to changes in iron metabolism, increased hepcidin, anemia of inflammation, and a persistent acute phase response.[24]

CONCLUSION

Normochromic normocytic anemia is the most common type of anemia in patients admitted with ischemic stroke in our population followed by microcytic anemia while macrocytic anemia is the least common type. Elderly female with previous comorbidities like diabetes mellitus and prolonged disease duration are more likely develop anemia. Iron deficiency is most consistent cause of anemia which is more likely in patients with underlying chronic disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Mohammad Haroon:** Conceptualization, writing, supervision.
2	**Jamal Khan:** Data curation, methodology.
3	**Irfan Ullah:** Statistical analysis.
4	**Shah Umam:** Methodology.
5	**Osama Ali Khan:** Writing.
6	**Ejaz Khan:** Data entry.

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ORIGINAL ARTICLE

Serum ferritin-based assessment of iron deficiency in individuals with β-thalassemia trait.

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ABSTRACT… Objective: To evaluate the potential coexistence of iron deficiency and BTT. Additionally, this study assesses the effect of iron deficiency on haematological indices of individuals with BTT. **Study Design:** Cross-sectional study. **Setting:** Noor Thalassemia Foundation, Lahore. **Period:** May 2024 to May 2025. **Methods:** Model involved the random selection of 74 participants, including parents of known beta thalassemia major cases and patients with beta thalassemia trait (HbA2 >3.5%), who visited the OPD department of Noor Thalassemia Fondation in Lahore. 5ml venous blood was drawn and subjected to complete blood count (CBC), HLPC, and serum ferritin measurement. **Results:** Out of 74 participants, 65 were females and 9 were males. Iron deficiency, characterized by a serum ferritin concentration below 15 ng/mL, was found in 23 individuals, while 42 individuals had a serum ferritin concentration above 15 ng/mL. Mean levels of HbA_2 were 5.6±0.4%, mean haemoglobin concentration was 10.24±1.36g/dL, mean MCV was 64.73±7.32fL, and mean MCH was 19.94±4.04%. The mean value of serum ferritin levels in our study population was 34.74±32.27 ng/mL. **Conclusion:** A total of 23 individuals (31%) were found to be iron deficient. Iron deficiency reduced the red blood cell count, haemoglobin concentration, and MCV while it increased the RDW in BTT individuals ($p<0.05$), indicating that iron deficiency significantly affects the haematological indices in carriers of BTT.

Key words: Beta Thalassemia Trait, Iron Deficiency in BTT, Iron Deficiency, Serum Ferritin.

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INTRODUCTION

β-thalassemia trait, also called β-thalassemia minor, is a heterozygous genetic condition that results from mutations in the HBB gene, encoding the beta globin chain of hemoglobin. The normal ranges of haemoglobin are from 13.5 to 17.5 g/dL for adult males and 11.5 to 15.5 g/dL for adult females.[1] Although individuals with β-thalassemia trait do not have any symptoms, they are characterized by low to normal haemoglobin, low mean corpuscular hemoglobin (MCH), and low mean corpuscular volume (MCV). β-thalassemia trait is widely distributed in various regions, particularly South Asian, Middle Eastern, Mediterranean, and African populations.[2] In Pakistan, around 10 million people are carriers of beta thalassemia.[3]

Iron deficiency anemia is an acquired form of anemia generally caused by chronic blood loss, such as gastrointestinal bleeding[4] and menorrhagia in females; impaired iron absorption due to GI reasons such as Celiac disease and gluten enteropathy; poor dietary intake. It is the most prevalent type of anemia, especially in children under 5 and women of reproductive age worldwide. A 2018 study found that iron deficiency anemia affected 28.6% of children under five and 18.2% of women of reproductive age in Pakistan.[5]

Both β-thalassemia trait and iron deficiency anemia exhibit the hematological features of hypochromic, microcytic anemia, making their differentiation challenging solely based on blood indices. However, despite these overlapping features, the pathophysiology of β-thalassemia trait and iron deficiency anemia differ significantly. The β-thalassemia trait has no medical management, but iron deficiency anemia can be managed by iron therapy. β-thalassemia trait is associated with a positive iron balance due to increased iron absorption, a compensatory response to ineffective erythropoiesis. Therefore, in β-thalassemia trait, iron supplementation is not required unless iron deficiency for identifiable reasons is present.

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In such cases, an improved iron-enriched diet can also help correct iron deficiency.

Serum ferritin, along with other markers of iron profile such as serum transferrin saturation, serum iron, and TIBC, are used in the differential diagnosis of hypochromic, microcytic anemia. Serum ferritin represents the body's iron stores and is considered a reliable biomarker to diagnose iron deficiency. It is instrumental in differentiating between iron deficiency and BTT when hematological indices are inconclusive. It also plays a critical role in detecting iron deficiency in patients diagnosed with BTT. The World Health Organization (WHO) recommends that serum ferritin levels below 15 ng/mL in adults and below 12 ng/mL in children under 5 years are significant diagnostically for iron deficiency.[6] Investigating coexistent iron deficiency in patients with β-thalassemia trait in vulnerable groups, such as women and children, is necessary. Omitting iron therapy can exacerbate anemia and worsen clinical conditions such as fatigue, reduced exercise capacity, and decline of neurocognitive function.[7]

The coexistence of iron deficiency in BTT has been reported in many population-based studies. Still, its prevalence varies widely depending on the geographical region and socioeconomic status of the patients. This study aims to investigate whether iron deficiency coexists with β-thalassemia trait or not, and also to find the prevalence of iron deficiency, assessed through ferritin levels, in patients with BTT. Along with differentiating between BTT and coexistent iron deficiency in BTT, this study also explores the effect of iron deficiency on hematological indices in subjects with β-thalassemia trait. This study will contribute to the more accurate identification of iron deficiency in individuals with BTT, thereby aiding in the improvement of anemia and overall well-being.

METHODS

This cross-sectional study was conducted at the Hematology outpatient department at Noor Thalassemia Foundation, Lahore, between May 2024 and May 2025 after approval from ethical review committee (NTF-R04-24-19/4/24). A random selection of parents of β-thalassemia major and patients of β-thalassemia trait diagnosed on the basis of haemoglobin electrophoresis (HbA_2 >3.5%) was made. The inclusion criteria comprised individuals aged greater than 18 years with no history of iron supplementation or blood transfusion in the recent 3 months. Individuals with chronic inflammatory disease, liver or kidney disorders, or a history of blood transfusion or iron supplementation were excluded from the study. After obtaining informed consent from the patients, 5 ml of blood was drawn for laboratory evaluation. Laboratory investigations involved CBC performed using Sysmex Kx21 (Sysmex corporation, Kobe Japan), HPLC using BioRad D10 Hemoglobin testing system (Bio-Rad laboratories, USA)and serum ferritin level assessment performed on Siemens Atellica using chemiluminescence immunoassays (Siemens,Medical Solutions, USA).

All the data were recorded and assessed through IBM SPSS version 25.0. The occurrence of iron deficiency in BTT subjects was determined descriptively. Furthermore, Independent T-test was employed to compare mean values of HbA_2, Red Blood Cells (RBC), Haemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red cell distribution width (RDW) and ferritin in two groups; one group with BTT and other group with coexistent iron deficiency.

RESULTS

Our study population enrolled 74 subjects diagnosed with β-thalassemia trait. Out of these, 65 were females (88%) and 9 were males (12%). The female-to-male ratio in our study was approximately 7.3:1. Participants ranged from 18 to 57 years of age, with the majority (92%) falling within the 20 to 49 years age group.

The haematological parameters, including HbA_2, RBC count, Hb, MCV, MCH, MCHC, RDW, and Serum ferritin levels, were measured and recorded as mean ± standard deviation and are presented in Table-I.

Out of these 74 participants, Iron deficiency (serum ferritin <15ng/mL) was identified in 23 subjects (31%), all of them were females (100%), while

no males exhibited iron deficiency- a statistically significant difference ($p<0.05$). Latent iron deficiency (serum ferritin 15 to 30 ng/mL) was identified in 22 subjects (29%). Among them, 3 were males (14%) and 19 were females (86%). A total of 29 subjects (40%) had serum ferritin >30ng/mL, indicating normal iron status.

Our study participants were categorized into two groups: Group A included individuals with β-thalassemia trait only, and Group B included those with concurrent iron deficiency.

Independent t-test showed statistically significant differences in values of hematological indices and serum ferritin between both groups (Table-II)

TABLE-I

Parameters	Mean±S.D
HbA_2 (%)	5.6±0.4
RBC ($x10^{12}$/L)	5.32±0.79
Hb(g/dL)	10.24±1.36
MCV(fL)	64.73±7.32
MCH(%)	19.94±4.04
MCHC(%)	30.22±2.20
RDW(fL)	41.21±4.36
Ferritin(ng/mL)	34.74±32.27

TABLE-II

	Group A BTT Only	Group B Concurrent Iron Deficiency	P-Value
HbA_2 (%)	5.57±0.87	3.95±0.3	$<0.05^S$
RBC ($x10^{12}$/L)	5.46±0.79	5.2±0.79	0.21^{NS}
Hb(g/dL)	10.09±1.03	9.2±1.4	$<0.05^S$
MCV(fL)	65.84±7.09	61.6±7.4	$<0.05^S$
MCH(%)	20.17±3.5	19.20±5.02	0.35^{NS}
MCHC(%)	30.42±2.25	29.79±2.01	0.27^{NS}
RDW(fL)	38.5±3.8	46.6±7.2	$<0.05^S$
Ferritin(ng/mL)	46.16±32.91	9.3±3.69	$<0.05^S$

DISCUSSION

The study evaluated the iron status, assessed through serum ferritin, among individuals with β-thalassemia trait. Our findings revealed the significant frequency of iron deficiency in individuals carrying β-thalassemia trait, and highlighted the hematological differences between BTT carriers and those with concurrent iron deficiency.

Among 74 participants, females showed a marked preponderance. BTT is known to have equal gender predisposition. The female predisposition in our studies may reflect the sample bias, the willingness of females to participate, and the greater number of females in society.

The mean HbA_2 levels (5.6±0.4%) align with the diagnostic criterion for BTT (HbA_2 >3.5%).[8] The mean value of haemoglobin (10.24±1.36g/dL) indicates a mild degree of anemia that is consistent with BTT.[9] Mean values of MCV (64.73±7.32fL) and MCH (19.94±4.04%) show microcytosis and hypochromia that are characteristic features of BTT.[10]

Iron deficiency affected 31% of participants, all of them were females. This substantial rate of iron deficiency observed in females reinforces the known gender disparity in iron deficiency. A similar study conducted by Salman et al. found that 34.7% of females with BTT were iron deficient.[11] Almost all the women suffering from iron deficiency in our study were in their reproductive years (20 to 45 years). Women in their reproductive ages are at higher risk of iron deficiency, where factors such as menstrual blood loss, pregnancy, and increased iron requirements contribute to the iron depletion.[12] Additionally, 29% of individuals showed latent iron deficiency, and 86% of them were females, showing broader patterns of latent iron deficiency in females. The high prevalence of iron deficiency and latent iron deficiency demands the need for routine iron assessment in BTT patients, especially females.

Individuals were stratified into two groups: Group A (individuals with BTT only) and Group B (BTT individuals with concurrent iron deficiency).

Group B showed significantly lowered HbA_2 levels (3.95±0.3%) as compared to Group A (5.57±0.87%) ($p<0.05$), reaffirming that iron deficiency can suppress HbA_2 levels. This phenomenon has been documented in many study cohorts[13] and highlights the need to rule out iron deficiency before diagnosing BTT based on HPLC or Hb electrophoresis, to avoid misdiagnosis and enhance diagnostic accuracy.

Group B showed significantly lowered levels of haemoglobin as compared to group A (9.2±1.4 g/dL) vs (10.09±1.03 g/dL), ($p<0.05$), indicating more severe anemia in those with concurrent iron deficiency. This suggests that the compounded erythropoietic impairment because of iron deficiency and thalassemia leads to reduced haemoglobin synthesis in individuals with concurrent iron deficiency. An existing literature states that carriers typically present with mild anemia, i.e, their haemoglobin ranges from 9 to 12 g/dL.[14] These findings suggest that if BTT individuals exhibit moderate anemia (haemoglobin <10g/dL), they must be screened for iron deficiency. Improving concurrent iron deficiency can improve the level of haemoglobin in BTT patients, as documented in studies.[15]

Significantly reduced MCV in group B relative to group A ($p<0.05$) shows the additive microcytic effect of iron deficiency on thalassemic RBCs. Elevated RDW in group A (46.6±7.2 fL) as compared to group B (38.5±3.8fL) shows the significant differences ($p<0.05$) and marked anisocytosis- a feature associated with iron deficiency.[16]

While the RBC count was higher in group A relative to group B, this difference lacked statistical significance ($p = 0.21$). BTT typically involves a compensatory increase in erythropoiesis due to chronic mild anemia[17], resulting in increased RBC count. However, the concurrent iron deficiency impairs the red cell production and haemoglobin synthesis, potentially normalizing or reducing RBC count despite the underlying β-thalassemia trait.

MCH and MCHC were also reduced in group B, indicating increased hypochromia. However, differences were not statistically significant, suggesting that though hypochromia is increased in the presence of iron deficiency, it may not consistently reflect the significant variation in the study population.

The study had a few limitations. It included a small number of males (n=9) that limited the gender based comparison. Only one marker of iron profile, i.e., serum ferritin, was evaluated. It is suggested to conduct a study that includes a balanced number of males and females to better assess the iron levels in males. Moreover, a comprehensive iron profile including serum transferrin saturation, serum iron, and TIBC should be incorporated to enhance diagnostic accuracy.

CONCLUSION

Our findings confirmed that iron deficiency can coexist with the beta thalassemia trait. Iron deficiency was found in 31% participants, and all of them were females. Additionally, 29% individuals, comprising 14% males and 86% females, were found to have latent iron deficiency. Women of reproductive age emerged as a group showing the most susceptibility to iron deficiency due to physiological processes such as menstruation, pregnancy, and increased nutritional requirements.

The high prevalence of iron deficiency in our study underlines the clinical significance of monitoring iron status in individuals with BTT, particularly women of reproductive age. Iron deficiency has significantly reduced the RBC count, haemoglobin, and MCV, and raised RDW ($p<0.05$) in BTT participants.

The findings highlight the need of evaluating iron status in BTT individuals presenting with low haemoglobin concentration, increased microcytosis (reduced MCV) and Raised RDW, must be evaluated to correct the iron deficiency and improve the haematological indices in individuals with BTT.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
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2	**Saima Mansoor Bugvi:** Study design, proofreading, data analysis.
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ORIGINAL ARTICLE

Prenatal exposure and risk of medication in Autism spectrum disorder.

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ABSTRACT… Objective: To investigate correlations between prenatal medication exposure and ASD risk. **Study Design:** Cross-Sectional Observational Study. **Setting:** Department of Speech Language Pathology, The University of Lahore. **Period:** 22nd April 2024 22nd October 2024. **Methods:** Involving 45 mothers of autistic children. The research spanned 12 months, employing a purposive sampling technique and a self-designed questionnaire. Data analysis utilized SPSS software, focusing on demographic characteristics and questionnaire responses. **Results:** Findings reveal a variety of factors potentially associated with ASD, including abrupt medication changes (26.7%), pre-clampsia (35.6%), maternal age (60% within 25-30 age group), neurological conditions (37.8%), cousin marriages (37.8%), and complications during delivery (22.2%). The study emphasizes the complexity of ASD and highlights potential risk factors. **Conclusion:** The research concludes that while no specific prenatal factor is implicated in ASD etiology, certain associations suggest that exposure to pregnancy complications may increase the risk. The study underscores the need for a nuanced understanding of ASD and early intervention strategies.

Key words: Autism Spectrum Disorder, Communicative Disorder, Prenatal Exposure.

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INTRODUCTION

Autism Spectrum Disorder (ASD) represents a profound and pervasive developmental challenge, significantly affecting communication and social interaction across an individual's lifespan. Typically diagnosed in childhood, ASD introduces a complex array of hurdles, impacting verbal and non-verbal communication, behavioural patterns, attachment dynamics, and cognitive functions.[1] This condition, characterized by a spectrum of symptoms and severity, results in a unique experience for each individual.The recognition and formal diagnosis of autism only emerged in 1943, with Donald Grey Triplett marking the first documented case. Born in Mississippi in 1933, Triplett's diagnosis by Dr. Leo Kanner led to the identification and classification of autism as "case 1." Initially, features associated with autism were incorporated under schizophrenia. The acknowledgment of autism as a distinct entity paved the way for further research and understanding, evolving into a multidimensional developmental disorder encompassing various characteristics.[2]

Referred to as Autism Spectrum Disorder due to the vast variability in its presentation, ASD manifests with a spectrum of characteristics and severity levels. Individuals with ASD may exhibit highly developed verbal skills or face significant communication challenges. Social interaction difficulties, poor eye contact, and repetitive behaviors are common traits.[3] The uniqueness of each person's experience underscores the intricate nature of ASD, with symptoms ranging from mild to severe and subject to change over time. The diagnostic criteria include challenges in social interaction, communication issues, and restricted/ repetitive behavioral patterns.

The precise causes of ASD remain elusive, but various factors are suspected contributors. Genetic elements play a pivotal role, with research indicating a strong familial link. Environmental factors such as exposure to heavy metals, prenatal medication, and maternal health during pregnancy are also considered. Contrary to misinformation, vaccines have been scientifically discredited as a cause of ASD.

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The complexity of ASD is further underscored by the presence of comorbid conditions and the influence of parental age and mental health.[4]

Diagnosing ASD involves assessing three key developmental domains: social interaction, communication, and repetitive behaviors. Lack of empathy, language difficulties, and repetitive actions are commonly observed. The absence of a standardized laboratory test necessitates reliance on behavioral observations and checklists. A comprehensive understanding of an individual's behavioral patterns and social interactions becomes crucial for accurate diagnosis.[5]

This research aims to explore the prenatal exposure to medications as a potential environmental factor contributing to the development of ASD. ASD's etiological factors involve a complex interplay of genetics and environment, with epigenetics playing a significant role. Maternal exposure to certain medications during pregnancy has been associated with an increased risk of ASD. Understanding these environmental contributors is crucial for comprehensive insights into the origins of ASD and developing effective strategies for prevention and intervention.[6]

METHODS

A Cross-Sectional Observational Study design was employed to gather insights into the prenatal exposure of medication and its potential correlation with Autism Spectrum Disorder (ASD). The research was conducted at the Department of Speech Language Pathology, The University of Lahore from 22nd April 2024 22nd October 2024. with a specific focus on the mothers of autistic children as the target population over duration of 12 months after obtaining approval from the Research Ethical Committee (REC-UOL-119-06-2023-19/6/23). The sample size for this study was determined at 45 participants, chosen with a 90% confidence level and a 10% margin of error. The inclusion criteria comprised mothers with autistic children, while speech therapists were excluded from participation. To collect relevant data, a self-designed questionnaire served as the primary data collection instrument. The questionnaire was formulated based on expert opinions and an extensive review of existing literature in the field. The target participants for data acquisition were mothers of autistic children, ensuring a direct and informed perspective on the variables under investigation.

The methodology employed a purposive sampling technique, enabling the selection of participants with specific characteristics relevant to the research focus. This approach aimed to provide a concentrated and relevant dataset for analysis.

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software, version 20, a standard tool for statistical analysis. Descriptive statistics, including mean and standard deviation (Mean ± SD), were utilized to summarize continuous variables. The choice of statistical methods aimed to facilitate a comprehensive understanding of the relationships between prenatal medication exposure and the presence of Autism Spectrum Disorder. In summary, the research methodology involved a targeted and specific approach, utilizing a well-designed questionnaire to collect data from a carefully selected sample of mothers of autistic children. The adoption of a cross-sectional observational study design and purposive sampling technique, coupled with robust statistical analysis using SPSS, contributed to a rigorous and systematic investigation into the variables of prenatal medication exposure and Autism Spectrum Disorder.

RESULTS

The study comprised 45 mothers of autistic children, with a diverse distribution across age groups. The majority fell within the 25-30 age bracket (60%), followed by those aged 35-40 (22.2%). A smaller percentage represented the age groups of 20-25 (15.6%) and 45-50 (2.2%). Regarding family history, 22.2% reported a neurological disorder in their family, with 37.8% indicating a history of depression. Additionally, 37.8% acknowledged cousin marriage within their families, and 15.6% reported a neurological condition in their husbands. The study also explored complications during delivery, with 22.2% of participants experiencing such issues as shown in table No.1.

TABLE-I		
Demographic characteristics of participants		
Characteristic	**Frequency**	**Percentage**
Age (years)		
20-25	7	15.6
25-30	27	60
35-40	10	22.2
45-50	1	2.2
Neurological Disorder in Family		
Yes	10	22.2
No	31	68.9
Maybe	4	8.9
Cousin Marriage		
Yes	17	37.8
No	28	62.2
Husband's Neurological Condition		
Yes	7	15.6
No	28	62.2
Maybe	10	22.2
Cousin Marriage		
Yes	17	37.8
No	28	62.2

The research questionnaire delved into various aspects related to prenatal exposure and potential factors contributing to autism spectrum disorder. Participants, comprised of mothers with autistic children, were probed on lifestyle, medications, and environmental factors during pregnancy.

Responses revealed a significant portion of mothers (26.7%) abruptly stopped medications, raising concerns about the potential impact on their offspring. Additionally, a considerable number of participants (35.6%) reported experiencing pre-clampsia during pregnancy, a condition associated with an increased risk of autism spectrum disorder.

In exploring the age of conception, a predominant percentage fell within the 25-30 age group (60%), indicating a potential correlation between maternal age and autism. Neurological conditions, both in participants and their family members, were scrutinized. Depression was reported by 37.8%, emphasizing the need to understand the interplay of mental health factors in autism.

Genetic considerations were examined, with 22.2% reporting a family member with autism. This underscores the genetic component in autism spectrum disorders. The prevalence of cousin marriages among participants (37.8%) adds complexity to the genetic landscape and potential risk factors.

Herbal medication usage during pregnancy was minimal (2.2%), aligning with broader health recommendations. Complications during pregnancy, such as panic attacks (22.2%), were reported. Notably, 75.6% of participants consulted physicians about their medications, reflecting a proactive approach to mitigate potential risks.

The study touched upon cousin marriages, a factor observed in 37.8% of participants. While previous research suggests a link between paternal neurological conditions and autism, only 15.6% reported such conditions in their husbands.

Complications during delivery were acknowledged by 22.2% of participants, contributing to the broader discussion on the role of birth-related factors in autism. Notably, 42.2% did not fill a consent form before treatment, indicating a potential gap in understanding the risks associated with medical interventions during pregnancy.

Awareness about prohibited medications during pregnancy varied, with 26.7% lacking this knowledge. Additionally, 28.9% did not have the opportunity to discuss medication risks, highlighting potential challenges in disseminating information.

The study revealed that 26.7% of participants had switched or stopped medications without consulting their doctors. This points to a need for improved communication between healthcare providers and expectant mothers.

Awareness of medication adverse effects varied, with 24.4% lacking knowledge. The occurrence of viral infections after conceiving (8.9%) adds another layer to the exploration of environmental factors in autism.

Metabolic changes during conception, such as fatigue (11.1%) and muscle cramps (17.8%), were reported. Finally, 28.9% of participants were unaware of changes in their child during the first 6 months, emphasizing the challenges in early detection and intervention for autism spectrum disorder.

These questionnaire responses collectively contribute to a nuanced understanding of the multifaceted factors potentially influencing autism spectrum disorders as shown in Table-II.

TABLE-II

Questionnaire responses

Question	Frequency	Percentage
Prenatal Exposure of Medication		
Depression	17	37.8
Panic Attack	10	22.2
Cousin Marriage	17	37.8
Paternal Neurological Condition	7	15.6
Underweight Child After Birth	9	20
Complications During Delivery	10	22.2
Muscle Cramps	8	17.8
Fatigue	5	11.1
Suddenly Stopped Medications	12	26.7
Viral Infection	4	8.9
Pre-clampsia	16	35.6
Environmental Issues	4	8.9
Age When Conceived Child		
20-25	7	15.6
25-30	27	60
35-40	10	22.2
45-50	1	2.2
Neurological Conditions in Family		
Depression	17	37.8
ADHD	2	4.4
OCD	1	2.2
None	25	55.6
Autism in Family		
Yes	10	22.2
No	31	68.9
Maybe	4	8.9
Herbal Medications During Pregnancy		
Ethanol Consumption	1	2.2
Excessive Use of Vitamins	1	2.2
None	43	95.6
Aysha Nauman		
Unconsciousness	3	6.7
Nervous Breakdown	1	2.2
Panic Attack	10	22.2
None	31	68.9
Aysha Nauman		
Yes	34	75.6
No	9	20
Maybe	2	4.4
Aysha Nauman		
Yes	17	37.8
No	28	62.2
Husband's Neurological Condition		
Yes	7	15.6
No	28	62.2
Maybe	10	22.2
Complications During Delivery		
Yes	10	22.2
No	34	75.6
Maybe	1	2.2
Filled/Read Treatment Form		
Yes	23	51.1
No	19	42.2
Maybe	3	6.7
Awareness of Prohibited Medications		
Yes	31	68.9
No	12	26.7
Maybe	2	4.4
Awareness of Risks and Consultation		
Yes	31	68.9
No	13	28.9
Maybe	1	2.2
Sudden Stop or Switch of Treatment		
Yes	12	26.7
No	32	71.1
Maybe	1	2.2
Knowledge of Medication Adverse Effect		
Yes	31	68.9
No	11	24.4
Maybe	3	6.7
Viral Infections After Conceiving		
Yes	4	8.9
No	37	82.2
Maybe		

DISCUSSION

The results of the study shed light on various factors potentially associated with autism spectrum disorder (ASD) in children, emphasizing the complexity of the disorder. Correlating these findings with previous studies provides valuable insights into the existing body of knowledge.[7]

One notable aspect is the prevalence of abrupt medication changes reported by 26.7% of participants. This aligns with studies that have explored the impact of maternal medication during pregnancy on neurodevelopment. Research, such as that conducted by Rai et al. (2018), emphasizes the need for caution in altering medications without medical consultation, as certain drugs may pose risks to fetal development.[8]

The reported cases of pre-clampsia (35.6%) during pregnancy are consistent with studies linking maternal hypertensive disorders to an increased risk of ASD. A study by Mann et al. (2016) found a significant association between pre-clampsia and neurodevelopmental disorders in offspring, reinforcing the idea that prenatal complications may contribute to the etiology of ASD.[9]

The age of conception, with a majority falling within the 25-30 age group (60%), correlates with existing literature indicating a maternal age effect on autism risk. Advanced maternal age has been identified as a potential risk factor, supported by studies like Sandin et al. (2016), which reported an increased risk of ASD in children born to mothers over the age of 35.[10] Neurological conditions, particularly depression (37.8%), within the study participants and their family members, align with research emphasizing the role of maternal mental health in autism risk. A study by Brown et al. (2019) highlighted the association between maternal depression and an elevated risk of ASD in offspring, suggesting the importance of mental health considerations in prenatal care.[11]

The prevalence of cousin marriages (37.8%) among participants adds a genetic dimension to the study. While cousin marriages themselves may not directly correlate with ASD risk, genetic factors intertwined with familial relationships have been explored in studies like Ghaziuddin et al. (2002), emphasizing the intricate genetic landscape of ASD.[12]

Complications during delivery reported by 22.2% of participants correlate with studies investigating perinatal factors and their association with ASD. Previous research, such as that by Gardener et al. (2009), has identified birth-related complications as potential contributors to neurodevelopmental disorders, including ASD.[13]

The lack of filled consent forms before treatment in 42.2% of participants echoes concerns raised in studies emphasizing the importance of informed consent during pregnancy. Research by Haw et al. (2017) stresses the significance of comprehensive communication between healthcare providers and expectant mothers to ensure informed decision-making.[14]

In summary, the discussion of the questionnaire results aligns with existing research, providing contextualization to the multifaceted factors associated with autism spectrum disorder. The correlations drawn from previous studies enhance the understanding of the complex interplay between prenatal factors and the risk of ASD in children.[15]

CONCLUSION

On the basis of obtained findings it is concluded that the evaluation there is insufficient evidence to implicate any one prenatal factor in autism aetiology, although there is some evidence to suggest that exposure to pregnancy complications may increase the risk.

LIMITATIONS

Lack of knowledge of health precautions influences the rate of autism in children. Limited time span for the research can cause variation in the results. Individual opinion of every participant can affect the background of the research. Lack of standardized practice for autism assessment in special settings influences the uniformity of opinion on autism related difficulties in children with childhood disorders.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Ahmed:** Data collection, analysis, paper writing.
2	**Hamza Manzoor:** Discussion writing, review of manuscript.
3	**Saira Zaman:** Data collection.
4	**Athar Adnan Uppal:** Literature review.
5	**Nasir Riaz:** Data entry.
6	**Aysha Nauman:** Critical revision.

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ORIGINAL ARTICLE

Establishment of reference range of her human epidermal growth factors receptor (HER2) by chemiluminescence method in healthy females.

Maham Shakoor[1], Asim Mumtaz[2], Atika Masood[3], Atiqa Arshad[4], Zainab Yousaf[5], Zaniab Akram[6]

ABSTRACT… Objective: To establish reference range for serum HER2 levels in normal Asian females and provide a comprehensive overview of its current understanding to step towards improving the accuracy and utility of serum HER2 as biomarker. **Study Design:** Cross Sectional study. **Setting:** Farooq Hospital Westwood, College of Allied Health Sciences, Akhtar Saeed Medical & Dental College Lahore. **Period:** October 2024 to December 2024. **Methods:** The female participants visited aged 30-70 years, free of symptoms and signs suggestive of any breast abnormality were included. The 120 female participants were enrolled for establishing reference value of serum HER2 levels. The venous blood sample was drawn for HER2 levels. The auto analyzer was used for HER2 estimation. The data was analyzed through the IBM SPSS V.27.0. **Results:** A total 120 females were enrolled. The mean + SD was 45.0 + 9.879. The weighted average test was used to determine 25th and 95th percentile value in order to establish lower reference limit and upper reference limit of HER2 assay. The established reference range was 9.41 to 14.03 ng/ml. The results revealed that 25% data was below 9.41ng/ml and 95 % of females HER2 levels were under 14.03ng/ml. **Conclusion:** The present study established a preliminary reference range for serum HER2 in healthy females, contributing to improved breast cancer diagnostics and monitoring in our region.

Key-words: Asian Females, Human Epidermal Growth Factor Receptor 2, Reference Range.

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INTRODUCTION

In Pakistan, breast cancer is a serious health issue that has become more common in recent years. In Pakistan, about 38.5% of females have breast cancers, making it the most prevalent cancer among women.[1] An estimated 90,000 new cases of breast cancer are diagnosed each year, and the incidence has been continuously increasing.[2] However, breast cancer is frequently discovered in Pakistan at an advanced stage, which lowers the likelihood of a successful course of treatment and raises the death rate.[3] As the breast cancer is a heterogeneous disease, distinct tumor regions may exhibit different genetic changes or traits.[4] There are various subtypes of this cancer, each with unique clinical characteristics and reactions to treatment.[5]

Human Epidermal Growth Factor Receptor 2, or HER2, is a protein that is essential for cell division, growth, and proliferation. It belongs to the protein family known as the epidermal growth factor receptor (EGFR). Many cancer types are frequently linked to HER2 overexpression or amplification, most notably breast cancer (20-30%).[6] HER2-positive tumors in breast cancer have excessive HER2 protein on their cell surfaces, which causes the cells to grow out of control and makes the cancer more aggressive. Compared to other types of breast cancer, HER2-positive breast cancer is more aggressive and may have a worse perspective. This protein has recently become a very important biomarker and target for diagnosis, prognosis, and treatment in breast cancer patients. The HER2 protein has three parts: the transmembrane, extracellular, and intracellular tyrosine kinase domains. The extracellular domain can be released into the blood after cleavage and shedding from the tumor cell surface by metalloproteases. Therefore, it can be detected in the serum. In 18% of primary breast cancers and 46% of metastatic breast cancers, serum HER2 levels are higher.[7]

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There are several evidence regarding the correlation of serum HER2 levels and tissue HER2 protein overexpression as well as poor prognosis in a metastatic type of breast cancer.[8,9] HER2 status is a critical factor in breast cancer treatment decision-making. Patients with HER2-positive breast cancer are typically recommended to receive HER2 targeted therapy in addition to standard treatments like chemotherapy and surgery. This personalized approach to treatment has led to better outcomes for patients with HER2-positive breast cancer.[10]

Despite the growing interest in serum HER2 level as a biomarker, there is lack of data on reference ranges for serum HER2, particularly in specific demographic groups such as Asian females. Biomarker levels can be influenced by genetic and ethnic variations, and extrapolating reference ranges from Western populations to Asian populations might not be suitable. Serum HER2 levels may be impacted by the fact that Asian women, for example, typically have lower body mass indices (BMIs) and distinct hormonal profiles than Western women. Serum HER2 levels may be impacted by environmental and lifestyle factors in addition to demographic ones.

For instance, it has been demonstrated that HER2 expression are modulated by diet, exercise, and exposure to environmental toxins. Asian populations frequently follow unique dietary habits, such as consuming large amounts of green tea and soy products, which contain bioactive compounds that may affect HER2 signaling pathways. Moreover, obesity and metabolic syndrome, which are linked to changed HER2 expression, are more common in Asia as a result of urbanization and changing lifestyles. These results underline the necessity of more investigation to develop population-specific reference ranges. For serum HER2 testing to be accurate and reliable in clinical practice, a population-specific reference range must be established.[11,12]

The most popular methods for measuring serum HER2 levels are chemiluminescence immunoassays (CLIAs) and enzyme-linked immunosorbent assays (ELISA), which can identify the extracellular domain of HER2 that has been released into the blood. However, it can be difficult to interpret results from various labs and studies due to the absence of standardized assays and reference ranges. Assay sensitivity, specificity, and reproducibility variations can produce contradictory results, highlighting the necessity of standardized procedures and clearly defined reference intervals.[13,14]

Given the increasing prevalence of HER2-positive breast cancer in Asia, it is especially important to establish a reference range for serum HER2 levels in healthy Asian females. In order to improve the precision and usefulness of serum HER2 as a biomarker, the present study set a reference range for serum HER2 levels in healthy Asian females and provides understanding to step towards improving the accuracy and utility of serum HER2 as biomarker. The present study can improve outcomes for patients with HER2 positive breast cancer and increase the clinical relevance of HER2 testing by filling these gaps.

METHODS

The study is cross-sectional and was conducted at the Farooq Hospital Westwood Branch, College of Allied Health Sciences, Akhtar Saeed Medical & Dental College Lahore. The intuitional review board authorized this study (Letter No: CAHS-08/2024-MLT-61). The non-probability convenient sampling technique was followed. The female participants visited during the month of October 2024 to December 2024, aged 30-70 years, free of symptoms and signs suggestive of any breast abnormality were included. Females with any breast related abnormality, and used or using any medications were excluded. The 120 female participants were enrolled for establishing reference value of serum HER2 levels.

After verbal informed consent, the demographic details of each participant were recorded. Under aseptic conditions, venous blood sample was drawn for HER2 levels in yellow top vaccutainer, labeled with individual's name and identification number. The sample was allowed to clot and serum was separated through centrifugation at 3000rpm. The serum was stored in labeled eppendorf cups at -80 till further analysis. Chemiluminescence-based auto analyzer Maglumi X8 by SNIBE was used for analysis. It uses nano-magnetic microbeads separation technology, the luminescence substrate

being N-(aminobutil)-N-(ethyl)-isoluminol (ABEI). The performance characteristics of the assay are given (Table-I). The samples were run in a batch. The internal quality control provided in the reagent kit was run with each batch analysis.

TABLE-I

Performance characteristics of HER2 assay

Precision (Intra-assay CV%)	Analytical Sensitivity	Calibration Traceability	Interfering Substances	Hook Effect
2.84%	2.0 ng/mL 0.5-350ng/mL	Snibe Internal Reference Material	Substances upto the following concentrations did not interfere with the assay ▪ Bilirubin 30mg/dL ▪ Hemoglobin 1000mg/Dl ▪ Triglycerides 1000mg/dL	None

The Statistical Package for Social Sciences (IBM SPSS V.27.0) was employed to analyze the data. The Kolmogorov-Smirnov (K-S) test was employed to evaluate the normality of the data. The age was represented as the mean ± (standard deviation). The reference values were calculated using non-parametric methods due to the non-normal distribution of the data. The 25th and 95th percentile values were determined using the weighted average test to establish the lower and upper reference limits of the HER2 assay.

RESULTS

From total 120 females, the minimum to maximum age was 30-70 years. The mean + SD was 45.0 + 9.879. Normality of data was analyzed by using K-S test which showed that data was not normally distributed as p value was < 0.05 (p=0.005). The present study was conducted to establish upper reference limit and lower reference limit of HER2 assay, which is used as diagnostic and prognostic biomarker of HER2 positive breast cancer. The estimated value of HER2 assay is given (Table-II).

The data was not normally distributed so the weighted average test was used to determine 25th and 95th percentile value in order to establish lower reference limit and upper reference limit of HER2 assay (Table-III). The established reference range was 9.41 to 14.03 ng/ml. The results revealed that 25% data was below 9.41ng/ml and 95 % of females HER2 levels were under 14.03ng/ml.

TABLE-II

Descriptive statistical analysis for estimated value of HER2 assay

Descriptive Analysis	Serum HER2 Levels
Median + Inter quartile range	11.3800 + 1.855
Standard error of mean	0.16866
Kit literature cut-off value	15.0 ng/ml
Observed minimum value	7.75 ng/ml
Observed maximum value	14.70 ng/ml

TABLE-III

25th and 95th Percentile values of HER2 assay

	Percentiles	
Weighted average	25th	95th
	9.41 ng/ml	14.03 ng/ml

DISCUSSION

HER2 overexpression is most commonly detected in breast Cancer.[13] HER2 is an integral membrane protein that weighs 185 kD. The extracellular domain of HER2 is separated from other components of HER2 and enters the bloodstream after its breakdown by metalloproteases. Currently, the most frequently employed methods for evaluating the expression of HER2 are immunohistochemistry, which involves the immunostaining of the HER2 ECD, and Fluorescence In Situ Hybridization (FISH), which involves the fluorescent labelling of amplified HER2 DNA. In breast cancer patients, serum HER2 levels have been reported to be correlated with tissue HER2 status.[15] Since determining the tissue HER2 status requires biopsy which is an invasive and time taking procedure, therefore serum HER2 levels are being studied as biomarker of HER2 positive breast cancer.[16]

The establishment of reference range for serum HER2 levels is essential for accurate clinical interpretation in breast cancer diagnostics and monitoring.[13] In present study, the reference range for serum HER2 in healthy females was determined to be 9.41-14.03 ng/mL, based on a sample size of 120 healthy female participants. This range

provides a critical baseline for distinguishing normal physiological levels from pathological elevations seen in HER2-positive breast cancer patients. The present study findings are in consistent with previous studies conducted in Asian populations but show slight variations when compared to Western data. For instance, a study conducted in Nepal determined the optimal cutoff value of serum HER2 levels to be 16.02 ng/ml which is close to the upper reference limit established in present study.[17] Whereas, in different studies conducted in Western countries, the cut off has been found to be between ranges 8.83-21ng/mL.[13,18]

Several other factors may contribute to variations in serum HER2 levels, including age, hormonal status, and BMI. Studies demonstrated that postmenopausal women tend to have slightly elevated HER2 levels compared to premenopausal women, possibly due to hormonal fluctuations.[11] Although the present study did not stratify participants based on menopausal status, future research should explore this aspect to refine reference ranges further. Additionally, there is impact of assay methodologies on HER2 measurements, underscoring the need for standardized testing protocols to ensure consistency across laboratories.[14] In present study, the state-of-the-art random access fully automated system (Maglumi X8) for the analysis of serum HER2 level was used. This system is the ultimate development of conventional ELISA plate readers that required immense time and manpower resources with many potential sources of errors.[19] Naoki et al. conducted a study and concluded that CLIA was more sensitive method than ELISA for measuring serum HER2 levels.[20]

The establishing a reference range for serum HER2 in healthy Asian women has important clinical ramifications, especially for the treatment of breast cancer. HER2-positive breast cancer is a more aggressive subtype that necessitates targeted treatments like trastuzumab, is linked to elevated serum HER2 levels. Clinicians can decrease false-positive diagnosis and improve their interpretation of borderline cases by establishing a normal range. Furthermore, since decreasing HER2 levels frequently correspond with therapeutic efficacy, this reference range can help with tracking treatment response.[21] In order to validate these reference ranges across an array of Asian subpopulations, future research should incorporate larger, multi-center cohorts. Furthermore, longitudinal research evaluating HER2 variations over time in healthy individuals may offer more profound understanding of its biological variability.

CONCLUSION

The present study improved breast cancer monitoring and diagnosis in our region by establishing a preliminary reference range for serum HER2 in healthy females. The clinical utility of these findings will be improved by additional studies with larger cohorts and in-depth subgroup analysis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Maham Shakoor:** Concept of project, data collection.
2	**Asim Mumtaz:** Review.
3	**Atika Masood:** Drafting.
4	**Atiqa Arshad:** Literature search.
5	**Zainab Yousaf:** Writeup manuscript, data collection.
6	**Zaniab Akram:** Statistical analysis.

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ORIGINAL ARTICLE

Diagnostic accuracy of diffusion weighted magnetic resonance imaging in differentiating benign and malignant meningioma taking histopathology as gold standard.

Shamoona Rashid[1], Sadia Zafar[2], Syeda Mehwish Zehra[3], Hina Rauf[4]

ABSTRACT… Objective: To evaluate the ability of diffusion-weighted MR Imaging to distinguish malignant meningiomas from benign, taking histopathology as the gold standard. **Study Design:** Cross-Sectional Validation Study. **Setting:** Department of Radiology, Aziz Fatimah Hospital and Allied Hospital, Faisalabad. **Period:** October 2024 to April 2025. **Methods:** A total of 225 patients aged between 20 to 60 years with suspected meningiomas were enrolled. DWI-MRI was performed using a 1.5 Tesla scanner (b-values 0, 500, and 1000 s/mm²). Findings were interpreted by a consultant radiologist and compared with histopathology. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using SPSS version 20.0; a p-value < 0.05 was considered significant. **Results:** DWI-MRI showed a high diagnostic accuracy (86.67%) in distinguishing malignant from benign meningiomas, with sensitivity 88.52%, specificity 84.47%, PPV 87.10% and NPV 86.14% (p = 0.0001). **Conclusion:** DWI-MRI is a reliable, non-invasive imaging modality with high diagnostic accuracy for differentiating benign and malignant meningiomas and can significantly aid in preoperative assessment and treatment planning.

Key words: Diffusion-Weighted Imaging, DWI-MRI, Histopathology, Meningioma, Magnetic Resonance Imaging.

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INTRODUCTION

Meningiomas are the most common type of primary intracranial tumors, contributing to nearly one-fifth of all brain and spinal tumors.[1] Their global incidence is estimated at about 8–10 cases per 100,000 people annually, with frequency increasing with age.[2] Improved availability of neuroimaging and rising life expectancy have contributed to a higher detection rate, and autopsy findings reveal that around 1–2% of the population may harbor small, asymptomatic meningiomas.[3] These tumors typically originate from arachnoid cap cells and are usually located along the cerebral convexities, falx cerebri, and skull base. Intraventricular locations are rare.[4] Meningiomas are most frequently diagnosed in middle-aged individuals and occur more often in females.[5] The highest incidence observed between 45 and 55 years of age, with increasing frequency in the elderly. The average age at diagnosis for posterior fossa meningiomas is reported to be 43.5 years.[6]

The development of meningiomas is strongly associated with genetic alterations, particularly mutations in the NF2 gene, while hormonal influences, especially progesterone sensitivity, also play a role. Prior cranial radiation exposure and inherited conditions such as neurofibromatosis type 2 further increase the risk. Advancing age and female gender are recognized as additional contributing factors.[7]

Clinical presentation depends on tumor size and location. Small meningiomas may remain asymptomatic, whereas larger lesions can cause headaches, seizures, or focal neurological deficits such as weakness, vision problems, or speech disturbances. Cognitive or personality changes may also appear in tumors affecting the frontal lobes.[8]

Most meningiomas are benign, slow-growing masses with well-demarcated borders and broad dural attachments.

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On magnetic resonance imaging (MRI), the "dural tail sign" - a tapering enhancement along the dura adjacent to the tumor - is considered characteristic, being present in 50–70% of cases.[9] Tumors less than 2.5 cm in size are often asymptomatic; however, larger tumors may produce progressive neurological symptoms.[10] Although the majority of meningiomas are benign, around 10% are atypical or malignant. These higher-grade variants demonstrate more aggressive behavior, including bone and parenchymal invasion, and are linked to higher rates of morbidity, mortality, and recurrence of up to 29–41%. Early and accurate distinction between is, therefore, essential for guiding surgical planning, determining the extent of resection, and deciding the need for adjunctive radiotherapy.[11]

According to the World Health Organization (WHO) classification, meningiomas are categorized into Grade I (benign, accounting for 80–85%), Grade II (atypical, about 15–20%), and Grade III (anaplastic/malignant, 1–3%). While Grade I tumors usually have a favorable prognosis, higher grades demonstrate aggressive behavior, higher recurrence rates, and worse clinical outcomes. The Ki-67 proliferation index has been proposed as an additional marker to predict aggressiveness.[12]

From a clinical perspective, the increasing incidence of meningiomas poses a significant healthcare burden due to their long-term follow-up needs, recurrence potential, and surgical demand. With populations living longer, the detection and management of these tumors are expected to rise, highlighting the need for accurate, non-invasive pre-operative grading.[13]

MRI is the foremost diagnostic tool for the detection of suspected meningiomas, significantly enhancing diagnostic accuracy and surgical planning.[14] DWI-MRI is a functional approach that measures water molecule motion at the cellular level and has shown promise in the characterization of brain tumors. Research on gliomas has demonstrated an inverse relationship between ADC values and tumor grade, and comparable trends are now being observed in meningiomas.[15]

Evidence on the diagnostic reliability of DWI-MRI for distinguishing benign from malignant meningiomas is limited, particularly in local settings. This study evaluates its performance against histopathology to determine its reliability as a non-invasive, pre-operative grading tool. If proven accurate, DWI-MRI could be integrated into routine practice to improve surgical planning and reduce complications associated with high-grade tumors.

METHODS

This cross-sectional validation study was conducted at the Radiology Department of Aziz Fatimah Hospital and Allied Hospital, Faisalabad, over a period of six months, from October 2024 to April 2025. Total 225 patients were enrolled. The sample size was calculated using a 95% confidence level, 10% margin of error, and based on an expected prevalence of malignant meningiomas of 23%, with previously reported sensitivity and specificity of DWI-MRI as 84.4% and 82.3%, respectively. Ethical approval was obtained (Ref. no. IEC/417-25) for this study was obtained from the institutional Ethical Committee of Aziz Fatimah Medical and Dental College Faisalabad before initiating data collection, and informed written consent was secured from all participants.

Total 225 patients aged between 20 - 60 years were enrolled, with a symptom duration of more than one month and a lesion size greater than 1 cm on imaging. Exclusion criteria comprised patients with a previously diagnosed meningioma presenting for follow-up, pregnant women, individuals with a known allergy to intravenous contrast, renal dysfunction, and patients who were claustrophobic and unable to undergo MRI.

All subjects underwent 1.5 Tesla MRI system (GE Healthcare Signa HD). DWI-MRI was performed using a single-shot spin-echo echo-planar imaging sequence with TR/TE/NEX of 4200/140 ms/1, and diffusion encoding were carried out by applying gradients in sequence along the X, Y, and Z axes with b-values set at 0, 500, and 1000 s/mm^2. The imaging parameters included a slice thickness (5 mm), interslice gap (1 mm), a FOV (240 mm), and a matrix (128 × 256), with a total acquisition time of approximately 80 seconds. Orthogonal and trace images, and ADC maps, were generated. ADC

values were computed by the MRI software and recorded in 10^{3} mm^2/s, with regions of interest (ROIs) placed both within the lesion and in the contralateral normal brain parenchyma.

MRI findings were interpreted by a consultant radiologist with a minimum of three years of post-fellowship experience. Each lesion was categorized as benign or malignant based on its diffusion characteristics and ADC values. All patients subsequently underwent biopsy or surgical resection, and the histopathological diagnosis was considered the gold standard for comparison. Demographic and clinical data, along with imaging and histopathological findings, were recorded on a structured proforma for analysis. Data analysis was performed using SPSS version 20.0. An Independent t-test was applied to compare the mean ADC values between the two groups. A p-value of <0.05 was considered statistically significant at a 95% confidence interval. Diagnostic performance of DWI-MRI was evaluated by determining its specificity, sensitivity, NPV, PPV, and overall diagnostic accuracy through 2×2 contingency tables, taking histopathology as the gold standard.

RESULTS

A total of 225 patients were evaluated, with ages ranging from 20 to 60 years (mean: 45.62 ± 8.75 years). Most of the patients (71.11%) were in the 41– 60 year age group. There were 121 males (53.78%) and 104 females (46.22%), yielding a male-to-female ratio of 1.2:1. The mean duration of symptoms was 5.23 ± 1.89 months, and the average lesion size was 4.48 ± 1.34 cm. Baseline demographic characteristics are shown in Table-I.

All patients underwent DWI-MRI, followed by histopathological confirmation. Based on 2×2 contingency analysis, DWI-MRI correctly identified 108 malignant cases (true positives), while 87 were true negatives. There were 16 false positives and 14 false negatives. The association was found to be statistically significant (p = 0.0001) and is presented in Table-II.

For distinguishing malignant from benign meningiomas, DWI-MRI demonstrated a sensitivity of 88.52%, specificity of 84.47%, PPV of 87.10%, NPV of 86.14%, and an overall diagnostic accuracy of 86.67%.

TABLE-I.

Baseline characteristics of study population (n = 225)

Variable	Frequency (%) or Mean ± SD
Age (years)	45.62 ± 8.75
20-40	65 (28.89%)
41-60	160 (71.11)
Gender	
Male	121 (53.78%)
Female	104 (46.22%)
Duration of Symptoms	5.23 ± 1.89 months
≤ 6 months	172 (76.44%)
> 6 months	53 (23.55%)
Lesion Size (cm)	4.48 ± 1.34
≤ 5 cm	174 (77.33%)
> 5 cm	51 (22.67%)
Place of Residence	
Rural	109 (48.44%)
Urban	116 (51.56%)

TABLE-II.

Diagnostic Accuracy of DWI-MRI vs. Histopathology

	Histopathology Positive	Histopathology Negative
DWI-MRI Positive	108 (TP)	16 (FP)
DWI-MRI Negative	14 (FN)	87 (TN)
P-value		0.0001

Stratified analysis revealed notable variations in the diagnostic accuracy of DWI-MRI across different subgroups. Male patients demonstrated a higher diagnostic accuracy (91.73%) compared to females (80.77%). Accuracy was also significantly higher among patients with a disease duration of more than six months (98.11%) compared to those with a shorter duration. Similarly, lesions larger than 5 cm yielded slightly higher accuracy (86.27%) than smaller lesions. When evaluated by place of residence, patients from rural areas showed greater diagnostic accuracy (95.41%) than those from urban areas (78.45%). Additionally, patients aged between 41–60 years exhibited a marginally higher diagnostic accuracy (87.50%) compared to those aged 20–40 years (84.62%). These subgroup outcomes are summarized in Table-III.

TABLE-III.

Summary of Stratified Diagnostic Accuracy of DWI-MRI

Variable		Sensitivity	Specificity	Accuracy
Age	20-40 years	78.13%	90.91%	84.62%
	41-60 years	92.22%	81.43%	87.50%
Gender	Male	98.44%	84.21%	91.73%
	Female	77.59%	84.78%	80.77%
Duration	≤ 6 months	83.33%	82.95%	83.14%
	> 6 months	100.00%	93.33%	98.11%
Size	≤ 5 cm	87.25%	86.11%	86.78%
	> 5 cm	95.00%	80.65%	86.27%
Residence	Rural	98.48%	90.70%	95.41%
	Urban	76.79%	80.00%	78.45%

DISCUSSION

Meningiomas rank among the most prevalent benign tumors within the brain and frequently present in the cerebellopontine angle (CPA).[16] Imaging techniques are essential for accurate diagnosis and for surgical intervention.[17] This study aimed to evaluate the effectiveness DWI-MRI in distinguishing malignant meningiomas from benign ones, using histopathological examination as the gold standard. The findings demonstrate that DWI-MRI has high diagnostic performance, with a sensitivity of 88.52%, specificity of 84.47%, and overall accuracy of 86.67%. These results support the growing body of evidence highlighting DWI-MRI as a valuable, non-invasive imaging modality for preoperative evaluation of meningiomas.

Our findings align closely with those reported by Sohu et al., who observed sensitivity and specificity of 84.4% and 82.3%, respectively, for DWI-MRI in grading meningiomas, though these figures are slightly lower than those observed in our study.[18] Similarly, Surov et al., found that the sensitivity, specificity, and diagnostic accuracy of DWI-MRI were 72.9%, 73.1%, and 73.0%, respectively, which are also lower than our findings, possibly due to differing patient populations and MRI protocols.[19] In a 2020 meta-analysis that pooled data from multiple studies, Siempis et al., found the average sensitivity and specificity of DWI in grading meningiomas to be 80% and 76%, respectively, with an area under the ROC curve of 0.91, supporting its clinical relevance.[20] These metrics are in agreement with our results, reinforcing the diagnostic role of DWI in routine neuroimaging protocols.

Our study is also consistent with findings by Sacco et al., where sensitivity ranging from 72.9% to 93.8% and specificity from 64.8% to 97.4%, further confirming the reliability of DWI as a non-invasive diagnostic tool.[21] Similarly, a recent study by Mousam Panigrahi et al., using a threshold-based DWI approach found a sensitivity of 66.7% and specificity of 75% in differentiating benign from malignant meningiomas.[22] Another recent study reported even higher diagnostic performance, with DWI achieving 81.8% sensitivity and 97.4% specificity in differentiating benign from malignant meningiomas. These diagnostic values further support the utility of DWI as a reliable and non-invasive imaging tool in the preoperative assessment of meningioma grade.[23]

In addition, a study by Xiaoyu Huang et al., emphasized that factors such as gender, tumor diameter, peritumoral edema, and ADC_{min} were significantly associated with brain invasion in meningiomas. Their predictive model incorporating these variables achieved an AUC of 0.924, with a sensitivity of 92.2%, indicating excellent diagnostic performance.[24] These findings suggest that combining DWI parameters with clinical and morphological features may further enhance preoperative prediction of aggressive tumor behavior.

In our study, stratified analysis showed higher diagnostic accuracy in male patients, those with lesions larger than 5 cm, and patients with disease duration exceeding six months. These variations may reflect advanced tumor progression, which could present more distinct imaging characteristics on DWI.[25] Interestingly, patients from rural areas demonstrated higher diagnostic accuracy, possibly due to later presentation and more defined pathological changes.[26]

While this study offers valuable insights, it has certain limitations. Being conducted at a single tertiary care center with non-probability sampling restricts the broader applicability of the results. Additionally, inter-observer variability in interpretation was not

assessed. Although our study focused solely on DWI, future research should explore integration with conventional MRI features and multi-sequence analysis. To confirm and enhance the diagnostic value of DWI-MRI in meningioma grading, larger, multicenter prospective studies employing standardized DWI protocols are needed.

CONCLUSION

DWI-MRI demonstrates high sensitivity, specificity, and diagnostic accuracy in differentiating malignant from benign meningiomas when compared with histopathology. Its non-invasive nature, accessibility, and diagnostic performance make it a valuable adjunct for preoperative tumor characterization. Stratified subgroup analysis further supports its utility in varied clinical settings. DWI should be considered a routine imaging tool for meningioma evaluation, especially where biopsy is contraindicated or delayed.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
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ORIGINAL ARTICLE

A comparative study of intrathecal 1mg nalbuphine as adjunct to 15mg of bupivacaine 0.75% versus 15mg of bupivacaine 0.75% alone in spinal anesthesia for infraumbilical surgery.

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ABSTRACT… Objective: To compare mean duration of analgesia when 1mg Nalbuphine is added to 15mg of Bupivacaine 0.75% versus 15mg of Bupivacaine 0.75% alone in spinal anesthesia for infraumbilical surgeries. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Anesthesia, Allied Hospital, Faisalabad. **Periods:** April 2024 to October 2024. **Methods:** Total 60 subjects undergoing elective infraumbilical surgery under spinal anesthesia were assigned to two groups; Group A received inj. 0.75% Bupivacaine 15mg along with inj. Nalbuphine 1mg (0.1ml) in subarachnoid space via 25 gauge Quinke type spinal needle and Group B received 0.75% bupivacaine 15mg alone in subarachnoid space using 25guage spinal needle. Analgesia duration (hours) was calculated from sensory block onset to first request of analgesia using VAS score. Analysis of data was done using SPSS.23, for statistical significance p-value ≤0.05 was taken. **Results:** Sensory and motor block onset in Group A vs B noted was 3.25 ± 0.41 minutes & 6.36 ± 0.66 minutes vs 4.31 ± 0.39 minutes & 7.90 ± 0.63 minutes (p<0.001). Duration of postoperative analgesia was longer in Group A 5.77 ± 0.57 hours vs 5.03 ± 0.29 hours in Group B (p < 0.001). **Conclusion:** These findings suggest that intrathecal Nalbuphine added to Bupivacaine can considerably prolonged the duration of analgesia versus when Bupivacaine used alone in spinal anesthesia for infraumbilical surgeries irrespective of age, gender, or comorbidity status.

Key words: Analgesia Duration, Bupivacaine, Infraumbilical Surgeries, Nalbuphine.

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INTRODUCTION

According to IASP, pain is defined as "an unpleasant sensory and emotional experience associated with, or resembling actual or potential tissue damage.[1]" Analgesics, or pain-relieving medications, are commonly used to manage pain and can be directed via various routes, depending on required level of pain relief.[2] However, limitations in pain control and undesirable side effects from high doses of these drugs have prompted ongoing efforts to find safer and more effective alternatives.[3] As a result, adjuvant medications have been introduced to enhance analgesic efficacy while minimizing drug-related adverse effects.[4]

Spinal anesthesia is commonly used for infraumbilical surgeries due to its effectiveness, rapid onset, and favourable safety profile.[5] Bupivacaine, a widely used local anesthetic in spinal blocks, offers dependable sensory and motor blockade.[6] Nevertheless, its duration of action is limited, often necessitating additional postoperative pain management, which can lead to increased patient discomfort and the need for supplemental analgesics.[7] Thus, improving the duration and quality of postoperative analgesia remains key area of interest in anaesthesiology.

Nalbuphine, synthetic opioid that is highly lipid-soluble and acts as kappa receptor agonist and mu receptor antagonist, providing effective analgesia particularly for visceral pain.[8] When used alongside bupivacaine, it has been shown to enhance postoperative pain relief while reducing side effects.[9]

This study aims to assess and compare effectiveness of 1 mg Nalbuphine added to 15 mg of 0.75% Bupivacaine versus 15 mg of 0.75% Bupivacaine alone in patients undergoing infraumbilical surgeries under spinal anesthesia. Several studies have examined the use of Nalbuphine with other

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anesthetics or as adjuvant in spinal anesthesia.[10] However, to date, no local study has evaluated combination of Nalbuphine with 0.75% Bupivacaine compared to Bupivacaine alone for infraumbilical surgeries. The rationale for using Nalbuphine as an adjunct in spinal anesthesia lies in its potential to extend sensory block duration and enhance postoperative pain control, while offering favourable side effect profile compared to other opioids making it a promising agent in regional anesthesia.

METHODS

This randomized trial was conducted at Department of Anesthesia, Allied Hospital Faisalabad, over six months period following approval of synopsis by CPSP. Prior to data collection ethical approval was also obtained from institution [No.48.ERC/FMU/2023-2024/394 Dated 02-02-2024]. Total 60 patients were registered using non-probability consecutive sampling. The sample size was with population mean taken was 348.33 and test value of population mean was 256.17, with pooled standard deviation of 56.6, 90% power of study, 5% level of significance, and 95% confidence level.[10] Calculated sample size was 60 (30 in each group).

Eligible participants included both male and female patients between 18 to 50 years, with ASA I or II, planned for elective infraumbilical surgeries under spinal anesthesia. Patients were excluded if they had any contraindications to spinal anesthesia, cerebral disease, bradycardia, morbid obesity, pregnancy, lactation, known hypersensitivity to study drugs, or were classified as ASA III or IV.

After obtaining written informed consent, participants were grouped using computer-generated random number table. Group A received intrathecal injection of 0.75% bupivacaine 15 mg combined with nalbuphine 1 mg (0.1 ml), while Group B received 0.75% bupivacaine 15 mg alone. All intrathecal injections were administered using 25-gauge Quinke-type spinal needle. Preoperatively, all patients received Tab alprazolam0.5 mg on night before surgery. In operating room, baseline parameters; heart rate, BP, and SpO_2 were recorded and preloaded with 500 ml Ringer's lactate. Time of intrathecal injection was considered as "0" minutes for study timeline. Sensory block level was assessed with 27G hypodermic needle every 2 minutes until two consecutive tests confirmed no sensation at the relevant dermatome. Hemodynamic parameters were monitored until complete recovery. Duration of analgesia was recorded from time of sensory block onset to first request for analgesia, defined as Visual Analog Scale (VAS) score >4.(11) VAS scores were assessed at different intervals postoperatively. The requirement and dose of rescue analgesia were also documented. All data were recorded by the principal investigator using standardized proforma.

SPSS v23 was used for data analysis. Categorical data represented by frequencies/percentages, and continuous variables by mean±standard deviation. Independent sample t-test/Mann-Whitney U test applied for normal and non-normal distributed data, respectively. Categorical variables were analysed using chi-square/Fisher's exact tests; p-value of less than 0.05 was deemed statistically significant. Stratification was used to control for effect modifiers in order to account for any confounding factors. Stratification was followed by reanalysis.

RESULTS

As shown in Table-I; mean age of group A and B patients noted was 37.33 ± 8.21 years and 35.97 ± 7.77 years, (p = 0.510). Group A comprised of males 63.3% and females 36.7%, whereas Group B included 56.7% males and 43.3% females; (p = 0.792). ASA physical status distribution showed that most patients in both Groups A and B, belongs to ASA Status I (66.7% and 53.3%; p = 0.430). BMI in Group A and B calculated was 27.07 ± 1.53 kg/m^2 and 27.43 ± 1.48 kg/m^2, p = 0.324. Regarding comorbidities, 17 patients (56.7%) in Group A and 13 patients (43.3%) in Group B were diabetic (p = 0.439), while 18 patients (60%) in Group A and 14 patients (46.7%) in Group B were hypertensive (p = 0.438). Total 13 patients (43.3%) in Group A and 10 patients (33.3%) in Group B were smokers (p = 0.596). No patients in either group reported a history of drug addiction. Baseline SpO_2 (%) and respiratory rate was similar in both groups; p 0.247 and 0.881, respectively. There was no statistically significant difference seen in baseline heart rate, (p = 0.155), systolic (p = 0.833), and diastolic BP (p = 0.656) among both groups. Time of spinal injection was also comparable between groups (p = 0.760).

Sensory block onset was faster in Group A (3.25 ± 0.41 minutes) compared to Group B (4.31 ± 0.39 minutes) p-value<0.001. Likewise, onset of complete motor block was significantly earlier in Group A (6.36 ± 0.66 minutes) than in Group B (7.90 ± 0.63 minutes) (p < 0.001). Duration of surgery was significantly shorter in Group A (98.43 ± 4.64 minutes) compared to Group B (102.30 ± 4.82 minutes); p = 0.002. Duration of postoperative analgesia was also significantly longer in Group A 5.77 ± 0.57 hours vs 5.03 ± 0.29 hours in Group B (p < 0.001). Median (IQR) values were 5.75 (0.92) for Group A and 5.05 (0.5) for Group B.

Stratified analysis of duration of analgesia revealed that Group A (receiving nalbuphine with bupivacaine) consistently showed longer median duration of analgesia compared to Group B (receiving bupivacaine alone) across various subgroups as shown in Table-II. When analyzed by age, patients in the 31–40 and 41–50 year groups in Group A had significantly longer analgesia than those in Group B (p = 0.001 and p = 0.002, respectively), while difference in 20–30year group was not statistically significant (p = 0.165). Gender-based comparison showed significantly prolonged analgesia in both males and females in Group A compared to Group B (p < 0.001 and p = 0.001, respectively). Among patients with/without diabetes Group A demonstrated significantly longer duration of analgesia than Group B (p = 0.009 and <0.001, respectively). Similarly, hypertensive and non-hypertensive patients in Group A experienced significantly longer analgesia (p < 0.001 and p = 0.029, respectively). Group A again showed significantly longer duration of analgesia compared to Group B (p < 0.001) among smokers and non-smokers.

TABLE-I

Patients characteristics in study groups

		Group-A	Group-B	P-Value
		30	30	
Age (years) mean±SD		37.33±8.21	35.97±7.77	0.510(t)
Gender	Male n(%)	19(63.3%)	17(56.7%)	0.792(c)
	Female n(%)	11(36.7%)	13(43.3%)	
ASA Status	I n(%)	20(66.7%)	16(53.3%)	0.430(c)
	II n(%)	10(33.3%)	14(46.7%)	
BMI (kg/m2) mean±SD		27.07±1.53	27.43±1.48	0.324
Diabetes n(%)		17(56.7%)	13(43.3%)	0.439(c)
Hypertension n(%)		18(60%)	14(46.7%)	0.438(c)
Smoking n(%)		13(43.3%)	10(33.3%)	0.596(c)
Drug addict n(%)		0(0%)	0(0%)	-
SpO2(%)		97±0.79	97.23±0.82	0.247(ζ)
Respiratory Rate (B/min)		14±0.85	14±0.87	0.881(ζ)
Heart Rate (BPM)		74±1.62	75±1.37	0.155(ζ)
Systolic Blood Pressure (mmHg)		121±4.56	121±5.16	0.833(t)
Diastolic Blood pressure (mmHg)		77±3.67	78±4.35	0.656(ζ)
Time of Spinal Injection (HH:MM)		9.11±0.27	9.09±0.27	0.760(ζ)
Time of Onset of Sensory block (Min)		3.25±0.41	4.31±0.39	<0.001(ζ)*
Time of Onset of Motor Block complete		6.36±0.66	7.90±0.63	<0.001(ζ) *
Duration of surgery (Min)		98.43±4.64	102.30±4.82	0.002(t) *
Duration of Analgesia (Hours)	Mean±SD	5.77±0.57	5.03±0.29	<0.001(ζ) *
	Median(IQR)	5.75(0.92)	5.05(0.5)	

Note: (c): Chi Square test, (t): independent sample t-test (ζ): Mann Whitney u test (*): statistically significant (p-value<0.05)

Table-II

Duration of analgesia (hours) stratified for various variables

		Duration of Analgesia		P-Value(ζ)
		Group-A	Group-B	
		30	30	
		Median (IQR)	Median (IQR)	
Age (Years)	20-30	5.70(1.50)	5.30(0.30)	0.165
	31-40	5.70(1.13)	5.00(0.60)	0.001*
	41-50	6.00(0.80)	4.90(0.45)	0.002*
Gender	Male	5.70(0.90)	5.00(0.50)	<0.001*
	Female	6.10(1.00)	5.10(0.55)	0.001*
DM	Yes	5.70(1.20)	5.20(0.55)	0.009*
	No	6.10(0.70)	4.90(0.55)	<0.001*
HTN	Yes	6.10(0.70)	4.95(0.63)	<0.001*
	No	5.60(1.15)	5.15(0.47)	0.029*
Smoking	Yes	6.10(0.90)	4.90(0.35)	<0.001*
	No	5.70(1.10)	5.20(0.58)	0.001*

Note: (ζ) Mann Whitney u test (Normality assumption was not fulfilled) (*): statistically significant (p-value<0.05)

DISCUSSION

According to current study findings, sensory block onset in Group A and B noted was 3.25 ± 0.41 minutes and 4.31 ± 0.39 minutes; p-value <0.001. Motor block onset was 6.36 ± 0.66 minutes in group A and 7.90 ± 0.63 minutes in group B (p < 0.001). Duration of postoperative analgesia was also significantly longer in Group A 5.77 ± 0.57 hours vs 5.03 ± 0.29 hours in Group B (p < 0.001). Likewise, in study by Naik et al, addition of 1.6 mg nalbuphine to bupivacaine significantly increased mean duration of analgesia from 175.8 minutes to 303.8 minutes.[12] Similarly, Niharika et al, reported notable extension of analgesia duration with nalbuphine (4.65 hours) compared to bupivacaine alone (3.21 hours) and also reported quicker sensory block onset of 1.93 minutes with nalbuphine versus 3.30 minutes with bupivacaine alone.[13] Our results are further supported by Raut Dessai et al, who observed mean analgesia duration of 264.97 minutes with nalbuphine, which was significantly longer than 198.50 minutes in bupivacaine-only group, p<0.001.[14] In addition to prolonged analgesia, onset of both sensory and motor blocks was found to be faster when nalbuphine was used as adjuvant. When used as an adjunct in spinal anesthesia, nalbuphine was also hemodynamically safe in study by Mehdi et al.[15] In contrast, Shah et al, compared three groups (2 groups with different doses of nalbuphine (1.6mg and 2.4mg) in combination with bupivacaine and one group received only bupivacaine and found similar onset of sensory and motor blocks among groups (p > 0.05). However, analgesia duration found to be highest in group with injection nalbuphine 2.4mg, p <0.001.[16] As reported by Bachula et al, intrathecal nalbuphine 0.8mg to bupivacaine in spinal block significantly enhances onset of sensory and motor block and extends the duration of postoperative analgesia, in patients undergoing cesarean section. Although higher proportion of patients in bupivacaine-only group achieved maximum sensory block, group receiving nalbuphine experienced longer duration of sensory regression and analgesia.[17] Nalbuphine is associated with favorable profile, as multiple studies have shown no significant occurrences of common opioid-related complications such as respiratory depression or urinary retention, which are often seen with agents like fentanyl.[18,19] Furthermore, its use does not negatively impact hemodynamic stability. Compared to other opioids, nalbuphine has demonstrated superior efficacy by providing longer-lasting analgesia while also minimizing side effects, making it more suitable option for managing postoperative pain.[18] In current study nalbuphine 1mg dose was given. Recent evidence suggests intrathecal nalbuphine 1.2mg is most effective

dose when used as adjuvant to bupivacaine for postoperative pain relief. While lower doses such as 0.8 mg also offer moderate analgesia (around 247 minutes).[20] On the other hand, although higher doses like 1.6 mg may extend analgesia duration, they are more likely to cause side effects. Thus, 1.2 mg strikes best balance between efficacy and safety, offering prolonged analgesia with minimal adverse effects.[19] These findings suggest that nalbuphine is safe and effective adjuvant to bupivacaine, offering improved analgesic outcomes with minimal adverse effects, making it viable alternative to traditional intrathecal opioids.

This study has certain limitations. We did not compare different doses of nalbuphine to determine the optimal effective dose. Additionally, nalbuphine was not compared with other adjuvant drugs, limiting broader applicability. The safety profile, including long-term or rare adverse effects, was also not thoroughly assessed.

CONCLUSION

These findings suggest that intrathecal Nalbuphine added to Bupivacaine can significantly prolonged the duration of analgesia versus when Bupivacaine used alone in spinal anesthesia for infraumbilical surgeries irrespective of age, gender, or comorbidity status.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Evaluation of the effectiveness of multimodal analgesia with low-dose opioids in post-operative pain management for CABG patients: A quasi-experimental study.

Gulrukh Begum[1], Laila Shaukat[2]

ABSTRACT… Objective: To evaluate effectiveness of multimodal analgesia (MMA) with low-dose opioids in reducing postoperative pain and the need for stronger opioids (nalbuphine) in patients undergoing coronary artery bypass grafting (CABG). **Study Design:** Quasi-experimental study. **Setting:** Department of Anesthesia Peshawar Institute of Cardiology, A Tertiary Care Hospital. **Period:** November 2024 to March 2025. **Methods:** Was conducted with 30 CABG patients receiving a standardized MMA regimen (acetaminophen, gabapentin, ketorolac, and low-dose morphine) for 72 hours postoperatively. Effectiveness was defined as maintaining Visual Analog Scale (VAS) scores ≤6/10 without nalbuphine escalation. Data on pain scores, opioid consumption, mobilization time, hospital stay, and complications were analyzed using SPSS v23. **Results:** MMA was effective in 83.3% of patients (n=25), while 16.7% (n=5) required nalbuphine. Median VAS pain scores decreased from 4 (IQR 3-5) at 6 hours to 0 (IQR 0-0) at 72 hours. Sedation was significantly associated with effectiveness (56% vs. 0%, p=0.022). No significant associations were found with demographic or surgical variables (all p>0.05). Postoperative complications included nausea (36.7%), vomiting (23.3%), and respiratory depression (16.7%). **Conclusion:** MMA with low-dose opioids effectively controlled post-CABG pain in most patients, reducing the need for stronger opioids. Sedation may serve as a clinical indicator of effective analgesia.

Key words: CABG, Multimodal Analgesia, Nalbuphine, Opioid Reduction, Postoperative Pain.

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INTRODUCTION

Sternotomy, sternal/rib retraction, pericardiotomy, internal mammary artery harvesting, saphenous vein harvesting, surgical manipulation of the parietal pleura, chest tube insertion, and other musculoskeletal damage during surgery are some of the causes of pain following cardiac surgery.

Opiate analgesics have historically been the mainstay of postoperative pain treatment following heart surgery. Opioids do, however, have certain unfavorable dose-related side effects, including as nausea, vomiting, constipation, dizziness, mental disorientation, and respiratory depression, which can significantly affect a patient's recuperation and postpone discharge.[1,2] Targeting multiple pain pathways at once is the goal of multimodal pain management in order to increase therapy effectiveness and recovery.[3] Additionally, recent data indicates that inadequate management of acute postoperative pain affects patients' well-being and raises their chance of developing chronic pain.[4] Evidence-based multimodal opiate-sparing analgesia following non-cardiac surgery has grown in popularity over the past 20 years.[5] Both the opiate-sparing effect and the achievement of more effective pain control through both central and peripheral anti-nociceptive mechanisms serve as justifications for the use of various analgesics.[1,6]

Following heart surgery, NSAIDs have shown opiate sparing effects in randomized trials.[7] However, NSAIDs have raised safety concerns for cardiac surgeons and anesthesiologists due to the possibility of bleeding, renal impairment, and an elevated risk of cardiovascular death.[8] Gamma-aminobutyric acid (GABA) analog gabapentin is mostly used to treat neuropathic pain and epilepsy, but it has also been employed in recent years as part of multimodal regimens following non-cardiac

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surgery.[9] Its effectiveness following heart surgery has been studied in recent trials, although the findings have been conflicting. In theory, gabapentin and NSAIDs should work together to produce synergistic analgesic and opiate-sparing effects; in fact, this combination has shown some promise in other surgical populations.[10,11]

The purpose of this study was to assess the effectiveness of a multimodal analgesic regimen that included low-dose opioids and NSAIDs, gabapentin, and paracetamol in lowering post-operative pain following CABG and the need to escalate opioids. According to our hypothesis, the multimodal regimen reduced side effects and had a better analgesic efficacy, as seen by an improved pain score.

To assess the effectiveness of multimodal analgesia (MMA) with low-dose opioids in reducing post-operative pain and opioid consumption, specifically evaluating the need for escalation to nalbuphine, which is the standard opioid protocol at the institution, in patients undergoing coronary artery bypass grafting (CABG) with sternotomy.

METHODS

This quasi-experimental single-arm study was conducted at Department of Anesthesia Peshawar Institute of Cardiology, a tertiary care hospital, from November 2024 to March 2025 following ethical approval from the institutional review board (Ref No. IRC/25/215) (22-07-2025). A convenience sample of 30 adult patients (aged ≥18 years) undergoing elective CABG via sternotomy were enrolled after obtaining informed consent. Exclusion criteria included chronic pain or opioid dependence, severe renal/hepatic impairment, and allergies to any components of the MMA protocol.

Postoperatively, patients received a standardized MMA regimen consisting of acetaminophen (1 g IV every 6 hours), gabapentin (300 mg orally every 8 hours), ketorolac (15 mg IV every 6 hours), and low-dose morphine (0.05 mg/kg IV) for breakthrough pain over 72 hours. MMA effectiveness was defined as maintaining pain at VAS ≤6/10 without requiring escalation to nalbuphine; VAS ≥7/10 necessitating nalbuphine or stronger opioids classified the regimen as ineffective. Data on demographics (age, gender, BMI), clinical characteristics (comorbidities, surgical details), and outcomes (VAS scores at 6, 12, 24, 48, and 72 hours, nalbuphine escalation, time to first mobilization, hospital stay, and adverse effects—nausea, vomiting, respiratory depression, dizziness, sedation) were collected via standardized questionnaires and medical records.

Statistical analysis was performed using SPSS v23. Continuous variables (age, BMI, pain scores, mobilization time, hospital stay) were reported as mean ± SD or median (IQR), while categorical variables (gender, MMA effectiveness, adverse effects) were presented as frequencies (%). The primary outcome (MMA effectiveness) was stratified by patient and surgical variables, with associations assessed using Chi-square or Fisher's exact tests (significance: $p \leq 0.05$). Normality was evaluated via Shapiro-Wilk/Kolmogorov-Smirnov tests.

RESULTS

The study included 30 patients with a mean age of 59.9 ± 10.6 years and BMI of 30.7 ± 2.7. LVEF averaged 54.2 ± 5.7%, while the number of involved vessels was median 3 (IQR 2-3). Surgical duration averaged 284.7 ± 70.4 minutes with cross-clamp time of 78.6 ± 32.2 minutes. Postoperative pain scores (non-normal) were: 6hrs - median 4 (IQR 3-5), 12hrs - 3 (2-4), 24hrs - 2 (0-2), 48hrs - 2 (2-2), and 72hrs - 0 (0-0). Total opioid consumption was highly skewed (median 40, IQR 28-400). Mobilization time was median 13 days (IQR 7-27) and hospital stay median 5 days (IQR 3-7). The data showed normal distributions for age, BMI, and LVEF, while pain scores and opioid use were non-normally distributed.

The study included 17 (56.7%) males and 13 (43.3%) females. Cardiopulmonary bypass (CPB) was used in 28 (93.3%) cases. Postoperative complications included nausea 11 (36.7%), vomiting 7 (23.3%), sedation 14 (46.7%), respiratory depression 5 (16.7%), and dizziness 5 (16.7%). (Table-I)

The effectiveness of MMA was assessed in 30 patients, with 25 (83.3%) achieving adequate pain control and 5 (16.7%) reporting insufficient relief (Figure-1).

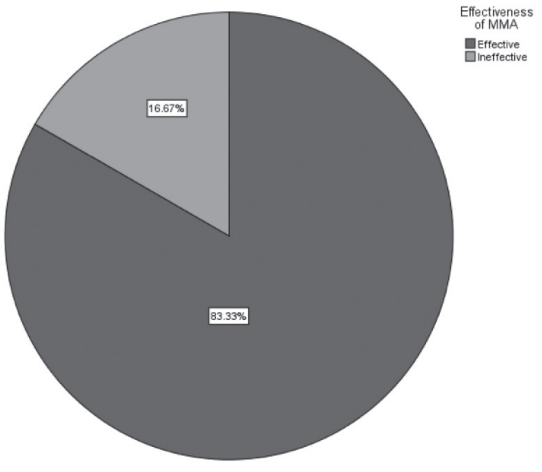
TABLE-I

Demographic and clinical characteristics (n=30)

Variable	Category	Frequency (%)
Gender	Male	17 (56.7%)
	Female	13 (43.3%)
CPB Use	Yes	28 (93.3%)
	No	2 (6.7%)
Nausea	Yes	11 (36.7%)
	No	19 (63.3%)
Vomiting	Yes	7 (23.3%)
	No	23 (76.7%)
Respiratory Depression	Yes	5 (16.7%)
	No	25 (83.3%)
Dizziness	Yes	5 (16.7%)
	No	25 (83.3%)
Sedation	Yes	14 (46.7%)
	No	16 (53.3%)

FIGURE-1

Effectiveness of MMA (Multi Modal Analgesia)



Most effective cases occurred in patients >40 years (96.0% vs 100% ineffective, p=0.649), males (56.0% vs 60.0%, p=0.869), and CPB users (92.0% vs 100%, p=0.513). Obese patients showed similar effectiveness rates (68.0% effective vs 60.0% ineffective, p=0.729). No significant associations were found for LVEF categories (96.0% >40% in both groups, p=0.649), surgery duration (72.0% >4hrs effective vs 60.0% ineffective, p=0.593), early mobilization (96.0% <24hrs in both, p=0.649), or hospital stay (80.0% <5 days effective vs 60.0% ineffective, p=0.334). (Table-II)

Postoperative complications analysis revealed sedation was significantly associated with effectiveness (56.0% effective cases had sedation vs 0% ineffective, p=0.022). Nausea (32.0% vs 60.0%, p=0.236), vomiting (20.0% vs 40.0%, p=0.334), and dizziness (12.0% vs 40.0%, p=0.125) were more common in ineffective cases but not statistically significant. Respiratory depression showed no difference (20.0% effective vs 0% ineffective, p=0.273). All ineffective cases (100%) occurred in non-sedated patients. (Table-III)

DISCUSSION

The present study demonstrated that a multimodal analgesia (MMA) protocol incorporating low-dose opioids was effective in controlling postoperative pain for 83.3% of CABG patients, significantly reducing the need for escalation to stronger opioids like nalbuphine. These findings align with several studies investigating MMA in cardiac surgery populations.[3,12] The progressive reduction in median VAS scores observed in our study (from 4 at 6 hours to 0 at 72 hours) mirrors the pain trajectory reported by Barr et al., suggesting consistent analgesic effectiveness across the critical postoperative period.[13]

The significant association between sedation and MMA effectiveness (p=0.022) represents a notable finding, as all ineffective cases occurred in non-sedated patients. This observation parallels work by Jannati M et al. that identified sedation levels as potential markers of adequate analgesia in opioid-sparing protocols.[17]

Our results showing no demographic or surgical predictors of MMA effectiveness contrast with some previous literature. While Fernandez RM et al.[16], reports that younger age and female gender as predictors of better MMA response, we found no significant associations with age (p=0.649), gender (p=0.869), or surgical duration (p=0.593).

Table-II

Association between patient characteristics and MMA effectiveness

Variable	Category	Effective (n=25)	Ineffective (n=5)	P-Value
Age Categories	<40 years	1 (4.0%)	0 (0.0%)	0.649
	>40 years	24 (96.0%)	5 (100.0%)	
Gender	Male	14 (56.0%)	3 (60.0%)	0.869
	Female	11 (44.0%)	2 (40.0%)	
Use of CPB	Yes	23 (92.0%)	5 (100.0%)	0.513
	No	2 (8.0%)	0 (0.0%)	
BMI Categories	Overweight	8 (32.0%)	2 (40.0%)	0.729
	Obese	17 (68.0%)	3 (60.0%)	
LVEF Categories	<40%	1 (4.0%)	0 (0.0%)	0.649
	>40%	24 (96.0%)	5 (100.0%)	
Surgery Duration	<4 hrs	7 (28.0%)	2 (40.0%)	0.593
	>4hrs	18 (72.0%)	3 (60.0%)	
First Mobilization	<24hrs	24 (96.0%)	5 (100.0%)	0.649
	>24hrs	1 (4.0%)	0 (0.0%)	
Hospital Stay	<5 days	20 (80.0%)	3 (60.0%)	0.334
	>5 days	5 (20.0%)	2 (40.0%)	

TABLE-III

Association between postoperative complications and MMA effectiveness (n=30)

Complication	Group	Effective n=25 n(%)	Ineffective n=5 n(%)	P-Value
Nausea	Yes	8 (32.0%)	3 (60.0%)	0.236
	No	17 (68.0%)	2 (40.0%)	
Vomiting	Yes	5 (20.0%)	2 (40.0%)	0.334
	No	20 (80.0%)	3 (60.0%)	
Respiratory Depression	Yes	5 (20.0%)	0 (0.0%)	0.273
	No	20 (80.0%)	5 (100.0%)	
Dizziness	Yes	3 (12.0%)	2 (40.0%)	0.125
	No	22 (88.0%)	3 (60.0%)	
Sedation	Yes	14 (56.0%)	0 (0.0%)	0.022*
	No	11 (44.0%)	5 (100.0%)	

These discrepancies may stem from variations in MMA protocols or patient populations. The lack of association with CPB use (p=0.513) contradicts findings by Van et al., who reported better pain control in off-pump CABG patients, suggesting our MMA protocol may mitigate the inflammatory effects of CPB.[14]

The 16.7% MMA failure rate in our study merits consideration. While lower than the 25-30% failure rates reported by Jin L et al in his trial.[17] The higher (though non-significant) rates of nausea (60% vs 32%) and vomiting (40% vs 20%) in ineffective cases echo observations by Cozowicz et al., suggesting inadequate pain control may contribute to these complications.[3]

Several limitations should be acknowledged. The single-arm design precludes direct comparison to conventional analgesia, and the modest sample size may have limited statistical power for some analyses. Additionally, the lack of standardized sedation scoring represents a potential measurement bias. Future studies incorporating randomized controlled designs, larger samples, and quantitative sedation assessment would strengthen these findings.

CONCLUSION

MMA with low-dose opioids effectively controlled post-CABG pain in most patients, reducing the need for stronger opioids. Sedation may serve as a clinical indicator of effective analgesia.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Comparison of pain scores between first and second session ESWL treatment for kidney stone patients.

Hafeez Ullah[1], Musab Umair Khalid[2], Syed Zafar Hussain[3], Usman Javed[4], Badar Murtaza[5], Faran Kiani[6]

ABSTRACT… Objective: To determine and compare pain scores between the first and second session ESWL treatment for kidney stone patients. **Study Design:** Descriptive, Case Series. **Setting:** Armed Forces Institute of Urology, Rawalpindi. **Period:** 1st January 2021 to 30th June 2021. **Methods:** A total of 133 patients with renal pelvis stone of 8-20 mm, 15 to 65 years old of the two sexual orientations were incorporated. Patients with stone in calycealdiverticulae with limited infundibulum, Renal ectopia or contortion, pregnancy, pyonephrosis and PUJO, claustrophobic and cardiovascular speed producer were prohibited. In the wake of taking informed assent, extracorporeal shock wave lithotripsy (ESWL) was finished in every patient. After this, anti-infection (infusion ceftriaxone 1gm IV x detail) and pain relieving (infusion dyclo IM x detail) was given to all patients before every meeting. Then extracorporeal shock wave lithotripsy (ESWL) was finished in every patient by single specialist (something like 3 years of post-cooperation experience). In all patients, two meetings were finished and torment score after first and second meeting (in no less than 10 days) was noted. **Results:** Age range in this study was from 15 to 65 years with mean time of 41.17 ± 8.83 years. Larger part of the patients 76 (57.14%) were between 15 to 40 years old. Out of 133 patients, 84 (63.16%) were male and 49 (36.84%) were females with male to female proportion 1.6:1. In our review, mean agony score after first meeting of ESWL was 5.29 ± 0.79 and after second meeting of ESWL was 3.75 ± 0.89 with p-worth of 0.0001. **Conclusion:** This study concluded that VAS scores is significantly lower in the second session of ESWL.

Key words: Extracorporeal Shock Wave Lithotripsy, Pain, Renal Stone.

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INTRODUCTION

Kidney stones represent a huge burden of disease on the planet. Beginning in 1976, the incidence of kidney stones increased markedly, a change likely driven by the weight epidemic[1]. Up to half of people with stones will develop stones again within 5 years which interspersed with intermittent forms that indicate the invasion of kidney stones. The main goal of kidney stone treatment is to maximize stone clearance without causing pain to the patient.[2] To achieve this, different non-obvious invasive modalities have been described, such as shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS).[3] The preferred method is SWL and for stones <2 cm is PCNL, but the treatment of stones 1 to 2 cm remains questionable.[4] This situation has been further exacerbated by the expansion of RIRS into the arsenal over the past two decades.[5]

Extracorporeal shock wave lithotripsy (ESWL) has long been used to treat kidney stones. Special rules mention ESWL as a reliable alternative treatment to ureteroscopy (URS) for the detection of upper ureteral stones less than 10 mm. favored. Disappointment in ESWL can lead to futile opening of the renal parenchyma, resulting in corona waves and difficulty, thus requiring permanent elective treatment, resulting in additional clinical costs.[6-7]

After ESWL, the system was performed under extensive sedation. Specialized modifications of the lithotripter allow the treatment to be performed without the use of general sedation, although lower levels of force are often used. Despite this, ESWL is still generally considered a distressing system. This can be caused by shock waves reaching superficial (skin and muscles) and deeper (ribs, nerves, and kidney capsules) structures. and unnecessary suffering.

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An elevated perception of pain may also limit potential opportunities to exert sufficient energy types of SWL devices, etc.).[8-9]

There is no information or close research on this topic. Due to the great pain during ESWL, the managers reduced the patient's nervousness and gave him great consistency and urged him to continue performing the method. Therefore, the current review aims to create close information and provide technical support to patients.

METHODS

In the wake of getting endorsement from institutional survey board (Uro-adm-Trg-1/IRB/2020/109) an observational review was directed at Military Foundation of Urology (AFIU), Rawalpindi where 133 patients going through extracorporeal shock wave lithotripsy (ESWL) were evaluated tentatively for torment appraisal from 1st January 2021 to 30th June 2021. The determined example size was 133 with 95% certainty level, 5% outright accuracy required and taking mean agony score after second meeting of ESWL as 5.23±2.94.11The testing method was non-likelihood, successive inspecting.

Measurements considered for the review included patients ranging in age from 15 to 65 years in one direction or the other, a single stone in the renal pelvis > 1 month of age based on the functional significance of the term, and a stone size of 8 to 20 mm.

Review prohibitions: Pregnancy (assessed by ultrasound), muscular or spinal torsion (preventing legal position), calyceal diverticular stones with elongated infundibulum, ectopia or renal malformation (horseshoe kidney or pelvic kidney), patients with PUJO (under examination in CTU), patients with pyonephrosis and sepsis (after clinical evaluation), patients with claustrophobia, patients with cardiovascular pacemakers, patients with intellectual disabilities and patients with elimination of calculations after the first visit.

Informed and dispassionate consent was obtained from each patient. Subsequently, antitoxin (ceftriaxone 1 g IV infusion x details) and analgesia (dyclo IM infusion x details) were administered to all patients before each meeting. Then, at this time, each patient's extracorporeal shock wave lithotripsy (ESWL) was performed by a single expert (approximately 3 years of post-collaboration experience). All patients completed two sessions and pain scores were recorded according to functional definitions after the first and second sessions (not less than 10 days). All information (age, orientation, stone length, stone size, BMI, diabetes, hypertension, place of residence, and VAS score at the first and second ESWL sessions) was recorded on a specially planned form.

Measurable verification was performed using SPSS Table 25.0. The mean and standard deviation of age, stone duration, stone size, BMI, ESWL length, and VAS score were determined in the first and second ESWL sessions. Determination of recurrence and relapse rate included counseling, diabetes mellitus (yes/no), hypertension (yes/no), place of residence (rural/metropolitan), history of renal medical surgery (yes/no), and affected side (right/left) Torment scores were observed across the range of the first and second ESWL sessions by applying free basic t-tests and paired t-tests, with p values ≤0.05 considered critical.

Impact modifiers like age, orientation, diabetes mellitus (yes/no), hypertension (yes/no), spot of living (country/metropolitan), past history of renal medical procedure (yes/no) and side impacted (right/left), length of stone, stone size and BMI. Post-delineation matched 't' test was applied to see their impact on VAS score and p-esteem ≤ 0.05 was viewed as critical.

RESULTS

Age range in this study was from 15 to 65 years with mean period of 41.17 ± 8.83 years. Greater part of the patients 76 (57.14%) were between 15 to 40 years old. Out of 133 patients, 84 (63.16%) were male and 49 (36.84%) were females with male to female proportion 1.6:1. Mean span of sickness in our review was 5.65 ± 2.28 months. Mean size of stone in our review was 14.11 ± 1.91 mm. Mean BMI was 27.40 ± 2.92 kg/m2. Appropriation of patients with status of other puzzling factors is displayed in Table-I. Correlation of agony scores between the first and second meeting ESWL treatment for

kidney stone patients is displayed in Table-II.

In our review, mean torment score after first meeting of ESWL was 5.29 ± 0.79 and after second meeting of ESWL was 3.75 ± 0.89 with p-worth of 0.0001.

Delineation of agony score concerning age, orientation, diabetes mellitus, hypertension, spot of living, past history of renal medical procedure and side impacted, span of stone, stone size and BMI is displayed in Table-III.

TABLE-I

Distribution of patients with status of other confounding variables (n=133)

Confounding Variables		Frequency	%age
Diabetes Mellitus	Yes	40	30.08
	No	93	69.92
Hypertension	Yes	32	24.06
	No	101	75.94
Place of living	Rural	54	40.60
	Urban	79	59.40
Previous history of renal surgery	Yes	36	27.08
	No	97	72.92
Side affected	Right	81	60.90
	Left	52	39.10

TABLE-II

Comparison of pain scores between the first and second session ESWL treatment for kidney stone patients.

	1st Session	2nd Session	P-Value
	Mean ± SD	Mean ± SD	
Pain score (VAS)	5.29 ± 0.79	3.75 ± 0.89	0.0001

DISCUSSION

After Schmiedt and Chaussy12 performed detailed shock wave lithotripsy (ESWL) for kidney stones in 1980, ESWL improved and was recognized as the first-line treatment option for small urinary tract stones.[10-12] The European Urology Rules recommend that ESWL is the best option for stones located in the kidney that measure <1 cm.[13] Unlike adaptive ureteroscopy and percutaneous nephrolithotomy, ESWL can be performed in short-stay facilities and the patient does not require systemic sedation.[14-16] Still, regardless of the benefits of SWL, the results of shockwave therapy can still be painful for patients, which may be one of the reasons why some patients consider whether to opt for SWL.[17-18] Additionally, thoughts of torture during SWL may cause the patient to change positions, which may alter the therapeutic shock wave center and therefore negatively affect SWL achievement rates.[19-21]

As SWL technology has advanced, the analgesic needs necessary to control pain during SWL have been significantly reduced.[22] Several clinical factors, such as sex, age, weight profile (BMI), and stone area, have been interpreted as predictive variables of ESWL-related pain. Encounter of ESWL in patients with kidney stones.[23-25]

The age range in this study was 15 to 65 years, with a mean duration of 41.17 ± 8.83 years. Most of the patients 76 (57.14%) were between 15 and 40 years old. Among the 133 patients, 84 were men (63.16%) and 49 were women (36.84%), with a male:female ratio of 1.6:1. 5.29 ± 0.79. The ESWL is 3.75 ± 0.89 and the p-value is 0.0001. In one review, VAS scores were significantly lower in the second ESWL session (5.23 ± 2.94 vs. 6.41 ± 2.37).[26-27]

Several studies have examined the association of different elements during SWL treatment with torture discrimination. Tokgoz et al 20 suggested that men may be more willing to endure the ordeal during SWL than women, and that the initial SWL session is often more pleasant for patients than the final session.[28] Gracious et al 21 also reported that emotional distress scores were affected by persistent age, sex, and stone area, but not by stone size or laterality.[29]

The ordeal during ESWL depends on the type of fuel source and how much energy is used. The need for painlessness is greater in women, younger patients, or patients applying higher voltages. And feel more pleasant afterwards. ESWL should be started at a lower voltage and increased slowly as treatment progresses. This gives the patient the opportunity to adapt to the treatment.[30]

The pathogenesis of discomfort in ESWL remains poorly understood, but is believed to be multifactorial.

TABLE-III

Stratification of pain score with respect to age, gender, diabetes mellitus, hypertension, place of living, previous history of renal surgery and side affected, duration of stone, stone size and BMI.

Co-morbid Conditions		1st session		2nd session		P-Value
		VAS score		VAS score		
		Mean	SD	Mean	SD	
Age (years)	15-40	5.39	0.75	3.70	0.89	0.0001
	41-65	5.14	0.83	3.82	0.89	0.0001
Gender	Male	5.26	0.75	3.79	0.89	0.0001
	Female	5.33	0.88	3.69	0.89	0.0001
Duration (months)	2-6	5.32	0.84	3.91	0.86	0.0001
	>6	5.20	0.69	3.38	0.87	0.0001
Size of stone (mm)	8-15	5.27	0.77	3.70	0.91	0.0001
	16-20	5.34	0.87	3.91	0.82	0.0001
BMI (kg/m^2)	≤27	5.16	0.77	3.79	0.91	0.0001
	>27	5.41	0.81	3.71	0.88	0.0001
Place of living	Rural	5.22	1.06	3.87	0.55	0.0001
	Urban	5.33	0.55	3.67	1.06	0.0001
Hypertension	Yes	5.50	0.67	3.78	0.94	0.0001
	No	5.22	0.82	3.74	0.88	0.0001
Diabetes mellitus	Yes	4.83	0.55	3.40	0.98	0.0001
	No	5.48	0.80	3.90	0.81	0.0001
Previous history of renal surgery	Yes	5.14	0.90	3.67	0.72	0.0001
	No	5.34	0.75	3.78	0.95	0.0001
Side affected	Right	5.02	0.81	3.64	0.90	0.0001
	Left	5.69	0.58	3.92	0.86	0.0001

Superficial cutaneous nociceptors and instinctive nociceptors, such as the periosteum, pleura, peritoneum, and external muscular nociceptors, are two important components responsible for pain during ESWL.[26] The size and location of the weight, the area of the front of the shock wave, the cavitation shock, the stress at the top of the shock wave, the size of the central area and the area of the shock wave at the skin also tends to cause pain. In the case of using shock waves to obtain large discontinuities in stones.[27]

Continued improvements have made ESWL more feasible in negligible darkness, allowing short-term ESWL to be performed without the need for general or spinal anesthesia. A CRITICAL QUESTION 28 Analgesics commonly used during ESWL include narcotics, narcotic hypnotics, nonsteroidal analgesics (NSAIDs), and local sedative ointments (e.g., EMLA). Associated with severe difficulties dyspnea, bradycardia, hypotension, nausea, regurgitation and delayed recovery time. Therefore, it is essential to choose a suitable method to relieve pain with fewer side effects. Although there are different examination reports analyzing changes in pain relief strategies during ESWL.[31]

CONCLUSION

This study reasoned that VAS scores is essentially lower in the second meeting of ESWL. Thus, we suggest that extracorporeal shock wave lithotripsy (ESWL) ought to be the essential methodology of decision in each patientwith renal stone of <2 cm and agony the board during ESWL ought to be engaged for getting the improved outcomes.

Ethical Approval

Ethical approval of this study was obtained

from Armed Forces Institute of Urology (AFIU), Rawalpindi.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Hafeez Ullah:** Acquisition, analysis.
2	**Musab Umair Khalid:** Design.
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4	**Usman Javed:** Final approval.
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ORIGINAL ARTICLE

Effect of spinal anesthesia versus general anesthesia on blood glucose concentration in patients undergoing elective cesarean sections.

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ABSTRACT… Objective: To compare mean blood sugar levels in patients undergoing elective cesarean sections through spinal versus general anaesthesia. **Study Design:** Prospective Cohort Study. **Setting:** Department of Anaesthesiology, Allama Iqbal Teaching Hospital DG Khan. **Period:** 1st March 2024 to 31st August 2024. **Methods:** Non-diabetic pregnant women aged 20 – 45 years with ASA-I status undergoing elective cesarean section were enrolled. Women with diabetes, eclampsia / preeclampsia, cardiomyopathy or allergy to anesthetic agents were excluded. Participants were categorized as exposed if opted for spinal anesthesia and unexposed if opted for general anesthesia. Blood glucose levels were measured preoperatively and 30 minutes of surgery using a standardized glucometer. Descriptive statistics are run using SPSS version 23. Numerical and categorical comparisons across the groups are made through t-test and chi-square test respectively at 5% significance level. **Results:** A total of 248 patients (124 per group) were included. Baseline characteristics including BMI, fasting duration, surgery duration and fluid type were comparable. Mean preoperative blood glucose was higher in spinal than general anesthesia group (83.9 ± 8.3 vs. 81.2 ± 8.6 mg/dl; p = 0.011). Post-operative glucose levels were significantly higher in spinal (126.4 ± 15 vs. 56.7 ± 9.8 mg/dl; p-value < 0.001). This difference remains significant across stratified groups. **Conclusion:** Spinal anesthesia was associated with significantly higher postoperative blood glucose levels compared to general anesthesia in non-diabetic women undergoing cesarean section. Monitoring perioperative glucose in spinal anesthesia may warrant further attention.

Key words: Blood Glucose, Cesarean Section, General Anaesthesia, Spinal Anaesthesia.

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INTRODUCTION

Because spinal anesthesia carries a lower risk of maternal and fetal problems than general anesthesia, it has emerged as the preferred anesthetic treatment for patients undergoing elective caesarean sections.[1] The stress reaction to surgery has a metabolic impact that includes reduced production of insulin and testosterone which are anabolic hormones and increased release of catabolic hormones like cortisol and catecholamines.[2] In addition to a relative insulin deficiency and decreased sensitivity of tissues to insulin, it increases the synthesis of glucose.[3] As a result, blood glucose levels will rise even if diabetes is not present already.[4]

Patients may suffer from these hyperglycemic reactions to surgical stressors during the perioperative phase, which can lead to negative consequences like slowed wound healing and a higher risk of infection.[5] Interestingly, even brief episodes of hyperglycemia impair immunity and raise the risk of infection.[6] Afferent neuronal trigger from trauma site, activates the stress response in surgical patients. By blocking afferent brain impulses, neuraxial anesthesia e.g., epidural or spinal anesthesia—inhibits the stress response after surgery, which includes hyperglycemia.[7]

In a study from Jordan, fifty-eight pregnant ladies undergoing elective c-section were enrolled (Group S contained 35 patients who were given spinal anesthesia, and group G contained 23 patients who wanted to have general anesthesia). The mean blood glucose concentration (BGC) was remarkably high in group G in contrast to group S in the times five minutes prior (80.2 ± 18.1 vs. 108.4 ± 16.7, p < 0.05) and half an hour following the operation (80.9 ± 17.7 vs. 121.1 ± 17.4, p < 0.05).[8]

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Kouzegaran S et al conducted a study on 60 patients (30 undergoing spinal anesthesia and 30 undergoing general anesthesia). They found lower levels of blood sugar (93.62 ± 15.81) in general anesthesia group than the spinal anesthesia group (110.26 ± 63.96) after surgery with remarkable difference ($P < 0.05$).[9]

Keeping in view the existing controversial results, we had planned this study to compare the mean blood sugar levels in patients undergoing spinal vs. general anesthesia. The local results from our setting will help working anesthetists to practice more suitable type of anesthesia which can reduce chances of stress-induce hyperglycemia and ultimately its associated morbidity. We hypothesized that mean blood glucose levels in women undergoing cesarean section 30-minutes post operatively would be higher in spinal anaesthesia group compared to general anaesthesia.

METHODS

This prospective cohort study was conducted at anaesthesia department of Allama Iqbal Teaching hospital DG Khan over a period of six months from 1st March 2024 to 31st August 2024 after approval from the institutional ethics review committee (ERC 75/MED/DGKMC, dated: 02-02-2024). Non-diabetic pregnant women 20 – 45 years, ASA-I status planned to undergo cesarean section were consecutively enrolled in the study after informed consent. Women with gestational as well as chronic diabetes, eclampsia / pre-eclampsia, cardiomyopathy and allergy to any anaesthetic agents were excluded from the study.

Women opting for general anaesthesia were taken as un-exposed and those opting for spinal anaesthesia were taken as exposed group. BMI was calculated pre-operatively by formula–weight in kg/height in meter.[2] Weight was measured on weighing scale and height on stadiometer.

All the participants remained nil per oral for 6 – 8 hours pre-operatively as per standard hospital protocol. During the fasting period, type of the fluid was decided by surgical team and recorded. All the procedures were performed as per standard hospital protocol. Briefly, upon arrival in operation theatre all participants were given prophylactic antibiotic, dexamethasone, ranitidine and metoclopramide before starting anaesthesia. General and spinal anaesthesia were instituted by consultant anaesthetist as per hospital protocol. Duration of surgery (minutes) was recorded in all cases. Intraoperatively same type of the fluid was infused to all participants. The baseline blood sugar levels were obtained five minutes prior to induction with GA and right before administration of local anaesthesia in SA group. Post-surgery blood glucose levels were obtained at 30-minutes. Blood sugar (mg/dl) was assessed using a single blood glucose monitoring kit with a lancet device.

A minimum sample size of 248 patients (124 in each group) was calculated using OpenEpi online software through formula for mean difference assuming mean blood glucose 93.62 ± 15.81 mg/dl in GA and 110.26 ± 63.96 mg/dl in SA groups at 80% power and 95% confidence level.[9] Data analysis was performed through SPSS version 23. Normality of numerical data was assessed through histogram visually and Shapiro-Wilk test statistically. Descriptive statistics in the form of mean ± SD for numerical and frequency and percentages for categorical comparison were run. Numerical data between the groups was compared through independent sample t-test and chi-square test for categorical data. Effect modification was controlled through stratification. P-value of < 0.05 was considered significant for all comparisons.

RESULTS

The mean age of the participants was 30.6 ± 3.4 years and 52.4% (n=130) were above 30-years. The mean BMI was 25.2 ± 3.1 kg/m^2 and 35.5% (n=88) were obese. Mean duration of fast before surgery was 7.1 ± 0.8 hours and mean duration of surgery was 47.4 ± 1.7 minutes. In 57.7% (n=143) women intravenous fluid without glucose was infused. Age, BMI, fasting status, duration of surgery and type of fluid infused were comparable between cesarean section performed under general and spinal anaesthesia [Table-I].

The mean blood sugar before surgery in study participants was 82.5 ± 8.6 mg/dl. The mean blood sugar levels were higher in spinal anaesthesia group

pre-operatively compared to general anaesthesia (83.9 ± 8.3 vs. 81.2 ± 8.6, p-value = 0.011). Post-operatively blood sugar levels were significantly higher in spinal anaesthesia group pre-operatively compared to general anaesthesia (126.4 ± 15.0 vs. 86.7 ± 9.2, p-value < 0.001) [Table-II].

Post stratification the mean blood sugar levels remained higher in spinal anaesthesia group compared to general anaesthesia group [Table-III].

TABLE-I

Characteristics of pregnant women undergoing caesarean delivery (N=248)

Characteristics	All (N=248)	General Anaesthesia (n=124)	Spinal Anaesthesia (n=124)	P-Value*
Age (years)	30.6 ± 3.4	30.2 ± 3.6	30.9 ± 3.2	0.096
≤ 30-years	118 (47.6)	65 (55.1)	53 (44.9)	0.127
> 30-years	130 (52.4)	59 (45.4)	71 (54.6)	
BMI (kg/m^2)	25.2 ± 3.1	25.4 ± 3.3	24.9 ± 2.8	0.277
Obesity – Yes	88 (35.5)	50 (56.8)	38 (43.2)	0.111
No	160 (64.5)	74 (46.3)	86 (53.8)	
NPO duration (hrs.)	7.1 ± 0.8	7.1 ± 0.7	7.1 ± 0.8	0.885
Surgery duration (mint.)	47.4 ± 1.7	47.2 ± 1.9	47.6 ± 1.6	0.066
Fluid – with glucose	105 (42.3)	53 (50.5)	52 (49.5)	0.898
without glucose	143 (57.7)	71 (49.7)	72 (50.3)	

BMI: body mass index, NPO: nil per oral *t-test for numerical and chi-square test for categorical comparison

TABLE-II

Blood sugar levels of pregnant women undergoing caesarean delivery (N=248)

Random Blood Sugar (mg/dl)	All (N=248)	General Anaesthesia (n=124)	Spinal Anaesthesia (n=124)	P-Value*
Before Surgery	82.5 ± 8.6	81.2 ± 8.6	83.9 ± 8.3	0.011
30 minutes after Surgery	106.4 ± 23.4	86.7 ± 9.2	126.4 ± 15.0	< 0.001

***** Independent sample t-test

TABLE-III

Factors affecting post-operative blood sugar levels of pregnant women undergoing caesarean delivery (N=248)

Factors		General Anaesthesia (n=124)	Spinal Anaesthesia (n=124)	P-Value*
Age (years)	≤ 30	87.1 ± 9.1	123.2 ± 15.1	< 0.001
	> 30	86.3 ± 9.4	128.2 ± 15.4	< 0.001
Obesity	Yes	87.5 ± 8.2	124.4 ± 15.5	< 0.001
	No	86.1 ± 9.8	126.8 ± 15.4	< 0.001
Fluid type	With glucose	85.5 ± 9.7	125.5 ± 16.9	< 0.001
	Without glucose	87.6 ± 8.8	126.5 ± 14.3	< 0.001

***** Independent sample t-test

DISCUSSION

Due to sympathetic nerves stimulation and the release of certain hormones, including cortisol, norepinephrine, and adrenaline, the pain and anxiety associated with operative procedures raise blood sugar levels.[10] Using spinal or general anaesthesia to lessen the pain and stress of the procedure may stop the release of hormones that raise blood sugar levels and sympathetic activation. Consequently, there will be no rise in blood sugar levels.[11] Some researchers have only looked at how blood sugar levels alter while under spinal anaesthesia. According to the findings, variations in blood sugar are influenced by the kind of medication used for spinal anaesthesia.[12]

In our study, we observed that post-operatively blood sugar levels were significantly higher in spinal anaesthesia group pre-operatively compared to general anaesthesia (126.4 ± 15.0 vs. 86.7 ± 9.2, p-value < 0.001). Our results offer a fascinating diversion from the accepted fact on the impact of anaesthesia on perioperative glucose regulation. Spinal anaesthesia has historically been linked to a lower stress response, which improves glucose homeostasis maintenance. For example, a prospective cohort study published by Samuel et al, on patients undergoing pelvic and lower abdominal surgeries revealed that the group under general anaesthesia had significantly higher mean blood glucose levels at the end of the procedure and 60 minutes after the procedure. This suggests that spinal anaesthesia is a better way to maintain perioperative glucose levels.[13]

According to El-Radaideh et al, patients undergoing elective caesarean sections under general anaesthesia had higher blood glucose levels five minutes prior to and thirty minutes following the conclusion of the procedure than patients under spinal anaesthesia.[8] Similarly, 40 non-diabetic women who were planned for an elective caesarean delivery were the subject of a study by Al-Harire HE et al. They discovered that during surgery blood glucose levels considerably rose in both groups. But in the GA group, the increase was more noticeable than in the SA group ($p < 0.05$).[14] A considerable decrease in the serum blood sugar level throughout the procedure compared to the pre-operation level was noted in a study by Fah et al on women who underwent caesarean sections under spinal anaesthesia.[15]

Our results, however, show that the spinal anaesthesia group had higher postoperative glucose levels, which is in contradiction to prior investigations. There are a few reasons for this disparity. First, different anaesthetic techniques may have different effects on the stress response depending on the type and length of surgical procedures. Second, there may be a role for patient-specific variables such baseline metabolic status, anxiety, and particular hormonal reactions. Third, glucose metabolism may be impacted by differences in intraoperative care, such as the use of vasopressors and fluid delivery.

The idea that spinal anaesthesia more effectively reduces the postoperative stress response is further supported by the observation made by Milosavljevic et al[16] that blood cortisol levels and glycemia were considerably greater in the general anaesthesia group compared to spinal anaesthesia group. The results of our investigation, however, point to the complexity of perioperative metabolic responses by indicating that this could not necessarily result in decreased postoperative glucose levels.

Nonetheless, our results are comparable to those published by Kouzegaran S et al. Following the procedure, they discovered that the group that had used the general anaesthesia method had significantly less blood sugar levels (93.62 ± 15.81) than the spinal anaesthesia group (110.26 ± 63.96).[9] Several recent investigations have investigated variables that could affect perioperative glucose levels while using various anaesthesia procedures. The impact of a single 8 mg dosage of dexamethasone on blood glucose levels in patients having spinal anaesthesia for surgery was examined by Joshi et al. They discovered that blood glucose levels significantly increased in diabetic patients following surgery, peaking three and twelve hours after the procedure. This implies that patients receiving spinal anaesthesia may experience hyperglycemia because of adjunct drugs like dexamethasone.[17]

In a comprehensive review and meta-analysis, Li

et al examined how various anaesthesia types affected diabetes patients' intraoperative blood glucose levels. They found that compared to general anaesthesia alone, combined general-epidural anaesthesia offered superior glycaemic management. However, the study also found that the effect of epidural anaesthesia on blood glucose was not statistically different from that of general anaesthesia, suggesting that the technique used for anaesthesia can affect glycaemic results.[18] These findings highlight the intricacy of managing blood sugar during surgery and imply that glycaemic results under various anaesthesia procedures might be influenced by variables like the use of adjunct medications, patient comorbidities, and particular surgical situations.

This study's rigorous inclusion/exclusion criteria and prospective cohort design, which reduced confounding from underlying medical illnesses like diabetes or hypertensive disorders, are its main strengths. The results' internal validity is improved by the two groups' similar baseline characteristics. Furthermore, the findings are made more robust using standardised procedures for anaesthesia and glucose testing as well as the comparatively high sample size.

Because this study was limited in its duration and only conducted at one centre, its findings might not be as applicable to larger groups. Despite being standardised, using a glucometer could not be as accurate as laboratory-based glucose analysis. Furthermore, the study did not take into consideration intraoperative factors that could affect blood glucose levels, such as individual anxiety levels, painkiller use, and stress response hormones (such cortisol). Because the choice of anaesthesia was patient-driven rather than randomised, selection bias may have been introduced.

A randomised controlled design should be used in future research to remove selection bias and strengthen the case for causality. External validity would be improved by multicentre trials with a variety of demographics. More thorough insights might also be obtained by assessing stress markers (such as cortisol and catecholamines) and considering long-term maternal and newborn outcomes. Routine care should include perioperative glucose monitoring, particularly for patients undergoing spinal anaesthesia during caesarean deliveries.

CONCLUSION

When compared to general anaesthesia, spinal anaesthesia produced noticeably higher postoperative blood glucose levels in non-diabetic women having elective caesarean deliveries. This highlights the significance of regular perioperative glucose monitoring and points to the necessity for more investigation into how spinal anaesthesia affects metabolism in obstetric patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Incidence and risk factors of acute kidney injury in term neonates.

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ABSTRACT… Objective: To determine the incidence and risk factors of acute kidney injury in term neonates. **Study Design:** Prospective Observational study. **Setting:** Neonatal Intensive Care Unit (NICU) of National Institute of Child Health, Karachi, Pakistan. **Period:** October 2024 to March 2025. **Methods:** A total of 190 neonates suspected to have AKI and admitted to the NICU were enrolled. The development of AKI during the study or discharge from the NICU was noted. Risk factors of AKI were also evaluated. Multivariate binary logistic regression analysis was performed for the determination of risk factors associated with the development of AKI in neonates taking p<0.05 as statistically significant. **Results:** Among 190 term neonates, 104 (54.7%) were male, and the mean age at admission was 2.92±1.89 days. There were 72 (37.9%) neonates who developed AKI, with stage 1 in 58.3%, stage 2 in 26.4%, and stage 3 in 15.3%. Mortality was higher in the AKI group (11.1% vs. 3.4%, p=0.035). Multivariate logistic regression identified maternal diabetes (adjusted odds ratio [aOR]: 3.22), pregnancy-induced hypertension (aOR: 2.85), IUGR (aOR: 3.75), and longer NICU stay (aOR per day: 1.16) as independent risk factors for AKI. Mortality was significantly high in AKI neonates (11.1% vs. 3.4%, p=0.035). **Conclusion:** This study demonstrated a high incidence of AKI among term neonates, with maternal diabetes, pregnancy-induced hypertension, maternal infection, IUGR at birth, and prolonged NICU stay identified as significant and independent risk factors.

Key words: Acute Kidney Injury, Maternal Diabetes, Mortality, NICU, Pregnancy Induced Hypertension.

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INTRODUCTION

In the neonatal intensive care unit (NICU) population, acute kidney injury (AKI) is highly prevalent, affecting all gestational groups, and is linked to substantial morbidity and mortality.[1-4] According to reports, neonatal AKI increases hospital stays, which raises healthcare costs drastically, exerting an extraordinary burden on nations with low-income economies.[5] The kidneys of newborns are not as developed as those of older children, making them more vulnerable to AKI.[6,7] According to several studies, the occurrence of neonatal AKI ranges between 18% and 70%.[8-12]

Different diagnostic criteria in newborns are employed, owing to which neonatal AKI presents a diversity in its occurrence, and these are difficult to follow in premature newborns as well.[13-16] Neonatal AKI can now be diagnosed with greater precision through the KDIGO modified diagnostic and classification criteria, which are based on quantitative changes in serum creatinine levels and/or a decrease in urine output.[17-21]

The rising sepsis prevalence and lack of awareness regarding neonatal AKI emphasize the need to evaluate incidence and associated risk factors.[18] In Pakistan, not much of the research has been done on AKI, more specifically on neonatal AKI, focusing on its prevalence, risk factors, and outcomes in various populations. This study was planned to determine the incidence and risk factors of AKI in term neonates. The findings of this study would not only add to the existing literature on the subject from Pakistani settings but also help clinicians improve diagnosis, prevent progression, intervene earlier, and better manage fluid balance in achieving improved long-term outcomes for neonates who experience AKI.

METHODS

This prospective observational study was conducted at the Neonatal Intensive Care Unit, National Institute of Child Health, Karachi, Pakistan, from October 2024 to March 2025 after achieving authorization from the Ethics Committee of the institution (letter

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number: IERB-21/2024). A sample size of 190 was calculated considering the anticipated frequency of AKI in neonates with gestational age >36 weeks as 41%[12], using a 95% confidence interval and a precision of 7%. The inclusion criteria were neonates with gestational age > 37 weeks and admitted to the NICU. All patients born within the hospital premises showing manifestation for AKI screening were enrolled into the study. Patients with urinary retention, dehydration, abnormal serum creatinine values at birth, and those requiring nutritional support through intravenous fluids were considered. The exclusion criteria were patients with <48 hours of stay in the NICU. Patients with lethal chromosomal anomalies, major kidney malformations, or those undergoing cardiac surgery within the first week of birth were also excluded. Sample selection was done employing a non-probability consecutive sampling technique. Parents/caregivers were briefed about the objective and safety of the study to take their consent to enroll their patients into the study. Demographic details of neonates like gender, age, and gestational age were noted. Maternal characteristics like maternal diabetes, pregnancy-induced hypertension, maternal infections at or near the time of delivery, and intrauterine growth restriction (IUGR) at birth were recorded. All neonates were treated as per the hospital protocol. AKI was defined and staged based on KDIGO criteria.[17]

The data was analyzed using "IBM-SPSS Statistics" version 26.0. The numerical variables were presented as mean and standard deviation (SD). The categorical variables were summarized through frequencies with percentages. The chi-square or the Fisher's exact test was applied to compare categorical variables. Numerical variables were compared using the independent t-test. Binary logistic regression was applied to determine factors associated with AKI, and adjusted odds ration (aOR) with 95% confidence interval (CI) was calculated. A p-value ≤0.05 was taken as statistically significant.

RESULTS

In a total of 190 term neonates, 104 (54.7%) were male, and 86 (45.3%) female. The mean age at admission was 2.92±1.89 days. Maternal diabetes was documented in 22 (11.6%) cases, pregnancy-induced hypertension in 18 (9.5%), and maternal infection in 28 (14.7%) cases. The incidence of AKI was noted in 72 (37.9%) neonates. According to the KDIGO criteria, 42 (58.3%) of the affected neonates had stage 1 AKI, 19 (26.4%) had stage 2, and 11 (15.3%) had stage 3. The duration of NICU stay was significantly longer in neonates with AKI (13.12±5.62 vs. 8.87±3.62 days, p<0.001). Maternal diabetes (22.2% vs. 5.1%, p<0.001), pregnancy-induced hypertension (16.7% vs. 4.2%, p=0.004), and maternal infection at or near delivery (25.0% vs. 8.5%, p=0.002) were significantly more frequent among neonates who developed AKI. IUGR at birth was more common in neonates who developed AKI (p=0.001). Table-1 is showing association of AKI in neonates with neonatal and maternal characteristics.

TABLE-I

Association of AKI with neonatal and maternal characteristics

Variables		Acute Kidney Injury		P-Value
		Yes (n=72)	No (n=118)	
Gender	Male	38 (52.8%)	66 (55.9%)	0.672
	Female	34 (47.2%)	52 (54.1%)	
Age at admission (days)		2.82±2.14	3.06±1.75	0.401
Gestational age (weeks)		38.01±1.25	38.28±1.03	0.217
Birth weight (kg)		2.65±0.35	2.73±0.31	0.102
NICU stay (days)		13.12±5.62	8.87±3.62	<0.001
Maternal diabetes		16 (22.2%)	6 (5.1%)	<0.001
Pregnancy induced hypertension		12 (16.7%)	5 (4.2%)	0.004
Maternal history of infection		18 (25.0%)	10 (8.5%)	0.002
Intrauterine growth restriction at birth		12 (16.7%)	4 (3.4%)	0.001

The stage of AKI at diagnosis was associated with both length of stay and risk factor burden, with stage 3 neonates having the longest median duration of NICU admission (median 15 days, IQR: 11–19). Of the 72 neonates with AKI, 6 (8.3%) required renal replacement therapy. Mortality was reported in 8 (11.1%) neonates with AKI in comparison to 4 (3.4%) neonates without AKI (p=0.035). Multivariate logistic regression identified maternal

diabetes (aOR:3.22, 95% CI:1.41–7.34, p=0.005), pregnancy-induced hypertension (aOR:2.85, 95% CI:1.09–7.47, p=0.032), IUGR at birth (aOR:3.75, 95% CI:1.16–12.16, p=0.027), and longer duration of NICU stay (aOR per day:1.16, 95% CI:1.07–1.26, p<0.001) as independent risk factors for AKI (Table-II).

TABLE-II

Multivariate logistic regression analyzing risk factors of AKI

Variables	Adjusted Odds Ratio	95% Confidence Interval (Lower-Upper)	P-Value
Maternal diabetes	3.22	1.41-7.34	0.005
Pregnancy induced hypertension	2.85	1.09-7.47	0.032
Maternal infection	2.31	1.01-5.27	0.048
Intrauterine growth restriction at birth	3.75	1.16-12.16	0.027
NICU stay (per day increase)	1.16	1.07-1.26	<0.001

DISCUSSION

The overall incidence of AKI was relatively high in the present study (37.9%). Agarwal et al.[22], through the Indian multicenter TINKER registry, reported an AKI incidence of approximately 26.6%. Farhadi et al.[23], in Iran observed a 26.6% prevalence of AKI, suggesting that geographic, ethnic, and healthcare system differences, along with varying inclusion criteria and AKI definitions, can influence observed rates. In contrast, Gedefaw et al.[24], in a study from Ethiopia, documented an incidence of 20.2% among NICU neonates, employing both clinical and laboratory definitions. The higher incidence in the current cohort may be attributed to a combination of rigorous screening, heightened surveillance for subtle changes in renal function, and possibly the burden of underlying maternal conditions common in the Pakistani population.

Stratification of AKI severity revealed that most affected neonates in this study experienced stage 1 AKI (58.3%). Farhadi et al.[23], reported relatively equal distribution among AKI stages but with a predominance of prerenal cases. The slightly higher proportion of stage 1 AKI may reflect early detection and intervention strategies implemented at the study center, as well as heightened clinical vigilance due to the use of standardized KDIGO criteria. In the TINKER registry.[22], and Rutledge et al.[25], a similar trend toward higher rates of mild AKI was observed, suggesting that improved diagnostic protocols globally are leading to earlier diagnosis, though the burden of severe AKI persists.

Maternal diabetes was present in 22.2% of AKI cases compared to 5.1% in non-AKI neonates. This association has been documented previously, where the metabolic and vascular effects of maternal hyperglycemia predispose neonates to compromised renal perfusion and glomerular injury.[26] Gedefaw et al.[24], similarly identified maternal and perinatal comorbidities as key predictors of AKI, while Agarwal et al.[22], and Farhadi et al.[23], also highlighted maternal diabetes and hypertension as recurrent risk factors in their respective cohorts. In the present study, pregnancy-induced hypertension was present in 16.7% of AKI neonates versus 4.2% in non-AKI neonates (aOR: 2.85, 95% CI: 1.09–7.47). This observation reinforces the importance of optimizing maternal health and antenatal care to mitigate preventable neonatal complications. Maternal infection at or near delivery was another significant risk factor, identified in 25.0% of AKI cases compared to 8.5% in non-AKI neonates (p=0.002). Infection-related inflammatory responses and sepsis are known contributors to renal hypoperfusion and direct nephrotoxic injury.[27] Gedefaw et al.[24], found that neonatal sepsis was an independent predictor of AKI, consistent with global trends in NICU populations. The high prevalence of perinatal infection underscores the need for infection prevention protocols, timely diagnosis, and appropriate antimicrobial therapy in perinatal and neonatal care settings.[25]

This study showed significant association between longer duration of NICU stay and the risk of AKI, with an aOR of 1.16 per additional day of admission (p<0.001). Rutledge et al.[25], observed that recurrent AKI (rAKI) in neonates was associated with prolonged hospitalization, with a median length of stay more than threefold higher than those without AKI. This relationship may reflect both the increased severity of illness among neonates developing AKI and the contribution of iatrogenic factors such as

nephrotoxic medications, invasive procedures, and nosocomial infections. The present study also explored the outcomes associated with AKI in the neonatal period. The requirement for renal replacement therapy was documented in 8.3% of neonates with AKI, a figure broadly consistent with previous cohorts reporting 5–15% rates of dialysis or hemofiltration in severe cases. In-hospital mortality among neonates with AKI was 11.1% (p=0.035). This increased mortality risk echoes the findings of El-Badawy et al.[28], who reported a threefold increase in mortality among AKI cases, and Alayed et al.[29], who found that AKI contributed to prolonged PICU stays, resource utilization, and increased case fatality. Gedefaw et al.[24], in their study found that neonates with perinatal asphyxia and sepsis demonstrated increased mortality rates, further substantiating the life-threatening nature of neonatal AKI.

Several limitations should be acknowledged in interpreting these results. The single-center design and exclusive inclusion of inborn term neonates limit the generalizability to outborn populations, preterm infants, or those with complex congenital conditions. The observational nature of the study introduces potential confounding and selection biases, and the follow-up was restricted to in-hospital outcomes without assessment of long-term renal function or growth.

CONCLUSION

This study demonstrates a high incidence of AKI among term neonates, with maternal diabetes, pregnancy-induced hypertension, maternal infection, IUGR at birth, and prolonged NICU stay identified as significant and independent risk factors. The findings reinforce the critical importance of antenatal risk factor modification, early diagnosis, and vigilant supportive care.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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5	**Aasma Kayani:** Critical revision.

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ORIGINAL ARTICLE

Effect of human milk fortification at different volume of feeds in pre-term newborns (< 32 weeks of gestation).

Muhammad Imran[1], Muhammad Usman[2], Muhammad Sarfraz Ahmad[3]

ABSTRACT… Objective: To assess how feeding volume of `human milk fortification (HMF) influences growth and bone mineral status in preterm infants. **Study Design:** Parallel-arm, Randomized Controlled Trial. **Setting:** Department of Neonatology, RTEH Indus Hospital, Muzaffargarh, Pakistan. **Period:** September 2024 to June 2025. **Methods:** A total of 132 preterm newborns born before 32 weeks of gestation, with Apgar scores below 7 at five minutes, admitted to the NICU within 24 hours and exclusively fed maternal human milk were enrolled. Infants were randomized into early (70–100 ml/kg/day), middle (101–130 ml/kg/day), or late (130–160 ml/kg/day) HMF initiation groups. Growth parameters, bone mineral status (BMS), and complications were recorded at 36 weeks post-menstrual age (PMA). Data were analyzed using ANOVA and chi-square tests, with statistical significance set at p<0.05. **Results:** Among a total of 132 preterm infants, 66 (50.0%) were male, and the mean gestational age was 30.1±1.1 weeks. At 36 weeks PMA, the early HMF group showed significantly greater weight gain (1021.8±156.3 g) and linear growth (3.7±0.8 cm), with higher head circumference increase (3.3±0.7 cm), compared to the late HMF group (p<0.001). Early HMF was associated with lower alkaline phosphatase (309.2±61.6 IU/L) and higher calcium and phosphorus levels. **Conclusion:** The early initiation of HMF at lower enteral feeding volumes in preterm infants is associated with improved growth and BMS at 36 weeks PMA.

Key words: Bone Mineral Status, Human Milk, Preterm, Postmenstrual Age.

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INTRODUCTION

Complications arising from pre-term birth are the primary cause of mortality among children below five years of age.[1] In 2019, preterm birth occurred in approximately 10.9% of live births globally, affecting around 15.2 million infants.[2] Preterm birth holds the highest cause-specific fatality rate, resulting in nearly 1 million deaths, which accounts for approximately one-third (36.1%) of deaths during the neonatal period.[3] Low birthweight (LBW) significantly overlaps with preterm birth, and premature birth with LBW is a significant cause of morbidity and morbidity worldwide.[5-7]

Human milk (HM) is known to be the best source of nutrition for both term and preterm infants.[8,9] The utilization of HM fortification (HMF) is 90–100% in the NICUs of the developed world.[10] Multicentric data from Australia exhibited that HMF was administered to infants ranging from 1250-2500 grams in weight, with 100% usage.[11] Another multicenter study from China analyzing very preterm infants found the mean birth weight as 1,204±261 grams, 1,255±257 grams, and 1293±251 grams in early, middle, and late HMF groups.[12] At the time of discharge, the mean body weight were 2,484±456a grams, 2,397±394 grams, and 2,287±402 grams respectively. The highest increase in body weight were noted in early and middle fortification groups. Another study reported no major differences in terms of weight gain with early or delayed fortification of HM.[13]

Despite advancements in neonatal care, achieving optimal nutrition for preterm infants remains challenging. Human milk fortification is commonly used to meet the increased nutritional needs of preterm babies. However, there is limited research on the effects of fortification at different volumes of feed. Understanding how varying feeding volumes impact the efficacy of human milk fortification is crucial for improving growth and developmental outcomes in preterm infants.

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This study aims to assess how feeding volume of HMF influences growth and bone mineral status (BMS) in preterm infants.

METHODS

This was a single-center, parallel-arm, randomized controlled trial conducted in the Department of Neonatology at RTEH Indus Hospital, Muzaffargarh, Pakistan. The study was carried during September 2024 to June 2025 following ethical approval from the institutional review board (letter: IHHN_IRB_2024_05_002, dated: 27-Aug-2024). Inclusion criteria were preterm newborns, born before 32 weeks of gestation, with an Apgar score below 7 at five minutes, admitted to the NICU within 24 hours after birth, and who were exclusively fed human milk of their respective mother. Exclusion criteria were the receipt of formula feed prior to 32 weeks post-menstrual age (PMA), major congenital anomalies, or human milk with a caloric content exceeding 26 kcal/oz before 32 weeks PMA. Sample size was calculated using G*Power (version 3.1.9.7), taking an effect size (f) of 0.40, alpha error probability of 5%, power of 95%, degrees of freedom of 5, and three groups, resulting in a total required sample of 130 infants, 132 participants (44 per group) were enrolled.

Following informed, written consent from the mother, eligible infants were randomized by the lottery method into one of three groups, early HMF, middle HMF, or late HMF, according to the volume of enteral feed at which fortification was initiated. The early HMF group began fortification at 70–100 ml/kg/day, the middle HMF group at 101–130 ml/kg/day, and the late HMF group at 130–160 ml/kg/day. Group allocation was concealed and performed by a staff nurse blinded to the intervention protocols. Enteral feeds were commenced per unit protocol under the supervision of the attending neonatologist, with human milk provided by the mother and commercial powdered HMF (Nan, Nestle) used for fortification. Initial HMF dosing was started with a quarter or half dose, increased as tolerated to the full dose as per product instructions. Feeding volumes was advanced by 10–20 ml/kg/day to a maximum of 170–200 ml/kg/day, with full enteral feeding defined as at least 150 ml/kg/day administered for more than 24 hours. At enrollment, demographic and perinatal data were recorded. BMS was evaluated via laboratory measurement of alkaline phosphatase, calcium, and phosphorus. Primary outcome measures as growth parameters, assessed at 36 weeks PMA using calibrated scales. Secondary outcomes included BMS, as well as complications. A dedicated proforma was be used for all study data entry.

Data were analyzed using IBM-SPSS Statistics version 26. Quantitative variables were expressed as mean and standard deviation, and categorical variables as frequency and percentage. Analysis of variance (ANOVA) was used for comparison of quantitative outcomes across groups, while the chi-square test or fisher's exact test were applied for categorical variables. A p-value below 0.05 was considered statistically significant.

RESULTS

Among a total of 132 preterm infants, 66 (50.0%) were male, and the mean gestational age was 30.1±1.1 weeks. The mean gestational age at birth was 30.2±1.1 weeks in the early HMF, 30.0±1.2 weeks in the middle group, and 30.1±1.0 weeks in the late group (p=0.697). The mean birth weight was 1242.9±165.2 grams, 1238.8±152.0 grams, and 1239.4±161.6 grams in the early, middle, and late HMF, respectively (p=0.992). The majority of infants in each group were delivered by cesarean section, comprising 79.5% in early and late HMF, and 81.8% in the middle HMF group (p=0.953), as shown in Table-I.

Infants in the early HMF group demonstrated the greatest weight gain (1021.8±156.3 grams), compared to 998.4±162.5 grams in the middle HMF group and 846.1±178.0 grams in the late HMF (p<0.001). In early HMF group the mean increase in length was 3.7±0.8 cm, compared to 3.6±0.7 cm, and 2.7±0.9 cm in the middle and late groups, respectively (p<0.001). Head circumference gain was significantly higher (p<0.001) in the early HMF (3.3±0.7 cm), and middle HMF group (3.2±0.7 cm), compared to the late HMF group (2.6±0.8 cm). Table-II is showing details about the comparison of 36 weeks PMA among study participants of study groups.

Mean alkaline phosphatase levels were lowest in the early HMF group (309.2±61.6 IU/L), followed by the middle (324.0±59.4 IU/L) and late HMF groups (381.2±66.7 IU/L), with the difference reaching statistical significance (p<0.001). The mean serum calcium was significantly higher in the early HMF group (9.3±0.6 mg/dl) and the middle group (9.1±0.7 mg/dl), compared to the late group (8.7±0.7 mg/dl), and the difference turned out to be statistically significant (p<0.001). The Mean serum phosphorus was highest in the early HMF group (5.7±0.9 mg/dl), followed by the middle (5.6±0.8 mg/dl), and late HMF groups (5.0±0.8 mg/dl), with p<0.001. Comparison of BMS at 36 weeks PMA among study groups is shown in Table-III.

Feeding intolerance (p=0.683), necrotizing enterocolitis (NEC) (p=0.592), bronchopulmonary dysplasia (p=0.650), culture-proven sepsis (p=0.760), intraventricular hemorrhage (p=0.760), or mortality (p=0.875) did not exhibited significant differences, and the details are given in Table-IV.

TABLE-I

Comparison of baseline characteristics of participants (N=132)

Characteristics		Early HMF (n=44)	Middle HMF (n=44)	Late HMF (n=44)	P-Value
Gender	Male	22 (50.0%)	21 (47.7%)	23 (52.3%)	0.913
	Female	22 (50.0%)	23 (52.3%)	21 (47.7%)	
Gestational age (weeks)		30.2±1.1	30.0±1.2	30.1±1.0	0.697
Birth weight (grams)		1242.9±165.2	1238.8±152.0	1239.4±161.6	0.992
Apgar score (5-minutes)		6.4±1.0	6.3±1.1	6.5±0.9	0.647
Mode of delivery	Cesarean section	35 (79.5%)	36 (81.8%)	35 (79.5%)	0.953
	Vaginal delivery	9 (20.5%)	8 (18.2%)	9 (20.5%)	

TABLE-II

Comparison of growth outcomes at 36 weeks postmenstrual age (N=132)

Characteristics	Early HMF (n=44)	Middle HMF (n=44)	Late HMF (n=44)	P-Value
Weight gain (grams)	1021.8±156.3	998.4±162.5	846.1±178.0	<0.001
Length incrase (cm)	3.7±0.8	3.6±0.7	2.7±0.9	<0.001
Head circumference	3.3±0.7	3.2±0.7	2.6±0.8	<0.001

TABLE-III

Comparison of bone mineral status at 36 weeks postmenstrual age (N=132)

Characteristics	Early HMF (n=44)	Middle HMF (n=44)	Late HMF (n=44)	P-value
Alkaline phosphatase (IU/L)	309.2±61.6	324.0±59.4	381.2±66.7	<0.001
Calcium (mg/dl)	9.3±0.6	9.1±0.7	8.7±0.7	<0.001
Phosphorus (mg/dl)	5.7±0.9	5.6±0.8	5.0±0.8	<0.001

TABLE-IV

Complications during hospital stay (N=132)

Characteristics	Early HMF (n=44)	Middle HMF (n=44)	Late HMF (n=44)	P-Value
Feeding intolerance	7 (15.9%)	6 (13.6%)	9 (20.5%)	0.683
Necrotizing enterocolitis	1 (2.3%)	2 (4.5%)	3 (6.8%)	0.592
Bronchopulmonary dysplasia	5 (11.4%)	6 (13.6%)	8 (18.2%)	0.650
Culture-proven sepsis	4 (9.1%)	3 (6.8%)	5 (11.4%)	0.760
Intreventricular hemorrhage	3 (6.8%)	4 (9.1%)	5 (11.4%)	0.760
Mortality	2 (4.5%)	3 (6.8%)	3 (6.8%)	0.875

DISCUSSION

This study indicated that early initiation of HMF was associated with significantly greater weight gain, linear growth, and head circumference increment at 36 weeks PMA. The weight gain at 36 weeks PMA was greatest in the early HMF group, with statistically significant differences compared to the late HMF group ((1021.8±156.3 grams vs. 846.1±178.0 grams, p<0.001). Linear growth (p<0.001), and head circumference increment (p<0.001) followed a similar pattern. Thanigainathan et al.[14], comparing early, versus late fortification of HM and found no clear differences variations in growth outcomes. The lack of significant differences in the meta-analysis may relate to methodological differences, smaller sample sizes, and earlier timing of fortification. The present trial, by using an intermediate early threshold and robust sample size, demonstrates a clear benefit to earlier HMF, suggesting that both timing and sufficient feed volumes may be important to maximize the anabolic effects of fortification in preterm infants.[15]

Improvement in BMS observed with earlier HMF initiation in this study is supported by evidence that timely provision of protein, calcium, and phosphorus is critical for bone mineralization in preterm infants. The early HMF group demonstrated significantly lower alkaline phosphatase levels compared to the late HMF group (309.2±61.6 IU/L vs. 381.2±66.7 IU/L, p<0.001), along with higher mean serum calcium and phosphorus. Lower alkaline phosphatase values in the early HMF group indicated reduced risk of metabolic bone disease. Tillman et al.[13], retrospectively compared early HMF versus late HMF, and found a lower incidence of elevated alkaline phosphatase levels in the early HMF, although no differences were detected in weight gain at 34 weeks PMA. The similarity in improved BMS between these findings and the current study may reflect the benefit of increased mineral intake when fortification is introduced earlier in the course of enteral feeding.[16]

Clinical safety is a central concern in the timing of HMF fortification. In the present study, the incidence of feeding intolerance did not differ significantly among groups, affecting 7 (15.9%) infants in the early HMF group, 6 (13.6%) in the middle group, and 9 (20.5%) in the late group (p=0.683). The occurrence of NEC was also not statistically different (p=0.592). Thanigainathan et al.[14], found little or no effect of early fortification on NEC risk, and with a systematic review by Kumar et al.[17], which also demonstrated comparable risks. The absence of increased risk with earlier HMF initiation in this setting suggests that concerns about adverse gastrointestinal outcomes should not preclude timely fortification, especially when careful monitoring and incremental dosing strategies are implemented. These findings provide reassurance for clinicians, particularly in low-resource settings, that early fortification can be safely implemented without elevating rates of serious morbidity. The lack of significant differences in rates of bronchopulmonary dysplasia, sepsis, intraventricular hemorrhage, and mortality among the three groups further supports the safety profile of early HMF introduction.

The present findings hold important clinical implications for the nutritional management of preterm infants. Early introduction of HMF at lower enteral volumes enables more rapid achievement of optimal protein and mineral intake, which is critical for catch-up growth and bone mineralization in this population.[18,-21] Researchers have also recommend individualized or targeted fortification strategies, and this study further supports the concept that the timing of standard fortification remains an underrecognized determinant of short-term growth and bone health.[9] Given the strong evidence that preterm infants are vulnerable to nutritional deficits and the proven association between adequate growth and neurocognitive outcomes.[22,23] This may be particularly relevant in resource-constrained environments as the timing of standard fortification is a modifiable factor.[24,25]

Some limitations of the present study warrant discussion. The trial was conducted at a single center, which may limit generalizability, especially given potential differences in clinical protocols, maternal milk composition, and local epidemiology of neonatal complications. Measurement of actual protein and energy intake from breast milk was not feasible, as the study relied on standard calculations and did not utilize point-of-care human milk analysis, which may introduce variability and

bias. Future multicenter randomized trials are recommended, including diverse populations, assessment of actual nutrient intake through human milk analysis, and longitudinal follow-up to evaluate neurodevelopmental and metabolic outcomes.

CONCLUSION

The early initiation of HMF at lower enteral feeding volumes in preterm infants resulted in improved growth and BMS at 36 weeks PMA without raising the risk of common neonatal complications. This study provides support for reconsidering the timing of HMF introduction in standard clinical protocols. Early nutritional optimization is likely to yield meaningful short-term and potentially long-term benefits for the most vulnerable infants.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Imran:** Data collection, data analysis.
2	**Muhammad Usman:** Conception, design, proof reading.
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ORIGINAL ARTICLE

Frequency and outcomes of cumulative excess oxygen exposure in ventilated pediatric ICU patients.

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ABSTRACT… Objective: To determine the frequency of cumulative excess oxygen exposure (CEOE) and its association with mortality in ventilated children. **Study Design:** Retrospective Cohort study. **Setting:** Pediatric ICU of Sindh Institute of Child Health and Neonatology, Karachi. **Period:** January 2023 to June 2023. **Methods:** The study sample size of 200 was determined using the OpenEpi sample size calculator employing a non-probability consecutive sampling method, and included children (1 month–15 years) admitted who required invasive ventilation ≥24 hours. CEOE was defined as mean hourly FiO_2 >0.21 with SpO_2 ≥95% in the first 24 hours of ventilation. Patients were stratified into quartiles: hypoxemia (SpO_2 <94%), no CEOE, and CEOE quartiles (Q1: >21–30%, Q2: 30–45%, Q3: 45–60%, Q4: ≥60%). Variables included hourly FiO_2 >21% with SpO_2 >95%, clinical parameters, admitting diagnosis, length of stay, comorbidities, and outcome (survival or exitus). Statistical analysis was performed using Chi-Square and Mann-Whitney U tests, with p <0.05 considered significant. **Results:** Among 115 patients, mean CEOE was 37.3 ± 11.9%, with overall mortality of 26.1%. Non-survivors had higher mean CEOE than survivors (41.2 ± 10.9% vs. 36.2 ± 12.0%; p<0.009). Mortality, multi-organ dysfunction, and PICU stay increased stepwise across CEOE quartiles. Logistic regression showed higher odds of mortality in Q2 and Q3 versus Q1, though not statistically significant after adjusting for age and gender. **Conclusion:** In ventilated children, excessive oxygen exposure was common and associated with increased mortality, organ dysfunction, and longer PICU stay. These findings highlight the need for vigilant oxygen titration and careful avoidance of hyperoxia to improve outcomes in pediatric critical care

Key words: Cumulative Excessive Oxygen Exposure, Hyperoxia, Mechanical Ventilation, Mortality, Pediatric Intensive Care.

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INTRODUCTION

Oxygen supplementation, along with invasive mechanical ventilation, constitutes the primary organ support provided to maintain oxygen saturation and partial pressure levels in pediatric intensive care units (PICU).[1] One of the primary objectives of resuscitation and intensive care is to ensure that tissue oxygen levels are maintained at suitable and safe levels.[2-4] Clinicians strive to avoid severe hypoxia whenever feasible, yet beyond this, consensus is limited. In fact, the apprehension about hypoxia frequently drives many to pursue supra-normal oxygen levels.[5] While the dangers of tissue hypoxia are widely acknowledged, the potential risks associated with excessive oxygen administration or other interventions aimed at correcting hypoxemia may not be fully recognized.[4] Excessive oxygen and hyperoxia has been reportedly associated with mortality in critically ill adults with trauma, brain injury, stroke, and cardiac arrest.[5] Although research on children is limited, emerging evidence highlights a significant association between hyperoxia and increased mortality in critically ill pediatric patients.[6-9] Oxygen toxicity associated with supplemental oxygen induces local and systemic effects, including cell signaling alteration, reactive oxygen species generation, inflammation promotion, and vascular endothelial dysfunction, compromising blood supply to vital organs like the brain and heart.[10] Current literature indicates a U-shaped curve, where increased mortality is observed with both hypoxia and hyperoxia extremes.[11] Targeting an SpO2 range of 88–92% is more effective than the previous standard practice of maintaining high normal oxygenation levels (>94%) in emergency admissions of invasively ventilated infants or children admitted to a PICU.

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The Oxy-PICU trial found that children in the conservative oxygenation group had better outcomes, including reduced mortality, fewer days of organ support, decreased hospital stay, lower financial burden, and less multiorgan dysfunction.[12] The objective of this study is (1) To determine the frequency of cumulative excessive oxygen exposure using SpO2 (2): To evaluate the relationship between hyperoxia and mortality among critically ill patients admitted to the intensive care unit

METHODS

This retrospective observational study was conducted in the one of the largest 24 bedded pediatric intensive care unit of a tertiary care hospital, following institutional review board approval (SICHN/Ex-007/2024) with a waiver of informed consent, over the period of 6 months from January 2023 to June 2023. The reporting of this observational cohort study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.[13] The inclusion criteria consisted of children aged 1 month to 15 years who were admitted to the pediatric ICU and required mechanical ventilation for at least 24 hours. Exclusion criteria: Patients with uncorrected cyanotic congenital heart disease, hypoxia (SpO_2 <94%), a PICU stay of less than 24 hours, or those who did not require mechanical ventilation.

The study sample size of 200 was determined using the OpenEpi sample size calculator, based on a 90% confidence level, a hyperoxemia frequency of 15.6%, 5% absolute precision, and employing a non-probability consecutive sampling method.

Cumulative excess oxygen exposure (CEOE) was defined as the average hourly FiO2 above 0.21 % when the corresponding hourly SpO2 was 95% or higher during the first 24 hours of mechanical ventilation.[14] (The 95% SpO2 threshold was selected because it best reflects the level commonly found in healthy children, offering a reliable indicator of normal oxygen saturation based on established data).[15,16] CEOE was computed and stratified by quartiles. Patients with a CEOE score of 0 were classified into a no CEOE group. Those with a CEOE score greater than 0 were divided into 4 quartiles. Consequently, the cohort of mechanically ventilated patients was categorized into five groups: hypoxemia with sato2<94%, no CEOE, and the first through fourth quartile CEOE groups, Q1<31 (>21-31), Q2:32-38%, Q3:39-44%, Q4:45-79%. For analysis, Q1 and Q2 were combined as 'low exposure' and Q3 and Q4 as 'high exposure' groups

Data will be collected using a specially designed questionnaire in SPSS version 26. The questionnaire is divided into three sections. Section A includes demographic variables such as age, gender. Section B covers clinical parameters including admitting diagnosis, and comorbidity, FiO2, SpO2, CEOE, which will be recorded on an hourly basis. If an Spo2 or Fio2 was not recorded in a given hour, the most recent recorded value will be carried forward (Approach used by Balcarcel et al.[14] If more than one value was recorded, the mean will be used, Thus, each encounter provided 24 hourly data points for SpO2 and FiO2 during the first 24 hours of ventilation.

Section C focuses on clinical outcomes, which will be assessed by recording the total hours of hyperoxia (SpO_2 ≥95%), cumulative excess oxygen exposure (CEOE), and the primary outcome variable — survival or death.

Data will be analyzed using SPSS 26. Descriptive analysis will be done to report the prevalence of hyperoxemia and time duration of CEOE. Frequency and percentages will be reported for all categorical variables such a, gender, admitting diagnosis, comorbidity etc. Mean±SD/ Median (IQR) will be reported for all numeric variables such as (Age in years, Oxygen Data (FiO2, SpO2 and CEOE), Outcome variables such as (Hours of Hyperoxia (≥95%), Hours of CEOE). Comparisons were performed using the Chi-square test for categorical variables and the Mann–Whitney U test for continuous variables, with $p<0.05$ considered statistically significant. logistic regression analysis to examine the association between CEOE quartiles and mortality.

RESULTS

During the six-month study period, a total of 1,815 patients were admitted to PICU,providing the cohort

from which 115 patients who met the predefined inclusion criteria, including at least 24 hours of mechanical ventilation and absence of hypoxemia were analyzed.

Demographic and Clinical Characteristics

Table-I represent the demographic and clinical characteristics of the study population. The cohort consisted of 61 males (53%) and 54 females (47%). The median age was 11 months with an interquartile range (IQR) of 6 to 18 months. The mean length of stay in the intensive care unit was 5.29 ± 2.87 days.

The mean cumulative excess oxygen exposure (CEOE) was 37.33 ± 11.85% during the first 24 hours of mechanical ventilation. Based on CEOE, patients were stratified into quartiles: Q1 (23.5%), Q2 (57.4%), Q3 (15.7%), and Q4 (3.5%). For further analysis, the lower two quartiles (Q1 and Q2) were combined and categorized as the lower CEOE group, while the upper two quartiles (Q3 and Q4) were merged to form the higher CEOE group. Outcomes were then compared between these two groups to assess the association between CEOE levels and clinical outcomes.

Regarding clinical outcomes, 85 patients (73.9%) survived, while 30 patients (26.1%) died during their ICU stay.

The most common admitting diagnosis was respiratory conditions, accounting for 49 patients (42.6%), followed by infectious diseases in 38 patients (33.0%), central nervous system (CNS) disorders in 20 patients (17.4%), cardiac conditions in 7 patients (6.1%), and gastrointestinal (GI) causes in 1 patient (0.9%).

Association of Excess Oxygen Exposure with Mortality

Table-II presents a comparative analysis of clinical and demographic variables between survivors and non-survivors. A total of 115 patients were stratified based on survival status to identify factors associated with mortality. The overall mortality rate was 26.1% (n=30).

There were no significant differences in age, length of ICU stay, gender distribution, primary diagnosis, or EOE quartiles between survivors and non-survivors. A statistically significant association was observed between hyperoxia and mortality (p = 0.009). Mortality was higher in patients with hyperoxia values greater than 37.3 (36.8%) compared to those with values ≤37.3 (15.5%).

TABLE-I

Descriptive statistics of study population (n:115)

Overall Descriptive	
Gender	**N (%)**
Male N (%)	61(53)
Female N (%)	54(47)
Age (In months) (Median -IQR)	11(6-18)
Length of stay (In days) (Mean ±SD)	5.287 ± 2.87
Diagnosis	
• Cardiac	7(6.1)
• CNS	20(17.4)
• INF	38(33.0)
• RESP	49(42.6)
• GI	1(.9)
CEOE (median)	37.333
CEOE	
• ≤37.333	58(50.4)
• ≥37.333	57(49.6)
Mortality	30(26.1)

Logistic Regression Analysis of Mortality by CEOE Quartiles

Table-III presents logistic regression analysis to examine the association between CEOE quartiles and mortality. In the univariable analysis, CEOE quartiles Q2 and Q3 showed higher odds of mortality compared to the reference group (Q1), though the associations did not reach conventional statistical significance (Q2: OR 3.48, 95% CI 0.94–12.89, p = 0.062; Q3: OR 4.00, 95% CI 0.85–18.84, p = 0.080). Similar trends persisted in the multivariable model after adjusting for age and gender, with Q2 showing a borderline significant association (OR 3.73, 95% CI 0.99–13.97, p = 0.051) and Q3 showing a comparable increase in odds (OR 4.40, 95% CI 0.92–21.01, p = 0.064).

Age and gender were not significantly associated with mortality in either model.

These findings suggest a potential dose-response relationship between higher oxygen exposure and

mortality, although statistical significance was not achieved, possibly due to sample size limitations.

DISCUSSION

In this retrospective cohort study of 115 mechanically ventilated pediatric patients, we examined incidence of CEOE and the relationship between cumulative excess oxygen exposure (CEOE) and mortality. Our study demonstrates that hyperoxia is common among mechanically ventilated pediatric patients, with a substantial cumulative excess oxygen exposure (mean 37.33 ± 11.85%) observed during the first 24 hours of ventilation.

TABLE-II

Comparison of clinical and demographic characteristics by mortality outcome Mann Whiteney U Test *Chi square test**

Mortality	Hyperoxia		P-Value	
	Less than equal to 37.33333 n (%)	Greater than 37.3333 N (%)		
Yes	9(15.5)	21(36.8)	.009*	
No	49(84.5)	36(63.2)21(36.8)		
Diagnosis				
Respiratory	24(41.4)	25(43.9)	.788*	
Non-Respiratory	34(58.6)	32(56.1)		
Gender				
• Male • Female	31(53.4) 27(46.6)	30(52.6) 27(47.4)	.930*	

length of stay in days	Hyperoxia	n:	Median (IQR)	Mean rank	P value
Age	less than equal to 37.33333	58	4.5(6-3)	52.16	0.055**
	greater than 37.3333	57	5(7.5-3)	63.94	
	less than equal to 37.33333	58	4.5(6-3)	55.12	0.349**
	greater than 37.3333	57	5(7.5-3)	60.93	

TABLE-III

Logistic regression analysis of mortality in relation to CEOE quartiles

	Mortality (n=%)	No Mortality (n=%)	Univariable	P-Value	Multivariable	P-Value
Gender						
Female	13(43.3)	41(48.2)	Ref	---	---	---
Male	17(56.7)	44(51.8)	1.219(527-2.817)	0.644	1.257(.528-2.993)	0.606
Age (Months)						
	10(5.5-21)	12(6-18)	.991(.970-1.012)	0.385	.988(.966-1.012)	0.324
CEOE (cat:)						
Q1	3(10)	24(28.2)	REF	REF	REF	
Q2	20(66.7)	46(54.1)	3.478(.938-12.891)	0.062	3.725(.993-13.972)	0.051
Q3	6(20)	12(14.1)	4(.849-18.836)	0.08	4.403(.919-21.012)	0.064
Q4	1(3.3)	3(3.5)	2.667(.206-34.555)	0.453	2.619(.198-34.621)	0.456

Notably, patients with higher levels of exposure tended to have increased mortality, underscoring the potential role of oxygen toxicity as a modifiable risk factor in the pediatric ICU. The overall mortality rate was 26.1%. Although demographic variables such as age, gender, and primary diagnosis were not significantly associated with mortality, patients who died had a higher mean CEOE compared to survivors.

While the length of stay (LOS) was numerically higher in patients with greater CEOE exposure, the difference across CEOE quartiles was not statistically significant.

Patients in CEOE quartiles Q2 and Q3 showed higher odds of mortality compared to Q1, with Q2 showing a borderline significant association after adjusting for age and gender, these findings suggest a potential dose-response trend between higher oxygen exposure and mortality risk, although statistical significance was not fully achieved.

Our study population was predominantly infants (IQR 6–18 months), which contrasts with local studies reporting a median age of 1.5 years by Naz et al[17] and a mean age of 3.5 years with IQR 1.2–7.0 by Nawaz et al.[18] However, male gender remained predominant across all cohorts. This difference may be attributed to the demographic profile of our hospital's catchment area, where infants represent the majority of patients requiring PICU admission.

The incidence of excessive oxygen exposure in our cohort (mean 37.3 ± 11.9%) was comparable to that reported by Naz et al[17] (32.5%), highlighting a consistent burden of hyperoxia among ventilated pediatric patients in local settings. In contrast, higher rates have been reported in other studies, such as Balcarcel et al[14] (63%) and Lilien et al[19] in bronchiolitis (45.9%). These differences may be explained by less frequent reliance on invasive PaO_2 monitoring in those studies, whereas our study utilized continuous SpO_2 as a practical surrogate for PaO_2, allowing closer titration of oxygen delivery.

Respiratory illnesses were the leading cause of PICU admission in our cohort, frequently requiring supplemental oxygen. However, excessive oxygen exposure in these patients can worsen lung injury, trigger multi-organ dysfunction, and is associated with higher mortality and prolonged PICU stay through the systemic effects of oxidative stress

A key finding of our study was that only a small proportion of patients fell into the higher CEOE quartiles (Q3: 15.7%, Q4: 3.5%). This pattern indicates that, while excessive oxygen exposure did occur, oxygen delivery in our PICU was more tightly titrated, minimizing prolonged hyperoxia and reflecting a cautious approach to oxygen management compared to what has been reported in other cohorts.

A substantial percentage of excessive oxygen exposure in this study was considered potentially avoidable, differing from other studies due to the high proportion of admissions (42.6%) requiring invasive mechanical ventilation for respiratory diseases.

In our study, mean cumulative excess oxygen exposure was significantly higher among non-survivors, suggesting an association with increased mortality. This aligns with findings by Geva et al[20], though Naz et al[17] reported no such relationship, likely reflecting differences in patient populations and monitoring methods.

Our findings demonstrate a clear dose-response relationship, with progressively higher CEOE quartiles associated with rising mortality, greater multi-organ dysfunction, and longer PICU stays.

The observed tendency to treat patients with high oxygen dosages aligns with findings from prior observational studies in critically ill adults, reflecting a "more is better" culture of oxygen supplementation.[21,22]

A key strength of our study lies in the noninvasive and continuous monitoring of SpO_2, enabling real-time FiO_2 titration at the bedside—now a standard in most ICUs. However, SpO_2 accuracy can be affected by low cardiac output, methemoglobinemia, skin pigmentation, or measurement artifacts.

LIMITATIONS

The study's limitations include its retrospective design, observational, single Centre based which inherently carries risks of selection bias and unmeasured confounders. Additionally, variations in local oxygen titration protocols between centers may limit the generalizability of our findings.

CONCLUSION

Moderate to high cumulative oxygen exposure is prevalent among children receiving invasive mechanical ventilation in pediatric ICUs. Future research is essential to define optimal oxygenation targets and minimize excessive oxygen exposure. Implementing a protocol-driven oxygen titration system managed by registered respiratory therapists could be an effective strategy to reduce excessive oxygen supplementation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Tasmina Panhwer:** Data collection, manuscript writing.
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ORIGINAL ARTICLE

Association of heart rate and oculocardiac reflex (OCR) during strabismus surgery in children.

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ABSTRACT… Objective: To determine the relationship between the baseline heart rate and the occurrence of the oculocardiac reflex in pediatric strabismus surgery using horizontal extraocular muscles. **Study Design:** Observational study. **Setting:** Mughal Eye Hospital, Lahore, Pakistan. **Period:** January-July 2024. **Methods:** Fifty children aged 3-12 years old who had elective surgery on strabismus (either esotropia or exotropia) were included. The baseline heart rate was used to classify patients as low (70-90bpm) and high (91-120bpm). All the surgeries were done under a standardised general anesthesia with intraoperative follow-up. The OCR was characterized as a 20 percent or more decrease in heart rate at baseline with extraocular muscle traction. Data were also analyzed with SPSS version 26, and associations were determined with the Chi-square test, and p was taken as significant ($p < 0.05$). **Results:** The mean age of participants was 7.6 ± 2.4 years, and the overall incidence of OCR was 58%. OCR occurred in 78.6% of patients with a low baseline heart rate and 31.8% of those with a high baseline heart rate, showing a statistically significant association ($p = 0.001$). OCR was more frequent during medial rectus surgery (35.7%) than lateral rectus (22.7%), though this difference was not statistically significant ($p = 0.320$). All OCR episodes were transient and managed successfully with cessation of traction and deepening of anesthesia. **Conclusion:** Children with lower baseline heart rates are significantly more prone to developing the oculocardiac reflex during strabismus surgery. Preoperative assessment of heart rate can thus serve as a simple yet valuable predictor for identifying high-risk patients and enhancing intraoperative preparedness.

Key words: Anesthesia, Baseline Heart Rate, Oculocardiac Reflex, Pediatric Ophthalmology, Strabismus Surgery.

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INTRODUCTION

A common ophthalmic procedure in children, strabismus surgery is often done to correct ocular misalignment and avoid long-term visual impairment and psychological effects.[1] However, after manipulating the extraocular muscles, the oculocardiac reflex (OCR), a trigeminovagal response marked by bradycardia or arrhythmia, is significantly linked to this surgery. Half Afferent signals from the trigeminal nerve's ophthalmic branch and efferent vagal stimulation mediate the OCR, which lowers heart rate and can cause anywhere from mild bradycardia to potentially fatal asystole.[2,3]

According to the definition and monitoring criteria employed, the incidence of OCR during pediatric strabismus surgery varies greatly, ranging from 14% to 90%.[3-5] A number of variables, such as patient age, anesthetic technique, depth of anesthesia, extraocular muscle manipulation type and sequence, and use of premedication or anticholinergic agents, affect the incidence and severity of OCR.[6-8] Younger children are especially vulnerable, and OCR is frequently linked to the first muscle operated on.[4,5] The incidence and magnitude of OCR have been demonstrated to be modulated by the depth of anesthesia and the selection of anesthetic agents, such as propofol, desflurane, or sevoflurane. Preventive measures have been studied with varying degrees of success, including the application of benzodiazepines, muscle relaxants, sub-Tenon block, intraoperative monitoring protocols, etc.[8-10]

Due to the unpredictability and the likelihood of severe cardiac complications, OCR remains one of the intraoperative priorities despite the ongoing improvements in perioperative care; further studies are needed to identify the correlation between the dynamics of heart rates and OCR presence in

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children who undergo strabismus operations.[2,11,12]

The discussion of the association between changes in heart rate and OCR will be essential to the development of effective management and prevention strategies, given the high prevalence and clinical significance of OCR during pediatric strabismus surgery. This paper seeks to explain this relationship in order to ensure that children have safer surgical experiences.

METHODS

This retrospective observational study was conducted to see whether there would be any relationship between baseline heart rate and the occurrence of the oculocardiac reflex (OCR) during strabismus surgery in pediatric patients. The study was carried out at Mughal Eye Hospital, Lahore, Pakistan after getting approval from ethical committee (Ref No. 0508/Admin/MEHT/RS), over an interval of seven months, continuing from January 2024 through July 2024. Fifty children, aged between three and twelve years at the time of the study, underwent elective strabismus surgeries, that is, esotropia or exotropia surgeries for horizontal extraocular muscles (medial or lateral rectus) during the operative period. To maintain homogeneous and healthy population features, prior to this study, children who had systemic illnesses, known cardiac abnormalities, previous ocular surgeries, and/or contraindications to general anesthesia were removed from the population sample.

Ethical approval for this study was obtained from the Institutional Review Board of Mughal Eye Hospital, and all procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from the parents or guardians of all participants after explaining the study purpose, procedures, and potential risks.

All procedures were carried out by skilled ophthalmic surgeons under established general anesthesia guidelines. The goal of anesthetic management was to keep the depth of anesthesia constant throughout all cases. Continuous electrocardiography (ECG), pulse oximetry, and non-invasive blood pressure monitoring were all part of the intraoperative monitoring. During traction on the medial or lateral rectus, the first horizontal muscle operated on, the oculocardiac reflex was evaluated. A 20% or greater drop in heart rate from the baseline value obtained just prior to muscle traction was considered the OCR. When OCR happened, the surgeon immediately relaxed the muscle traction and, in accordance with accepted clinical practice, deepened the anesthesia.

ECG or pulse oximetry was used to measure the baseline heart rate prior to surgery while the patient was relaxed and at rest. Patients were split into two groups according to baseline measurements: those with a low baseline heart rate (70–90 beats per minute, or bpm) and those with a high baseline heart rate (91–120 bpm). A structured proforma was used to gather data on the patient's age, sex, type of strabismus (esotropia or exotropia), muscle operated (lateral or medial rectus), baseline heart rate, and presence or absence of OCR.

All data analyses were performed using SPSS version 26. Continuous variables were shown in mean ± standard deviation (SD), whereas categorical variables were expressed in frequency and percentage. The association between baseline heart rate groups and the occurrence of OCR was analyzed using the Chi-square test, and any p-value found to be less than 0.05 was considered statistically significant.

RESULTS

Fifty pediatric patients undergoing horizontal strabismus surgery were studied to identify the correlation between baseline heart rate and OCR incidence. The participants' mean age was 7.6 ± 2.4 years, with slightly more males (56%) than females (44%). Esotropia was most common (54%), and the medial rectus was operated more often (56%) than the lateral rectus (44%). The mean baseline heart rate was 92.4 ± 12.1 bpm.

The overall rate of OCR during surgery was 58% (29 of 50 patients). When stratified by baseline heart rate categories, OCR was present in 78.6% (22 of 28) of children with a low baseline heart rate (70–90 bpm) and 31.8% (7 of 22) with a high baseline heart rate (91–120 bpm). This difference was statistically

significant (p = 0.001), indicating that children with lower resting heart rates were significantly more likely to experience OCR during extraocular muscle traction.

TABLE-I

Demographic and Clinical Characteristics of the Study Population (n = 50)

Variable	Mean ± SD / n (%)
Age (years)	7.6 ± 2.4
Sex (Male/Female)	28 (56%) / 22 (44%)
Type of Strabismus	
• Esotropia	27 (54%)
• Exotropia	23 (46%)
Muscle Operated	
• Medial Rectus	28 (56%)
• Lateral Rectus	22 (44%)
Baseline Heart Rate (bpm)	92.4 ± 12.1

TABLE-II

Association between baseline heart rate and occurrence of oculocardiac reflex (OCR)

Baseline Heart Rate Group	n	OCR Present (%)	OCR Absent (%)	P-Value
Low HR (70–90 bpm)	28	22(78.6)	6(21.4)	0.001
High HR (91–120 bpm)	22	7(31.8)	15(68.2)	
Total	50	29(58)	21(42)	

TABLE-III

Relationship between the type of muscle operated and OCR occurrence

Muscle Operated	Total (n)	OCR Present n (%)	OCR Absent n (%)	P-Value
Medial Rectus	28	10 (35.7%)	18 (64.3%)	0.320
Lateral Rectus	22	5 (22.7%)	17 (77.3%)	
Total	50	15 (30%)	35 (70%)	

Regarding the type of muscle operated, OCR was observed in 35.7% of medial rectus and 22.7% of lateral rectus cases; however, this difference was not statistically significant (p = 0.320). All OCR episodes were transient and resolved promptly with cessation of traction and deepening of anesthesia.

Overall, these findings indicate that a lower baseline heart rate is significantly associated with an increased risk of OCR during pediatric strabismus surgery, while the specific horizontal muscle manipulated does not independently affect OCR occurrence.

DISCUSSION

The current research examined the relationship between preoperative heart rate and OCR incidence during strabismus surgery in children. We found that OCR was experienced in 58% of patients, with a much greater rate among children with lower baseline heart rate (78.6%) compared to those with higher baseline heart rate (31.8%). Although OCR occurred more often during medial rectus traction (35.7%) than lateral (22.7%), this difference was not statistically significant. All episodes were transient and well controlled by cessation of traction and deepening of anesthesia.

These observations are in tandem with variable incidence of OCR that has been mentioned in past literature, ranging between 14-90 percent based on methodology, type of anesthesia, and the criterion of monitoring.

Our findings are consistent with those of Ha et al., who reported a comparable 30% incidence of the oculocardiac reflex (OCR) during pediatric strabismus surgery. At the traction of the muscle, the adrenergic phase, and the cutting of the muscle, the difference in the drop in HR in patients with OCR was substantially less than that in patients without OCR (all, $p<0.01$). In this investigation, we measured the maximal recovered HR after traction of the extraocular muscle (EOM), and it, interestingly enough, did not completely recover until cutting of the EOM, while in surgery for patients with OCR. The mean percentage of decreased HR compared to baseline HR was 10% at the cutting of the EOM in patients with OCR. We hypothesized that once OCR was initially entered, it would be comparably difficult for HR to return to baseline HR at all points during surgery. Therefore, it might be crucial for the surgeon to monitor the occurrence of OCR at the

first traction of the EOM.[3]

Again, a different study has also examined the neurophysiological processes involved in OCR and the importance of increased vagal discharge after trigeminal stimulation. Such mechanisms define the reason why the children with a more sympathetic tone during the baseline can have a more prominent reflexive vagal response, which leads to the increased risk of OCR.2.

We also find similar results to those of other researchers who reported that among the baseline physiological parameters, heart rate and age are good predictors of the occurrence of OCR.[9] In addition, Karaman et al.[7] and Yi and Jee[6] found that the depth of anesthesia and anesthetic agent choice moderate OCR incidence. In particular, light anesthesia is likely to enhance vagal sensitivity and, therefore, children are more prone to more and worse episodes of OCR.

It was also found in the current study that medial rectus traction induced OCR more frequently than lateral rectus traction, but this difference was not found to be significant. Investigations also report the same tendency, and they found a greater rate of OCR when surgery is performed on the medial rectus, perhaps because of the more easily injured sensory fibers and the one being nearer to the ophthalmic branch of the trigeminal nerve.[4,6]

The importance of anesthetic depth and the selection of drugs used in OCR modulation has been studied widely. As Oh et al. 8 and Choi et al. 10 discovered, sevoflurane was more effective in suppressing the reflex than desflurane and isoflurane. Such results are in concert with our protocol of ensuring standardized sevoflurane anesthesia, which could have helped in the moderate incidence rate of OCR (30%) in the cohort. Similarly, it was shown that OCR reduction was achieved through bispectral index (BIS)-guided anesthesia through ensuring optimal anesthetic depth and avoiding vagal fluctuations.[13]

Anticholinergic agents have also been used prophylactically. Zhao et al.[11] compared Glycopyrrolate with atropine and observed that both of them were similar in OCR prevention, but glycopyrrolate had fewer side effects. OCR episodes in our study were temporary and could be controlled by stopping traction and further deepening anesthesia without the need for pharmacologic support, which is in line with the recommendations of prior literature.[10,14]

In the comparison of our results with Klikic and Gulec[15], we discussed a similar age group of pediatrics. They were anesthetized with sevoflurane, yet they had a significantly greater rate of observed OCR (62.3%) than we (30%). This might be because of their future surveillance methodology and the small size of the cohort that enabled them to detect less severe cases. Although their research established that OCR happened more often during manipulation of the first extraocular muscle irrespective of the type, our findings revealed a moderate relationship between increased initial heart rate and the occurrence of OCR.

We also found that OCR was more frequent during medial rectus traction (35.7%) than lateral rectus (22.7%), but this was not statistically significant. This is in line with the findings of Kim et al., who found a considerably higher incidence of OCR under medial rectus traction ($p = 0.009$) among 73 pediatric patients.[16] The overall OCR incidence was considerably higher in their report (74%), which can be explained by the differences in anesthetic technique, definition thresholds (any decrease in heart rate), and characteristics of the patient population.

The existing findings underline the value of the predictive nature of the preoperative baseline heart rate as a non-invasive, simple form of risk stratification. Children with a resting heart rate of more than 90 beats per minute are to be considered at risk of OCR and thus are to be monitored and be ready for intervention. This useful predictor supports recent reviews that highlight customized perioperative care as a means of improving safety in pediatric ophthalmic surgery.

Our findings establish baseline heart rate as a straightforward, non-invasive, and clinically significant predictor of OCR risk, contributing new information to the body of existing literature. In

pediatric strabismus surgery, this parameter may help direct customized anesthetic management when combined with proven preventive measures. Despite the fact that our study offers insightful information, generalizability may be limited by its retrospective design and small sample size. More thorough knowledge of OCR pathophysiology and improved preventive measures may be possible with future multicentric prospective studies that include autonomic function testing and heart rate variability analysis.

CONCLUSION

This study found a strong relationship between lower baseline heart rate and the incidence of the oculocardiac reflex during pediatric strabismus surgery. Children with a baseline heart rate of ≤90 bpm were significantly more likely to develop OCR compared to those with higher heart rates. Although the type of muscle operated was not significantly associated, medial rectus traction showed a slightly higher frequency. All OCR cases were brief and managed effectively with prompt intervention. These findings emphasize the importance of preoperative heart rate measurement as a simple, non-invasive risk factor that can help improve intraoperative safety and preparedness in pediatric ocular surgery.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Frequency of retinopathy of prematurity in preterm low birth weight vs preterm very low birth weight admitted to Abbasi Shaheed Hospital, Karachi, Pakistan.

Tayyaba Anwer[1], Shaheen Masood[2], Urooj Mateen[3], Ilham Khanam[4], Nisha Usman[5], Dua Akhtiar[6]

ABSTRACT… Objective: To determine the prevalence of retinopathy of prematurity (ROP) in preterm low birth weight (LBW) versus very low birth weight (VLBW) among admitted infants. **Study Design:** Prospective Observational study. **Setting:** The Pediatric Department, Abbasi Shaheed Hospital, Karachi, Pakistan. **Period:** January 2025 to June 2025. **Methods:** A total of 100 preterm newborns (50 LBW, and 50 VLBW) of any gender, admitted to the NICU within 48 hours, and without congenital ocular abnormalities were included. All infants were examined and managed for ROP using standard protocols. Data were analyzed using SPSS version 26.0. Stratification of effect modifiers was done to observe their effect on ROP. Inferential statistics were applied taking p<0.05 as significant. **Results:** In 100 preterm newborns, 51 (51.0%) were females, and the mean age was 11.4±5.5. ROP was found in 61 (61.0%) infants. Those with ROP had significantly lower birth weight (1390.2±286.8 g vs 1604.6±361.3 g, p=0.001) and gestational age (29.7±2.0 vs 31.1±1.1 weeks, p<0.001), with VLBW seen in 67.2% versus 23.1% without ROP (p<0.001). Cesarean section delivery (80.3% vs 43.6%, p<0.001), lower Apgar scores, surfactant (34.4% vs 7.7%, p=0.002), steroid use (9.8% vs 0%, p=0.047), longer oxygen therapy and NICU stay, and all deaths (14.8%) were significantly associated with ROP. **Conclusion:** There is a substantial burden of ROP among preterm VLBW infants, with key risk factors including lower gestational age, lower birth weight, and prolonged oxygen therapy.

Key words: Apgar Score, Cesarean Section, Low Birth Weight, Mortality, Retinopathy of Prematurity.

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INTRODUCTION

Retinopathy of prematurity (ROP) is the most extensively recognized cause of vision impairment after preterm delivery.[1] Preterm newborns with ROP are those who require admission to NICU because of a variety of morbidities, such as sepsis, extremely low birth weight and the resulting underdevelopment of the lungs, and other conditions.[2,3] It has been observed that the retinal vascularization reaches full maturation approximately 40 weeks into the pregnancy, having begun to develop around week 16 of gestation.[4] Premature neonates are naturally undeveloped in the retinal vasculature, and the comparatively high oxygen flow.[5,6] The current American guidelines for ROP detection suggest ROP examinations for infants weighing less than 1500 g or with a gestational age ≤ 30 weeks. Infants with birth weights up to 2000 g may also be added to the list if the attending neonatologist determines that an examination is necessary due to a poor neonatal course. These standards result in a high number of low-yield tests on newborns who are bigger and better developed.[7]

Numerous countries have conducted population-based research on ROP, with varying definitions and reported results. According to research utilizing the pediatric inpatient care databases from USA, the incidence of ROP ranged between 12.8% and 19.9%.[8,9] A study conducted in Taiwan found that the incidence of ROP was 36.6% among premature infants with LOS of more than 28 days.[10] Any stage of respiratory failure was observed in 27-30% of newborns with birth weight ≤1500 g, gestational age ≤32 weeks, or an unstable clinical course in a network of Turkish NICUs.[11,12]

According to a Pakistani study, the prevalence of ROP was found to be 26.8% of these patients, with 25.6% of them having a weight of less than 1 kg, 65.1% having a weight between 1 and 1.5 kg, and 9.3% having a weight of more than 2 kg.[13] However, there is not much literature available in this regard to address the local population.

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The burden of LBW is highly prevalent in South Asia, it becomes importance to study the pattern how ROP burden differs among different categories of LBW. This study was planned to determine the prevalence of ROP in preterm LBW versus VLBW infants admitted to the Abbasi Shaheed Hospital, a tertiary care facility in Karachi. The findings of this study would not only be a valuable addition to the existing literature but also help the clinicians to know the actual burden of the disease among different categories of LBW and opt for the most suitable treatment options for patients falling into those LBW groups for better outcomes of the disease.

METHODS

This prospective observational study was performed at the Pediatric Department, Abbasi Shaheed Hospital, Karachi, Pakistan, from January 2025 to June 2025, after obtaining approval from the institutional ethics committee (letter number IRB/KMDC/KMU/080/2025, dated: 15-1-2025. A sample size of 58 (29 in each group) was calculated using the WHO sample size calculator, considering the anticipated frequency of ROP in LBW and VLBW as 74.7% and 25.6%, respectively[13], at 95% power of the study and 95% confidence level. The calculated sample size turned out to be too small for the study, therefore, it was enhanced to 50 patients in each study arm. Patients' inclusion was carried out following the non-probability consecutive sample technique. The inclusion criteria were infants of any gender, and born with a birth weight ≤2500 grams. Only those with a gestational age ≤37 weeks, admitted to the NICU within 48 hours of birth, and with no congenital ocular abnormalities were made part of this study. The exclusion criteria were infants with major congenital malformations affecting the eyes. Infants who died before their first ophthalmologic examination, or those with incomplete medical records, or those who had insufficient follow-ups were also excluded from the study. Birth weight between 1500 and 2500g was considered LBW, whereas a birth weight <1500g as VLBW.[16] Informed and written consents were obtained from parents/guardians.

Patients either admitted to the NICU or visiting outpatient ophthalmology clinics because of their referral for eye examination were enrolled into the study. Demographical data of the eligible patients like gender, age, birth weight, along with perinatal information were recorded. Information regarding oxygen therapy used, family history of eye disorders, surfactant administration, use of steroids, and maternal medical history were taken. ROP was diagnosed and classified according to the International Classification of Retinopathy of Prematurity (ICROP) criteria.[17] Following pupillary dilation with 0.5% tropicamide and 2.5% phenylephrine, a consultant pediatric ophthalmologist performed indirect ophthalmoscopy at 4 to 6 weeks postnatal age or at 31 weeks postmenstrual age, whichever was later. The presence and severity of ROP were assessed based on the location (zone I–III), stage (1: demarcation line, 2: ridge, 3: extraretinal fibrovascular proliferation, 4: partial retinal detachment, 5: total retinal detachment), and the presence of plus disease (dilatation and tortuosity of posterior pole vessels). The consultant pediatric opthalmologist having at least 5 years of experience examined and treated all patients as per standard protocols. The relevant data was stored on a predesigned proforma.

The collected data was analyzed using "IBM-SPSS Statistics version 26.0". Categorical variables were represented as frequencies and percentages, while the numerical data were shown as mean and standard deviation (SD). Stratification of effect modifiers was done to observe their effect on the outcome (ROP). The post-stratification chi-square or the Fisher's exact test, or independent sample t-test were applied taking $p<0.05$ as significant.

RESULTS

A total of 100 preterm newborns were enrolled, comprising 51 (51.0%) females. The mean age at the time of admission was 11.4±5.5 hours. The overall frequency of ROP was noted in 61 (61.0%) cases. Among those diagnosed with ROP, stage 1 was observed in 26 (42.6%), stage 2 in 17 (27.9%), stage 3 in 15 (24.6%), and stage 4 in 3 (4.9%) infants. Infants with ROP had a significantly lower mean birth weight (1390.2±286.8 g vs. 1604.6±361.3 g, $p=0.001$). The frequency of ROP was significantly higher in the VLBW (67.2% in ROP vs. 23.1% without ROP, $p<0.001$). The mean gestational age was significantly lower in the ROP cases (29.7±2.0

weeks vs. 31.1±1.1 weeks, p<0.001). The mode of delivery was significantly associated with ROP, with cesarean section accounting for 49 (80.3%) of ROP cases, compared to 17 (43.6%) in the non-ROP cases (p<0.001). Infants with ROP had significantly lower Apgar scores both at 1 minute (5.7±0.5 vs 7.3±0.8, p<0.001), and 5 minutes (7.3±0.8 vs 8.3±0.6, p<0.001). Table-I is showing comparison of baseline characteristics with respect to frequency of ROP.

ROP cases were found to have significant association with surfactant administration (34.4% vs 7.7%, p=0.002). Type of oxygen therapy was found to have significant association with the frequency of ROP (p=0.012). The mean duration of oxygen therapy was almost double in the ROP group (24.5±13.3 days vs. 13.1±4.0 days, p<0.001). ROP was significantly associated with the use of steroids (p=0.047). The mean duration of NICU stay was significantly longer for infants with ROP (31.0±15.8 days vs. 18.2±5.6 days, p<0.001). All cases with mortality (n=9, 14.8%) had ROP (p=0.009). Comparison of treatment related aspects and outcomes with respect to frequency of ROP are given in Table-II.

DISCUSSION

This study found a significant association of VLBW with the frequency of ROP with compared to LBW infants. The pronounced frequency of ROP among VLBW infants in this study aligns with the findings reported by Hwang et al.[18], from Korea, who documented an ROP incidence of 34.1% among VLBW infants, with increased risk correlating with lower gestational age, and birth weight. The Korean study also highlighted that 11.6% of infants developed stage 3 or greater ROP, paralleling the higher proportion of severe ROP cases in the present study, where stage 3 or higher accounted for nearly 30% of all ROP cases.[18] Bhuiyan et al.[19], in Bangladesh found a frequency of 23.5% for ROP among VLBW infants, and a striking 44.4% among extremely LBW neonates. The current study's elevated ROP frequency, particularly among VLBW infants may reflect local disparities in neonatal care protocols, higher rates of prematurity, and potentially limited access to preventive strategies such as timely oxygen monitoring and administration of antenatal corticosteroids. Comparison with work from rural India[20], which documented ROP prevalence of 17.4%, further emphasizes the higher burden observed in the present urban tertiary care context.[20]

TABLE-I

Comparison of baseline characteristics (N=100)

Characteristics		Retinopathy of Prematurity (n=61)	No Retinopathy of Prematurity (n=39)	P-Value
Gender	Male	36 (59.0%)	13 (33.3%)	0.012
	Female	25 (41.0%)	26 (66.7%)	
Age (hours)		11.5±5.0	11.1±6.2	0.755
Birth weight		1390.2±286.8	1604.6±361.3	0.001
Birth weight categories	Low birth weight	20 (32.8%)	30 (76.9%)	<0.001
	Very low birth weight	41 (67.2%)	9 (23.1%)	
Gestational age (weeks)		29.7±2.0	31.1±1.1	<0.001
Mode of delivery	Cesarean section	49 (80.3%)	17 (43.6%)	<0.001
	Vaginal delivery	12 (19.7%)	22 (56.4%)	
Apgar score	At 1-minute	5.7±0.5	7.3±0.8	<0.001
	At 5-minutes	7.3±0.8	8.3±0.6	<0.001
Parental history of eye disorders		6 (9.8%)	2 (5.1%)	0.328
History of parental smoking		14 (23.0%)	19 (48.7%)	0.008
Maternal diabetes		12 (19.7%)	10 (25.6%)	0.482
Maternal hypertension		32 (52.5%)	16 (41.0%)	0.264
Pre-eclampsia		14 (23.0%)	2 (5.1%)	0.018

TABLE-II

Comparison of treatment related aspects and outcomes (N=100)

Characteristics		Retinopathy of Prematurity (n=61)	No Retinopathy of Prematurity (n=39)	P-Value
Type of oxygen therapy	Continuous positive airway pressure	36 (59.0%)	13 (33.3%)	0.012
	Mechanical ventilation	25 (41.0%)	26 (66.7%)	
	Mechanical ventilation + Continuous positive airway pressure	18 (29.5%)	3 (7.7%)	
	Nassal cannula	-	5 (12.8%)	
Duration of oxygen therapy (days)		24.5±13.3	13.1±4.0	<0.001
Surfactant administration		21 (34.4%)	3 (7.7%)	0.002
Use of steroids		6 (9.8%)	-	0.047
Sepsis		49 (80.3%)	25 (64.1%)	0.071
Duration of NICU stay (days)		31.0±15.8	18.2±5.6	<0.001
Mortality		9 (14.8%)	-	0.009

Differences in ROP incidence between centers can be attributed to variations in screening criteria, survival rates of extremely premature infants, and quality of perinatal care. In contrast to the present study's high ROP burden, Awan et al.[21], in another local study reported an ROP incidence of only 3.2% among preterm infants with a mean gestational age of 31.9 weeks, and mean birth weight of 1632 g. A study from Bangladesh involving 154 infants <35 weeks gestation and <2000 g, reported an ROP prevalence of 19.5%.[22] Relatively lower prevalence of ROP may result from broader inclusion criteria, later screening initiation, or higher mean birth weights in the screened population.

This study documented significant association between ROP and prolonged oxygen therapy, with infants diagnosed with ROP receiving oxygen for a mean duration of 24.5 days, almost double that of those without ROP ($p<0.001$). This observation echoes findings from Boo et al.[23], in Malaysia, who identified prolonged oxygen therapy, invasive respiratory support, late-onset sepsis, and extreme prematurity as key risk factors of ROP. The relation between cesarean section and increased ROP prevalence in the current cohort stands in contrast to Boo et al.[23], who found vaginal delivery to be independently associated with higher ROP risk. The difference may be related to local clinical practices or underlying maternal and neonatal comorbidities influencing delivery mode selection and subsequent neonatal outcomes. Apgar scores were significantly lower among infants with ROP in this study, a pattern that is supported by Goldman et al.[24], who also identified low Apgar scores at five minutes as an independent risk factor for ROP in VLBW infants. The relationship with surfactant use likely reflects greater pulmonary immaturity among infants who later develop ROP, while the exclusive use of steroids among ROP infants in this study (9.8%) points to the potential dual role of steroids in both respiratory support and modulation of angiogenic processes in the retina. Multicenter analyses by Koc et al.[25], and Boo et al.[23], linked respiratory distress syndrome, bronchopulmonary dysplasia, and prolonged ventilation to increased ROP risk.

Length of NICU stay, and mortality were both substantially higher among infants with ROP. Koc et al.[25] also observed higher rates of morbidity and prolonged hospitalization among VLBW survivors, with major neonatal complications paralleling increased ROP incidence. The association between ROP, and mortality highlights the broader systemic vulnerability of these infants and reinforces the need for targeted surveillance and intervention strategies in the highest-risk subgroups. NICUs must prioritize strict control of oxygen supplementation, minimize unnecessary transfusions, enhance infection control, and promote the use of antenatal corticosteroids to reduce both the incidence and severity of ROP. Interdisciplinary collaboration

between neonatologists, ophthalmologists, and nursing staff is essential to ensure timely diagnosis, follow-up, and intervention.

Expanding future research to a multicenter or national registry would enhance the robustness and external validity of the results. A limitation is the lack of detailed data on the timing, concentration, and duration of oxygen therapy, which could provide further insights into modifiable risk factors. Future research should integrate neurodevelopmental assessment as a routine outcome measure for preterm infants at risk of ROP, enabling more holistic care and targeted early intervention.

CONCLUSION

There is a substantial burden of ROP among preterm VLBW infants, with key risk factors including lower gestational age, lower birth weight, and prolonged oxygen therapy. The identification of these factors supports the need for enhanced preventive strategies and early intervention in high-risk populations. Adoption of uniform ROP screening guidelines, improvements in perinatal and neonatal care, and multicenter data collection efforts can reduce the incidence of severe ROP and its lifelong sequelae in similar resource-limited settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	**Shaheen Masood:** Conception, Critical revision.
3	**Urooj Mateen:** Data analysis, methodology.
4	**Ilham Khanam:** Literature review.
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ORIGINAL ARTICLE

Predictive Value of Ultrasonography and Alkaline Phosphate (ALP) in Common Bile Duct (CBD) Stones.

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ABSTRACT… Objective: To assess the predictive performance of trans-abdominal US (TAUS) and serum ALP for detecting CBD stones in adults by taking MRCP as the reference standard. **Study Design:** Prospective Cross-validation study. **Setting:** Department of Gastroenterology, Kulsoom Bai Valika Hospital, Karachi, Pakistan. **Period:** Oct 2024 to Apr 2025. **Methods:** Adults (≥ 18 years) with clinical suspicion of common bile duct stones underwent TAUS (2–5 MHz convex probe) and serum ALP measurement within 6 hours of admission. All participants then received MRCP within 48 hours, interpreted by a radiologist blinded to TAUS and ALP results. In a subset proceeding to surgery (n=80), intraoperative findings and cholangiography confirmed stone presence and clearance. We calculated sensitivity, specificity, positive and negative predictive values, overall accuracy and area under the receiver-operating-characteristic curve (AUC) for TAUS, ALP ≥ 400 IU/L and their combination. **Results:** Of 210 enrolled patients (mean age 45.7 ± 12.5 years; 61.9 % female), MRCP confirmed choledocholithiasis in 122 (58.1 %). TAUS detected stones with 78.7 % sensitivity, 72.1 % specificity, 80.0 % PPV and 71.1 % NPV. ALP ≥ 400 IU/L yielded 65.6 % sensitivity, 42.0 % specificity, 61.1 % PPV and 46.8 % NPV. Among 80 surgically explored patients, 68 (85 %) had stones confirmed and 42 of 45 (93.3 %) underwent successful intraoperative cholangiographic clearance. **Conclusion:** High-resolution TAUS outperform ALP ≥ 400 IU/L for non-invasive choledocholithiasis detection and should remain the frontline diagnostic modality. MRCP or endoscopic ultrasound should be reserved for equivocal cases or intermediate-risk patients.

Key words: Alkaline Phosphatase, Choledocholithiasis, Diagnostic Accuracy, Magnetic Resonance Cholangiopancreatography, Pakistan, Ultrasonography.

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INTRODUCTION

Gallstone disease (GSD) is one of the most prevalent biliary disorders worldwide, with population-based studies estimating that up to 20 % of adults in SouthAsia harbour gallstones at some point in their lives.[1] Although the majority remain within the gallbladder, between 1 % and 15 % migrate into the common bile duct (CBD)[2], producing choledocholithiasis; an entity associated with obstructive jaundice, acute cholangitis and biliary pancreatitis if left untreated.[3] Rapid and accurate identification of CBD stones therefore underpins safe surgical planning and helps to avert the morbidity and cost of delayed or missed diagnoses.[2]

In highresource settings, magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound have become firstline, noninvasive tests because both approach the diagnostic yield of endoscopic retrograde cholangiopancreatography (ERCP) without its attendant procedurerelated risks.[4,5] Unfortunately, limited scanner availability, long waiting lists and prohibitive costs often restrict their routine use in Pakistan's public hospitals.[4] Consequently, clinicians continue to rely on two inexpensive and readily accessible surrogates: transabdominal ultrasonography (TAUS) and serum alkaline phosphatase (ALP).[4] US offers the attractive combination of low cost, bedside portability and the ability to demonstrate both intraductal echogenic foci and secondary ductal dilatation.[4,5] Yet its diagnostic accuracy is highly variable; published figures span from as low as 15% to as high as 40%, a range largely determined by stone size, anatomical location and operator skill.[4]

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Biochemical markers provide complementary pathophysiological information. ALP, a membranebound glycoprotein released from injured cholangiocytes, rises proportionally with the degree and duration of biliary obstruction.[6] A crosssectional survey from Lahore reported a positivepredictive value (PPV) of nearly 90 % for ALP concentrations ≥ 400 IU/L when intraoperative findings were taken as the gold standard.[7] In contrast, a British series demonstrated that while persistent ALP elevations (> 370 IU/L) were indeed associated with stones, the standalone sensitivity of the enzyme was only 42 %, underscoring the danger of using biochemistry in isolation.[5]

These disparate results highlight two enduring uncertainties: first, the optimal ALP cutoff point for maximising discrimination in different populations; and second, the incremental value obtained when ultrasonographic findings are interpreted in tandem with concurrent ALP levels. Existing Pakistani data are limited to retrospective or singlemodality evaluations, leaving a knowledge gap regarding how best to integrate imaging with biochemistry for frontline triage in resourceconstrained environments. The present study therefore set out to prospectively assess the predictive performance of TAUS and serum ALP for detecting CBD stones in adults presenting to a large tertiarycare hospital in Karachi by taking MRCP as the reference standard.

METHODS

This prospective cross-validation study was conducted in the Department of Gastroenterology, Kulsoom Bai Valika Hospital, Karachi from Oct 2024 and Apr 2025. Ethical approval was obtained from the institutional review board (ERC No: 664), and written informed consent was secured from all participants.

Sample size of 217 to 220 patients was estimated on Open Epi sample size calculator using PPV of ALP (≥400 IU/L) as 90%[7], margin of error as 4% and 95% confidence level. Patients of age more than and equal to 18 years of either gender presenting with cholelithiasis and elevated ALP (≥400IU/L) that underwent open cholecystectomy were included. Cholelithiasis was suspected in patients with rightupperquadrant pain (VAS>4) for ≥6 weeks and was diagnosed upon US evidence of stones in the gall bladder (echoic shadow). Exclusion criteria comprised known malignancy, chronic liver disease, empyema gallbladder, acute cholecystitis, previous biliary surgery, pregnancy, hemodynamic instability precluding imaging, and refusal to consent. Non-probability consecutive sampling method was employed for sample selection.

TAUS was performed within 6 hours of admission by credentialed sonographers using a Philips Affiniti 70 (2–5 MHz convex probe). Sonographers were blinded to ALP results. CBD diameter, presence of intraductal echogenic foci with posterior acoustic shadowing and gallbladder status were recorded. CBD dilatation was defined as > 8 mm. US was considered positive if any echogenic focus was visualized or if CBD dilatation coexisted with gallstones. A venous blood sample was obtained concurrently from all of the patients. ALP was measured on a Roche Cobas 6000 (IFCCtraceable method; upper reference limit 130 IU/L). ALP ≥400IU/L was considered as a positive test. Then all 210 participants underwent MRCP within 48 hours of admission on a 1.5 T scanner, using heavily T2weighted singleshot fast spinecho sequences in axial and coronal planes. A boardcertified radiologist; who was blinded to US and ALP results interpreted each MRCP. Choledocholithiasis was confirmed by the presence of one or more discrete signalvoid filling defects within the CBD. During surgical exploration, CBD stones were visualized directly or extracted using choledochotomy or transcystic approaches. In several cases, dilated bile ducts and impacted stones were observed, correlating with preoperative imaging and biochemical markers. The nature of the stones varied from soft, pigment-rich sludge to hard, cholesterol-laden calculi. Intraoperative cholangiography was employed in selected cases to delineate ductal anatomy and confirm stone clearance, thereby supporting or contradicting preoperative ultrasound and ALP findings.

Data was analyzed using SPSS version 23. Mean and SD were computed for continuous data and frequencies and percentages were computed for categorical. Two by two was used to calculated sensitivity, specificity, PPV, negative predictive

value (NPV) and diagnostic accuracy for TAUS and ALP≥ 400 IU/L by taking MRCP as reference standard. Twotailed p < 0.05 denoted significance.

RESULTS

Of 220 eligible patients, 4 declined or were lost, leaving 216; 6 were later excluded (three incomplete imaging, 3 indeterminate MRCP), yielding 210 for analysis. Baseline characteristics are presented in Table-I. The overall mean age was 45.7 years (SD=12.5), and sex distribution showed a modest female predominance (61.9 %). Overall, median ALT, total bilirubin and ALP were found as 200 (121.75–286.25) IU/L, 3.5 (2.18–5.64) mg/dl, and 450 (299.75–632.50) IU/L respectively.

MRCP confirmed CBD stones in 122 of 210 patients (58.1 %). TAUS correctly identified 96 of these 122 cases (sensitivity 78.7%) and correctly excluded 64 of 88 stonefree patients (specificity 72.1 %), yielding a PPV of 80.0 % and a NPV of 71.1 %. The area under the ROC curve for TAUS was 0.75. Using a threshold of ALP ≥ 400 IU/L, 80 of 122 stone cases were detected (sensitivity 65.6 %), but only 37 of 88 nonstone patients were correctly classified (specificity 42.0 %), with a PPV of 61.1 % and NPV of 46.8 %. The AUC for ALP was 0.64, indicating poor overall discrimination. When either US or ALP (≥ 400 IU/L) was positive, sensitivity remained at 78.7 % but specificity fell to 68.2 %, and the combined AUC was 0.73; not a meaningful improvement over TAUS alone. (Table-II & Figure-1)

Eighty patients (38% of the cohort) underwent surgical CBD exploration. Intraoperatively, stones were directly visualized or extracted in 68 patients (85%). Stone composition was mixed: 54% were hard, cholesterolladen calculi and 46% soft, pigmentrich sludge. Intraoperative cholangiography was performed in 45 cases and confirmed complete ductal clearance in 42 (93.3%).

FIGURE-1

ROC curve for the US and ALP≥ 400 IU/L

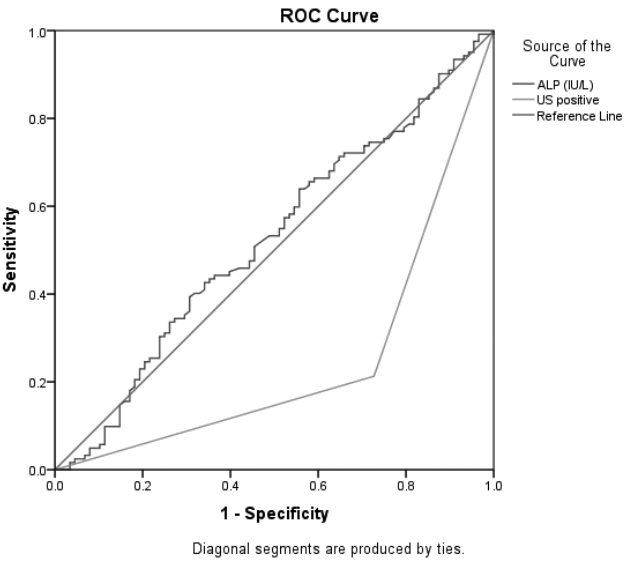

TABLE-I

Baseline demographics and laboratory parameters (n = 210)

Variable	Total Sample (n=210)	CBD Stones Present (n = 122)	CBD Stones Absent (n = 88)
Age, years (mean ± SD)	45.66 ± 12.48	45.71 ± 12.91	45.60 ± 11.94
Female sex, n (%)	130 (61.9)	61 (69.3)	69 (56.6)
ALT, IU/L (median [IQR])	200 [121.75–286.25]	239 [167.50–326.25]	150 [94–229]
Bilirubin total, mg/dL (median [IQR])	3.5 [2.18–5.64]	5.19 [3.53–6.51]	2.02 [1.27–2.99]
ALP, IU/L (median [IQR])	450 [299.75–632.50]	463.5 [301–637]	446 [300.50–603]

TABLE-II

Test accuracy of TAUS and ALP by taking MRCP as gold standard (n = 210)

Parameter	Sensitivity % (95 % CI)	Specificity % (95 % CI)	PPV % (95 % CI)	NPV % (95 % CI)	Accuracy (95 % CI)
TAUS	78.69 (70.35–85.58)	72.73 (62.19–81.68)	80 (73.75-85.07)	71.11 (63.10-77.99)	76.19 (69.84-81.78)
ALP ≥ 400 IU/L	65.57 (56.43-73	42.05 (31.60-53.05)	61.07 (55.74-66.14)	46.84 (38.38-55.47)	55.71 (48.72-62.55)

DISCUSSION

Our study confirms that choledocholithiasis in Pakistan disproportionately affects middleaged women, with 61.9 % of our overall cohort and 69.3 % of patients with MRCPconfirmed stones being female. This mirrors community surveys in Karachi showing gallstone prevalence of approximately 10.2 % and a clear female predominance.[8] The mean age of 45.7 years in our cohort similarly aligns with regional data indicating earlier onset of symptomatic disease compared with Western populations.[9] Intraoperative cholangiography in 80 surgically explored patients confirmed ductal clearance in 93.3 %, underscoring the value of operative imaging when preoperative diagnostics are equivocal.[10]

Transabdominal US delivered robust diagnostic accuracy, correctly identifying 78.7 % of MRCPconfirmed stones and excluding 72.1 % of nonstone cases. A recent systematic review and metaanalysis of 15 studies encompassing over 2000 patients reported pooled US sensitivity of 73 % and specificity of 91 % for choledocholithiasis, corroborating our findings in a Pakistani tertiarycare setting.[11] US's robust performance in our study also aligns with prior Pakistani data demonstrating sensitivity of 96% and specificity of 80.2% for CBD stone detection in tertiarycare settings.[12] While, in another Pakistani study US showed the lesser sensitivity of 29%, however, specificity was 85%.[7] Early study also demonstrated ultrasonographic sensitivity of 77% and specificity of 98% in obstructive jaundice, foreshadowing the gains achieved with today's highresolution machines.[13]

By contrast, serum ALP at a threshold of 400 IU/L underperformed, yielding only 65.6 % sensitivity and 42.0 % specificity. This confirms that a universal cutoff of 400 IU/L misses one in three true stones and falsely flags more than half of nonstone patients. This mirrors findings from a prospective analysis in which an ALP cutoff of 78 IU/L achieved 97.6 % sensitivity but only 72.6 % specificity, illustrating the sensitivityspecificity tradeoff inherent to biochemical markers.[14] Conversely, ALP's PPV in a study conducted at Lahore reached 90 % at thresholds ≥ 400 IU/L, but sensitivity remained low (42 %), limiting its utility as a standalone screen.[7] Biochemical markers alone cannot substitute for imaging, especially given the overlap of ALP elevations in gallbladder inflammation and other hepatobiliary conditions.

MRCP remains the noninvasive diagnostic gold standard, with pooled sensitivities and specificities exceeding 85 % and 90 %, respectively.[15] However, MRCP access in Pakistan is severely limited. According to the World Health Organization's Global Health Observatory, Pakistan had just 0.22 MRI units per million population as of 2013, a figure that has seen only marginal improvement in the ensuing decade.[16] A 2011 RADAID International report documented merely 19 MRI systems serving some 170 million Pakistanis, equivalent to 0.11 units per million and concentrated in private urban hospitals, leaving entire provinces without any MRI access.[17] The cost of MRCP (PKR 15 000–25 000; ~USD 85–140) places it beyond the reach of many publicsector patients, resulting in delayed or foregone definitive imaging.

Endoscopic ultrasound (EUS) has demonstrated superior sensitivity (96-100%) and specificity (92-100%) for choledocholithiasis compared to MRCP in previous studies.[4,18] When combined with samesession ERCP, EUS-directed interventions reduce patient burden and overall costs associated with repeat procedures.[19] Adoption of EUS in Pakistan is limited by equipment scarcity and a shortage of trained endosonographers, but initial experiences at tertiary centres have been encouraging, suggesting that broader EUS integration could alleviate MRCP shortages.[4]

Clinical practice guidelines increasingly advocate riskstratified approaches. The American Society for Gastrointestinal Endoscopy (ASGE) classifies verystrong predictors (e.g., CBD stones on US, bilirubin > 4 mg/dL) and recommends MRCP or EUS for intermediaterisk patients.[2] European associations similarly endorse selective imaging, balancing diagnostic yield against cost and resource utilization.[19] In Pakistan, adapting these algorithms with locally validated biochemical thresholds and transabdominal US criteria could optimize resource utilization.

Costeffectiveness analyses from comparable low and middleincome countries indicate that a tiered approach; initial transabdominal US, followed by MRCP only for those at intermediate risk can reduce unnecessary MRCP by up to 70% and save significant healthcare expenditure.[20] Similarly, laparoscopic common bile duct exploration, available in several Karachi surgical units, achieves stone clearance rates above 80% and may be more costeffective than repeated imaging or ERCP in selected cases.[21]

Our study's foremost strength lies in its prospective design with rigorous blinding and use of MRCP as a uniform reference standard for all participants, which minimizes spectrum and verification biases and reflects realworld practice in a busy tertiarycare hospital. Nevertheless, our singlecentre setting and reliance on examinations performed by highly trained sonographers may limit the generalizability of these findings to less expert environments. Only 38 % of patients underwent surgical confirmation, introducing potential verification bias, and we did not assess alternative biomarkers such as gammaglutamyl transferase or capture patientcentred outcomes like quality of life and downstream healthcare utilization. Looking ahead, multicentre validation across Pakistan's diverse healthcare facilities will be critical, as will costeffectiveness analyses tailored to local resource constraints, broader training programs to standardize ultrasound proficiency, and exploration of integrative predictive models including clinical scores and machinelearning approaches to optimize noninvasive diagnosis and guide resource allocation in settings where advanced imaging remains scarce.

CONCLUSION

Highresolution TAUS outperforms ALP ≥ 400 IU/L for noninvasive choledocholithiasis detection and should remain the frontline diagnostic modality. MRCP or endoscopic ultrasound should be reserved for equivocal cases or intermediaterisk patients. Future work should refine locally appropriate ALP thresholds, validate combined risk scores and expand access to advanced endoscopic imaging.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Ramsha Waseem:** Concept of study,
2	**Iram Dayo:** Data analysis, manuscript writing.
3	**Nimra Aslam:** Data analysis.
4	**Muhammad Ghayasuddin:** Final review.
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6	**Muhammad Ali:** Literature review.

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ORIGINAL ARTICLE

Comparison of the frequency of post-operative wound infection and mean length of ICU stay after tight versus standard glycemic control among diabetic patients undergoing CABG.

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ABSTRACT… Objective: To compare post-operative wound infection rates and average ICU stay length in diabetic patients undergoing coronary artery bypass surgery at Azra Naheed Medical College, Lahore, based on strict glycemic control versus standard glycemic control. **Study Design:** Randomized Controlled Trial. **Setting:** Azra Naheed Medical College, Lahore. **Period:** January 2023 to June 2023. **Methods:** Total 260 eligible diabetic patients scheduled for surgery provided informed consent following ethical committee approval. A lottery-based randomization process allocated patients to Group A (tight glycemic control, blood sugar levels 120-160 mg/dL) or Group B (standard glycemic control, blood sugar levels 161-200 mg/dL). Treatment was as per standard protocols, and blood sugar levels were monitored accordingly. Proforma entries documented ICU stay and wound infections during hospitalization, ensuring data confidentiality. **Results:** The study involved 260 cases, with 130 in each group. In Group-B, the mean age was 51.56+6.07 years, and in Group-A, it was 52.09+5.86 years. Males constituted 53.85% (n=70) in Group-B and 53.08% (n=69) in Group-A, while females were 46.15% (n=60) in Group-A and 46.92% (n=61). Wound infection development differed, with 29.23% (n=38) in Group-A and 59.23% (n=77) in Group-B. The remaining 70.77% (n=92) in Group-A remained infection-free. Regarding mean hospital stays, Group-A stayed for 3.92+0.95 days, while Group-B spent 5.73+0.76 days (p = 0.0001). **Conclusion:** Strict glycemic control significantly reduces postoperative infections and ICU stay duration in diabetic patients undergoing coronary artery bypass surgery compared to standard glycemic control.

Key words: Coronary Artery Bypass Surgery, CABG, Perioperative Glycemic Control, Diabetes Mellitus, Post-operative Hospital Stay, Standard Glycemic Control, Tight Glycemic Control, Wound Infection.

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INTRODUCTION

Diabetes mellitus (DM), a prevalent chronic condition characterized by compromised immune function, impacts an estimated 350 million individuals worldwide.[1] Pakistan has one of the ten greatest prevalence of diabetes patients globally, which is correlated with an elevated risk of coronary artery events.[2,3] A well-documented phenomenon in perioperative and postoperative cardiac surgery, hyperglycemia is associated with an unfavorable prognosis. It is associated with increased mortality, protracted hospital stays, and contamination of surgical wounds.[4] Consequently, in order to ensure favorable outcomes for patients undergoing coronary artery bypass surgery (CABG), glycemic control becomes crucial.[5]

Diverse glycemic control strategies have been suggested in an effort to improve the prognosis of these patients. These include strict glycemic control and standard glycemic control using a sliding scale model; however, the available literature indicates that these strategies have variable effects on ICU duration of stay and post-operative wound infection.[6] The two strategies did not correlate in a statistically significant way with the duration of ICU stay or postoperative wound infection, according to a study by Konstantinos et al.[7]

Pakistan has a rising diabetes rate. The International Diabetes Federation estimates 33,000,000 cases of diabetes in Pakistan in 2022, 26.7% of adults. Pakistan's type 2 diabetes prevalence is 11.77%, greater in cities than rural areas.

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Diabetes is a major public health issue and increases the risk of coronary heart disease. Hyperglycemia, which is common in diabetic and non-diabetic cardiac surgery patients, is linked to higher mortality, longer hospital stays, and surgical wound infections.[8,9] Thus, glucose management is essential for CABG patients' success.

Hyperglycemia affects postoperative healing and increases surgical infection risk, emphasizing the need to manage it. Diabetes is a major public health issue in Pakistan, hence effective prevention and management are needed.[10]

The purpose of this research is to compare the incidence of postoperative wound infection and ICU duration of stay following strict glycemic control versus standard glycemic control. Due to the lack of local literature and the inconsistent results found in the existing literature, this study will produce additional evidence based on our population. This information may offer clinician's insights into the most effective glycemic control technique to implement in diabetic patients undergoing coronary artery bypass grafting (CABG), with the ultimate goal of reducing morbidity and mortality rates.

METHODS

By comparing the incidence of post-operative wound infection and the average length of intensive care unit (ICU) stay among diabetic patients undergoing coronary artery bypass surgery at Azra Naheed Medical College, Lahore for ischemic heart disease under strict glycemic control versus standard glycemic control; this study aims to determine which modality is more effective.

The research was a randomized controlled trial; data collection was done for six months (from January'2023 to June'2023) subsequent to the approval of the synopsis by the CPSP and Ethical Review Board (ANMC/ME/01/23/060, Dated: 04-January-2023 in the name of Dr M. Ammar) at the Azra Naheed Medical College, Lahore.

Approximately 260 diabetic patients who met the inclusion criteria and were scheduled to undergo coronary artery bypass surgery at Azra Naheed Medical College, Lahore were approached and provided informed consent subsequent to the study protocol receiving approval from the hospital's ethical committee. The proforma contained notation pertaining to the demographic data of the individuals. The patients were allocated into two categories through a lottery-based randomization process. The patients in Group A (tight glycemic control) had blood sugar levels maintained between 120 and 160 mg/dL, while those in Group B (standard glycemic control) had blood sugar levels maintained between 161 and 200 mg/dL. Annexes detailing treatment protocols are included.

The selection criteria for the patients for this study was: 'Individuals of age 30 to 60 years, of either gender who have been diagnosed with diabetes for a minimum of five years and are undertaking coronary bypass surgery for ischemic heart disease.

Exclusion criteria for this study were: 'Patients who express a voluntary refusal to partake in the research; patients with renal dysfunction (estimated GFR<60ml/min/1.73m2), chronic obstructive pulmonary disease (FEV1/FVC ratio<0.7), or who were currently receiving immunosuppressive therapy, as confirmed on history and from their medical records; Patients who exhibit severe ventricular arrhythmias (ventricular tachycardia and/or fibrillation) within the first twenty-four hours of their intensive care unit (ICU) admission undergo cardioversion; Individuals who had undergone prior cardiac surgery; intraoperative and/or within the initial 48 hours after the procedure; mediastinal re-exploration for hemorrhage; support for hemodynamics with an intra-aortic balloon pump (IABP).

The sample size was determined, using an 80% power of test, a 5% level of significance, and an expected mean duration of ICU stay of 3.2+4.7 days for patients with strict glycemic control as opposed to 2+1.2 days for those with standard glycemic control.[5]

Consecutive non-probability sampling technique was used for selection of the patients.

The blood sugar level of all the patients was monitored and recorded in accordance with the

methodology. Patients were monitored, and proforma entries were made for the duration of ICU stay and the occurrence of wound infections during hospitalization. Data confidentiality was guaranteed.

The information was entered and analyzed utilizing version 23.0 of SPSS. Age and length of hospitalization were numerical variables analyzed in the form of means and standard deviation. The data for qualitative variables, such as the occurrence of wound infections and gender, was expressed as frequencies and percentages. Age, gender, and duration of DM were utilized to stratify the data in order to account for the effect modifiers. For statistical significance analysis, the independent t-test and post-stratification chi-square test were utilized according to the type of the variable; taking p-value less than 0.05 as statistically significant.

RESULTS

In order to compare the frequency of post-operative wound infection and mean length of intensive care unit (ICU) stay among diabetic patients undergoing coronary artery bypass surgery due to ischemic heart disease at Azra Naheed Medical College, Lahore, a total of 260 cases (130 in each group) that met the inclusion/exclusion criteria were enrolled.

The age distribution of the participants indicates that 15.38% (n=20) of Group-B and 87.69% (n=114) of Group-A were between the ages of 30 and 45, while 84.62% (n=110) were between the ages of 46 and 60. The mean + standard deviation for Group-A was 52.09+5.86 years and for Group-B it was 51.56+6.07 years.

Males comprised 53.85% (n=70) of Group-A participants and 53.08% (n=69) of Group-B participants, while females comprised 46.15% (n=60) of Group-A and 46.92% (n=61) of Group-B participants.

A comparison of wound infection development in both groups reveals that 29.23% (n=38) of participants in Group-A and 59.23% (n=77) of participants in Group-B developed an infection, while the remaining 70.77% (n=92) of participants in Group-A and 40.77% (n=53) in Group-B did not have any infection (p = 0.000). A comparison of the mean hospital stays in both groups reveals that Group-A stayed for 3.92+0.95 days, while Group-B spent 5.73+0.76 days; the p value was 0.0001. (as shown in the tables below)

Age, gender, and duration of DM were utilized to stratify the data in order to account for the effect modifier. For statistical significance analysis, the independent t-test and post-stratification chi-square test were utilized. A p-value less than 0.05 was regarded as statistically significant.

TABLE-I

Comparison of development of wound infection in both groups (N=260)

Wound Infection	Group-A (n=130)		Group-B (n=130)	
	No.	%	No.	%
Yes	38	29.23	77	59.23
No	92	70.77	53	40.77
Total	130	100	130	100

P value=0.0001

TABLE-II

Comparison of duration of hospital stay in both groups (N=260)

Duration of Hospital Stay (Days)	Group-A (n=130)		Group-B (n=130)	
	Mean	SD	Mean	SD
	3.92	0.95	5.73	0.76

P value=0.0001

Statistically significant differences were observed in the duration of hospital stays when age, gender, and tenure of diabetes were accounted for in the stratification process ($p < 0.0001$). Although the results of the stratification of wound infection data by age were not statistically significant for young adults, they were ($p = 0.001$) for the elderly. Furthermore, a statistically significant increase in the incidence of wound infections was noted among female patients, specifically in Group B ($p < 0.0001$). Additionally, the length of time that diabetes was present was found to be a substantial determinant in the occurrence of wound infections (p-value = 0.0001).

DISCUSSION

The objective of this study was to compare the duration of ICU stay and incidence of postoperative

wound infection between patients who received strict glycemic control and those who received standard glycemic control. In light of the scarcity of local literature and the incongruous findings observed in the extant research, this investigation has the potential to generate supplementary evidence concerning our demographic. With the ultimate aim of reducing morbidity and mortality rates, this information may provide clinicians with insights regarding the most efficacious glycemic control technique to employ in diabetic patients undergoing coronary artery bypass grafting (CABG).

Of 260 cases analyzed in total (130 cases in each category) in accordance with our research, 12.31% (n=16) in Group-A and 15.38% (n=20) in Group-B belonged to the 30-45 age group, whereas 87.69% (n=114) in Group-A and 84.62% (n=110) were between the ages of 46-60. The calculated mean and standard deviation for Group-A and Group-B were, respectively, 51.56+6.07 years and 52.09+5.86 years. Group-A consisted of 46.15% (n=60) males, while Group-B had 46.92% (n=61) males. Group-A exhibited a mean hospital stay of 3.92+0.95 days, whereas Group-B maintained a mean stay of 5.73+0.76 days (p value = 0.0001; significance level: 0.0001).

A previous study conducted by Subhani et al. found that patients undergoing post-operative wound infection were statistically significantly less likely to develop such infections when they were on strict glycemic control (33.87% vs. 61.29%).[11] Conversely, Chan demonstrated that patients undergoing strict glycemic control had a substantially shorter length of stay in the intensive care unit (4.1 vs 6.9 days) and a significantly lower incidence of postoperative wound infection (19.1% vs 35.2%) than those undergoing standard glycemic control.[12] Significant disparities were observed in the analysis of wound infection progression between the two groups in our research. A total of 38 participants, or 29.23%, contracted wound infections under strict control conditions; the remaining 70.77% (n=92) maintained infection-free status. In contrast, patients on conventional glycemic control had a greater incidence of wound infections, affecting 59.23% (n=77) of the 130 participants. Notably, a mere 40.77% (n=53) of the participants in Group-B remained unaffected by infections. A significant correlation (p = 0.0001) was observed between the type of glycemic control and wound infection, as determined by the statistical analysis.

In their study, Haga et al. compared the duration of intensive care unit (ICU) stays of patients with strict glycemic control (3.2+4.7 days) to those with standard glycemic control (2.2+1.2 days).[13] Our findings are in-consistent with those of Konstantinos et al., who did not observe a statistically significant correlation between the two strategies and the duration of postoperative wound infection or ICU stay.[14]

Ehab A. Wahby et al[15] conducted an additional investigation with the purpose of comparing the outcomes of diabetic patients undergoing coronary artery bypass graft (CABG) surgery when subjected to moderate versus strict perioperative glycemic control. Their findings indicated that strict glycemic control resulted in a more favorable outcome for diabetic CABG patients. Consistently advising diabetic patients undergoing CABG surgery to maintain perioperative blood glucose levels within the range of 110 to 149 mg/dL is both safe and worthwhile.

Zerre et al. identified an independent risk factor for sternal incision infection as an elevated blood glucose level within 48 hours of the procedure in their retrospective study[10] and a separate investigation conducted by Elassi et al. revealed that diabetic patients who underwent CABG surgery fared well, with the exception of sternal incision infection.[11] The initial examination of the correlation between strict glycemic control and reduced surgical wound infection occurred in 1991, when the American College of Cardiology and American Heart Association identified a heightened prevalence of such infections among patients with diabetes.[12]

It has been postulated that hyperglycemia may impact leukocyte function through mechanisms such as diminished bactericidal capability, phagocytosis, chemotaxis, and adherence to microbes. Furthermore, there is an inverse correlation between the degree of hyperglycemia and leukocyte function.[16]

In a meta-analysis examining the impact of strict glycemic control on patient morbidity and mortality, Haja et al. discovered that patients undergoing strict glycemic control required significantly less time for ventilation than the control group. However, substantial heterogeneity existed in the data, which the Lazar study significantly emphasized.[8]

In summary, the results of our study in accordance with most of the above studies justify the hypothesis that "there is a difference in frequency of postoperative wound infection and mean length of ICU stay with tight glycemic control as compared to standard glycemic control among diabetic patients undergoing coronary artery bypass surgery".

CONCLUSION

The incidence of postoperative wound infections and the average duration of intensive care unit (ICU) stays are considerably reduced in diabetic patients undergoing coronary artery bypass surgery when strict glycemic control is implemented, as opposed to standard glycemic control.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
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4	**Zafar Tufail:** Review of manuscript.
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ORIGINAL ARTICLE

Pattern of fodder chopper machine injury in Gujranwala, Punjab, Pakistan.

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ABSTRACT… Objective: To find out the pattern of injury caused by toka / Fodder Chopper machine in Gujranwala Punjab. **Study Design:** Observational Retrospective Study. **Setting:** Department of Surgery, Gujranwala Teaching Hospital, Gujranwala. **Period:** April 2021 to March 2023. **Methods:** All the patients having fodder chopper machine injury were the part of study and their pattern of injury was studied. Age of patient, sex, side of injury and extent with severity were recorded. **Results:** Out of 100 patients, 82 (82.00%) were male and 18(18.00%) were female. Mean age was 17 years. Digits, palm and wrist, distal forearm, proximal forearm and arm had 53(53.00%), 20 (20.00%), 11 (11.00%), 9(9.00%) and 7 (7.00%) injuries, respectively. Right upper limb is more common presentation 81.00% than left upper limb 19.00%. **Conclusion:** Fodder Chopper machine injuries are one of most common cause of disability and are very common in our region especially in our rural area and mostly effected are children of younger age group under 14 years. This is due to inexperience and no training and design of Toka/ Fodder Chopper Machine.

Key words: Disability, Fodder Chopper Machine, Side of Injury.

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INTRODUCTION

Pakistan is a country of farmers and Gujranwala is a city of Punjab surrounded by agriculture lands. In rural areas, it is daily practice to use Toka/Fodder chopper for preparation of food for domestic animals. Mostly these machines are locally made for conversion of hay to smaller pieces. With the shift of manual machine to electric machine the chances of injuries have increased a lot.[1]

In surgical emergencies of almost every hospital in Pakistan, patients with these Toka injuries present regularly, but their diversity and impact warrant further investigation. Patients with different patterns of injuries from different age groups and genders frequently appear in surgical emergencies.[2] Commonly affected are young individuals, with digits, wrists, and hands being the most commonly injured parts. Victims are predominantly those lacking proper training or experience. Disability in the younger generation not only causes personal suffering but also represents a loss of future productive human resources for the country, contributing to an increased socioeconomic burden.[3]

Fodder chopper injuries, while underreported in national databases, follow a predictable pattern across Punjab and can be reasonably extrapolated to Gujranwala.[4] Young males dominate the affected demographic, with a notable number of children also suffering injuries—often while assisting adults or playing near operating machines. Females, particularly non-professional or casual laborers, are also at risk, likely due to limited training and lack of awareness about machine safety protocols.[5] These injuries primarily involve the upper limbs, especially the fingers and hands, with outcomes ranging from deep lacerations to partial or complete amputations. Some rare but serious cases involve scalp avulsion injuries when head coverings are caught in the rotating blades. The right upper limb is more frequently affected, possibly due to its dominant use during operation.[6]

The majority of these injuries occur during routine agricultural tasks. Poorly maintained or unsafe machine designs lacking protective guards, absence of formal operator training, and the use of machines by non-professionals are major contributing factors.[7]

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Understanding these patterns can help guide preventative measures, including safer machine engineering, rural education campaigns, and targeted operator training, thereby reducing the incidence of such life-altering injuries in this vulnerable population.[8]

METHODS

This was observational retrospective study was carried out at Gujranwala Teaching Hospital Gujranwala Surgery department from April 2021 to March 2023, after the approval from the CPSP and Institutional Review Board (Letter No: No.Admn.182/GMC, Dated: 29/02/2021 in the name of Dr. Farhan Tahir) All the patients having fodder chopper machine injury were the part of study and their pattern of injury was studied. Age of patient, sex, side of injury and extent with severity were recorded. All the injuries other than than Toka/ Fodder Chopper Machine Injury were excluded so that exact extent of injuries by Toka Machine.

All the patients presented in Trauma Surgical of our Hospital either came directly or referred from Primary and Secondary Health center were managed initially according to ATLS guidelines. After initial resuscitation in Emergency patients were shifted to Operation Theatre for definitive Management and Plastic Surgeons, Pediatric Surgeons, Orthopedic Surgeons and Neurosurgeons were also included in the management plan.

All the detail of patient was recorded on file of ward that was studied and data collected from that which includes demographic details, site of injury, extent and pattern of injuries and what management done to patients. Mostly Right upper limb was involved with injuries ranging from amputations of distal phalanx hand Arm and forearm amputations.

RESULTS

There were 13(13.00%) male and 7 (7.00%) female patients between the ages of 1-10 years, between the ages 11-20 years there were 14(14.00%) male and 6(6.00%) female patients of fodder chopper/ Toka machine injuries were presented. Between the ages of 21-30 years 15(15.00%) male and 2 (2.00%) female patients, between 31-40 years 15(15.00%) male and 1 (1.00%) female patients, between 41-50 years 11(11.00%) male and 2 (2.00%) female patients, between the ages of 51-60 years 9(9.00%) male and 1 (1.00%) female patients, patients with ages 61 above 5(5.00%) male and 0 (0.00%) female patients were presented. Majority of patients were from 1 to 20 years of ages, as these ages are future of our generation and are not trained of these machines as depicted in Table-I.

In our study the frequency of fodder chopper machine injury according to site were right digits 37(37.00%) male and 7 (7.00%) female patients, left digits 8(8.00%) male and 2(2.00%) female patients, right palm and wrist 13 (13.00%) male and 3(3.00%) female patients, left palm and wrist 3 (3.00%) male and 1 (1.00%) female, right distal forearm 7 (7.00%) male and 2 (2.00%) female, left distal forearm 1 (1.00%) male and 1 (1.00%) female patients, right proximal Forearm 6 (6.00%) male and 1 (1.00%) female, left proximal Forearm 2 (2.00%) male and 0 (0.00%) female, right arm 5 (5.00%) male and 1 (1.00%) female, left arm 1 (1.00%) male and 0 (0.00%) female present. The occurrence of fodder chopper machine injuries were maximum of right digits as shown in Table-II.

There is a statistically significant association between age group and gender ($p < 0.05$). Younger females (1–20 years) are proportionately more affected than older females. No significant association between gender and injury site ($p > 0.05$). The pattern of injury by site is similar across genders.

TABLE-I

Age distribution according to gender (n=100)

Age in Years	Male	Female	Total
1-10	13(13.00%)	7(7.00%)	20(20.00%)
11-20	14(14.00%)	6(6.00%)	20(20.00%)
21-30	15(15.00%)	2(2.00%)	17(17.00%)
31-40	15(15.00%)	1(1.00%)	16(16.00%)
41-50	11(11.00%)	2(2.00%)	13(13.00%)
51-60	9(9.00%)	1(1.00%)	10(10.00%)
61 and above	5(5.00%)	0(0.00%)	5(5.00%)

TABLE-II

Distribution of injuries according to site of body (n=100)

Site of Injury	Male	Female	Total
Right Digits	37 (37.00%)	7 (7.00%)	43 (43.00%)
Left Digits	8	2	10
Right Palm and Wrist	13	3	16
Left Palm and Wrist	3	1	4
Right distal Forearm	7	2	9
Left distal Forearm	1	1	2
Right proximal Forearm	6	1	7
Left proximal Forearm	2	0	2
Right Arm	5	1	6
Left Arm	1	0	1

DISCUSSION

In Pakistan 65 % people live in rural area and is country in which agriculture is main profession of majority of people and therefore depend on farming for food. Cattle farming need toka/fodder chopper machine for cutting of food for cattle.

The study by Mehmood et al. (2015) highlights the significant burden of agricultural machinery-related injuries in rural Pakistan, with fodder cutter (Toka) machines identified as the most common cause, accounting for over 50% of the cases reviewed. Traumatic amputations of the upper limb were the predominant injury pattern, seen in nearly 58% of patients, typically resulting from direct hand entrapment during the manual feeding of fodder. The majority of affected individuals were young males, although female involvement was also noted, reflecting the shared responsibilities in agricultural labor. Complications such as wound infection were common, while rare but fatal outcomes like tetanus and Fournier's gangrene were also reported. The

study emphasized that most of these injuries are preventable and recommended safety campaigns, improved machine design, and timely access to specialized care, including the potential for re-implantation and revascularization in suitable cases. These findings underline the occupational hazards faced by rural populations and reinforce the need for preventive and policy-level interventions to reduce disability and mortality associated with agricultural machinery use.[9]

In Pakistan this Fodder chopper is mainly used as an agricultural tool. Since the use of automatic Fodder Chopper machine has increased the severity of injuries has also increased substantially. Injuries by these machines are usually non-fatal. A study of farm-related injuries in children under 16 reported 65 non-fatal accidents in one year and 33 deaths over four years. Machinery and falls were common causes. Despite safety improvements, farms remain dangerous. Better enforcement of safety laws and targeted education are needed to reduce these preventable injuries.[10]

In our country like Pakistan in which agriculture is a main profession have these Fodder chopper machine injuries a major cause of disability and injury, people of younger age groups were involved mostly due to active involvement.[11,12]

A national review (1990–2001) of fatal agricultural injuries among Canadian children aged 1–6 found a higher fatality rate (14.9 per 100,000) than the general unintentional injury rate (8.7 per 100,000). Most deaths occurred on farms, mainly from being run over by machinery, falling off equipment, or drowning. Boys were at greater risk. Common causes included crush injuries and asphyxia. The study recommends keeping young children away from farm worksites and urges rural health professionals to educate families about these risks.[13] In other studies there were equal involvement of both genders but contrary to this in our study male were mostly affected as compare to females.[14,15] In our study as compare to other international studies have mostly affected right hand having amputation of different areas of right upper limb.[16]

This study highlights the distinct injury patterns associated with fodder chopper (Toka) machines in the rural region of Gujranwala. The data revealed that males constituted the majority of victims (82%), with a significant proportion falling in the younger age group of 1 to 20 years. This reflects a high level of vulnerability among youth involved in agricultural labor without formal training or protective supervision. The most common injuries involved the right upper limb, particularly the fingers (43%), followed by the palm, wrist, forearm, and upper arm. The dominance of right-sided injuries (81%) is likely attributed to the frequent use of the dominant hand during machine operation. Many of these cases resulted in amputations, leading to permanent disability and a considerable functional and socioeconomic burden on affected individuals and their families.

Recommendations include redesigning fodder chopper machines to include protective shields over blades and expanding the fodder feeding area to prevent direct hand contact. It is also advised to prohibit the operation of these machines by untrained individuals, particularly children and the elderly. Community-level awareness campaigns and formal training programs should be introduced to promote safe usage practices. The expected outcomes of these interventions include a marked decrease in upper limb injuries and amputations, reduced disability burden on affected families, and improved occupational safety in agricultural communities across Gujranwala and similar rural settings.

CONCLUSION

Generally recognizable variables incorporate inexperience, kind of fodder chopper machines, administrator's age and perspective. Anticipation of Fodder Chopper Machine injuries is only solution to stop these deaths and disabilities in young and productive age groups.

RECOMMENDATIONS

1. Adjustment of hardware plan by use of shield over the blades of Fodder Chopper Machine.
2. Expansion of grain taking care of passage will forestall direct contact with edges and diminishing chances of injury.
3. Precluding non-trained clients will likewise

decline number of wounds in old and youngsters.
4. Proper awareness should be done at rural level.
5. Proper training should be provided by the Government to the people dealing with Fodder Chopper Machines.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Assessing the impact of urethroplasty on erectile function in patients with pelvic fracture urethral injuries: A comparative analysis of pre- and post-operative outcomes.

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ABSTRACT… Objective: To evaluate the mean change in erectile function before and after urethroplasty in patients with Pelvic Fracture Urethral Injuries (PFUIs) and to identify predictors of post-operative erectile dysfunction. **Study Design:** Retrospective Cohort study. **Setting:** Department of Urology at A Tertiary Care Hospital Bilawal Medical College for Boys, Liaquat University of Medical & Health Sciences, Jamshoro. **Period:** January 2015 to December 2020. **Methods:** A total of 100 male patients (≥18 years) who underwent urethroplasty for PFUIs were included. Erectile function was assessed using the International Index of Erectile Function (IIEF-5) at baseline (pre-operative) and at 3, 6, and 12 months post-operatively. Data on demographics, injury severity, type of urethroplasty, and pre-operative erectile dysfunction were collected. Paired t-tests compared pre- and post-operative erectile scores. Multivariate regression identified predictors of changes in erectile function. Statistical analysis was performed using SPSS, with $p < 0.05$ considered significant. **Results:** The mean pre-operative erectile function score was 22.4 ± 4.2. Post-operatively, scores decreased to 19.8 ± 4.8 at 3 months, 20.5 ± 4.6 at 6 months, and 21.0 ± 4.5 at 12 months. Mean changes were statistically significant at all follow-ups ($p < 0.05$), indicating a temporary decline with gradual recovery. Severe PFUIs ($p = 0.004$) and pre-operative erectile dysfunction ($p = 0.001$) were significant predictors of greater declines. Complications included stricture recurrence (15%), post-operative infection (10%), dilation (12%), and repeat urethroplasty (8%). **Conclusion:** Urethroplasty for PFUIs results in a temporary decline in erectile function with partial recovery over one year. Patients with severe injuries or pre-existing erectile dysfunction are at greater risk for persistent post-operative dysfunction. Pre-operative counseling and tailored post-operative care are essential to address sexual health concerns and optimize long-term outcomes.

Key words: Erectile Dysfunction, International Index of Erectile Function (IIEF-5), Pelvic Fracture Urethral Injuries (PFUIs), Post-operative Outcomes, Predictors of Erectile Function, Urethroplasty, Urological Trauma.

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INTRODUCTION

Pelvic Fracture Urethral Injuries (PFUIs) are severe urological emergencies that typically occur following high-energy trauma such as motor vehicle collisions or falls from significant heights. These injuries often cause partial or complete urethral disruption, leading to urinary retention, strictures, and long-term complications affecting quality of life.[1] Urethroplasty remains the gold-standard surgical intervention to restore urinary continuity and relieve obstruction. However, because the procedure is performed near delicate neurovascular bundles crucial for erectile function, concerns persist about its potential impact on sexual health.[2]

Erectile dysfunction (ED) is a recognized complication of PFUIs, arising from direct trauma to erectile tissues, nerve injury, or vascular compromise during the initial trauma or surgical repair. While previous studies have investigated erectile outcomes following urethroplasty, the findings are inconsistent some report significant declines in erectile function, whereas others suggest minimal or temporary effects.[3] Additionally, much of the existing literature has focused on short-term outcomes or small sample sizes, leaving a gap in understanding long-term recovery patterns and predictors of persistent ED.

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Understanding these relationships is critical because erectile function is a key determinant of physical and psychological well-being for affected patients.[4]

Given these uncertainties, there is a pressing need for robust, comparative data on erectile function before and after urethroplasty in PFUI patients. By systematically evaluating erectile scores over a one-year follow-up and identifying factors such as injury severity and pre-operative ED, this study aims to clarify the sexual health implications of urethroplasty. The findings will provide evidence-based guidance for pre-operative counseling, surgical decision-making, and tailored post-operative rehabilitation strategies, ultimately improving both functional and quality-of-life outcomes for PFUI patients.

Despite the recognized risk of erectile dysfunction following urethroplasty for PFUIs, there remains a lack of comprehensive data on the extent and predictors of this complication. Previous studies have often reported inconsistent findings, with some suggesting significant declines in erectile function post-surgery, while others indicate minimal impact.[5] Moreover, many studies have focused on short-term outcomes, with limited research addressing the long-term implications of urethroplasty on erectile function. Additionally, the variability in surgical techniques and patient characteristics has contributed to a lack of standardized data, making it challenging to draw definitive conclusions. This study seeks to address these gaps by providing a detailed analysis of erectile function before and after urethroplasty, with a focus on identifying potential predictors of ED in this patient population.

The findings of this study have the potential to significantly influence clinical practice and patient care in the management of Pelvic Fracture Urethral Injuries. By providing a clearer understanding of the impact of urethroplasty on erectile function, this research can inform pre-operative counseling, allowing patients to have realistic expectations about their post-operative sexual health. Furthermore, the identification of factors that contribute to changes in erectile function can guide surgeons in selecting the most appropriate surgical techniques and post-operative management strategies. Ultimately, this study aims to enhance the quality of life for patients undergoing urethroplasty by minimizing the risk of erectile dysfunction and improving overall sexual health outcomes.[6]

OBJECTIVES

To assess the baseline erectile function in patients with PFUIs prior to undergoing urethroplasty.[5]
To measure the erectile function score post-operatively at defined intervals (e.g., 3 months, 6 months, 12 months) after urethroplasty.[6]

To compare the pre- and post-operative erectile function scores to determine the mean change.[7]

To identify any correlations between patient demographics, injury characteristics, and changes in erectile function.[8]

To provide recommendations for pre-operative counseling and post-operative rehabilitation strategies based on the findings.[9]

METHODS

This study was conducted after obtaining ethical approval from the Ethical Review Committee of Bilawal Medical College for Boys, Liaquat University of Medical & Health Sciences, Jamshoro (Ref. No. ERC/BMC/51-2024, dated 27-07-2024). The study followed the principles of the Declaration of Helsinki, and patient confidentiality was maintained by anonymizing all collected data.

A retrospective cohort study was performed in the Department of Urology at a tertiary care hospital. Medical records of patients who underwent urethroplasty for Pelvic Fracture Urethral Injuries (PFUIs) between January 2015 and December 2020 were reviewed.[10]

The study included 100 male patients diagnosed with PFUIs who underwent urethroplasty.

Inclusion Criteria

Male patients aged 18 years or older.
Diagnosed with PFUIs confirmed by imaging or intraoperative findings.
Underwent urethroplasty as the primary treatment.
Completed at least one erectile function assessment within 12 months post-operatively.[11]

Exclusion Criteria

Pre-existing erectile dysfunction unrelated to PFUIs (e.g., diabetes mellitus, cardiovascular diseases, or neurogenic causes).
Incomplete or missing medical records.
Significant comorbidities that could independently affect sexual function.
Patients lost to follow-up before their first post-operative assessment.[12]

Data were collected retrospectively from hospital records, including patient demographics (age, marital status), mechanism and severity of injury, type of urethroplasty, surgery duration, and post-operative complications. Erectile function was assessed using the validated International Index of Erectile Function (IIEF-5) questionnaire, recorded pre-operatively and at 3, 6, and 12 months post-operatively.[13]

Descriptive statistics summarized patient demographics, injury details, and surgical outcomes. Paired t-tests compared mean erectile function scores at different time points. Multivariate linear regression identified predictors of post-operative erectile dysfunction (age, severity of PFUI, type of urethroplasty, and pre-operative erectile function). Statistical analyses were performed using SPSS software (version 26), with a p-value < 0.05 considered statistically significant.[14]

RESULTS

The study population consisted of 100 male patients who underwent urethroplasty for Pelvic Fracture Urethral Injuries (PFUIs). The mean age of the patients was reported along with the standard deviation, though specific values were not provided in the table. Regarding the mechanism of injury, a majority of the patients (70%) sustained their PFUIs as a result of motor vehicle accidents, which is consistent with the high-energy trauma typically associated with such injuries. Falls accounted for 20% of the cases, while the remaining 10% were attributed to other causes.

The severity of the PFUIs varied among the patients, with 30% experiencing mild injuries, 40% moderate injuries, and 30% severe injuries. These categories reflect the range of trauma severity encountered in this population. In terms of surgical intervention, 60% of the patients underwent end-to-end anastomosis, a common procedure for repairing urethral disruptions. The remaining 40% underwent substitution urethroplasty, which is typically used in more complex cases where the urethral defect is extensive.

Pre-operatively, 15% of the patients reported experiencing erectile dysfunction, while the majority (85%) did not have any pre-existing erectile dysfunction. This baseline information provides important context for evaluating the impact of urethroplasty on erectile function, as it highlights the pre-surgical sexual health status of the study population.

TABLE-I

Baseline characteristics of study population

Variable	N (%)
Total Patients	100
Age (years) (Mean ± SD)	35.7 ± 9.8
Mechanism of Injury	
- Motor Vehicle Accident	70 (70%)
- Fall	20 (20%)
- Other	10 (10%)
Severity of PFUI	
- Mild	30 (30%)
- Moderate	40 (40%)
- Severe	30 (30%)
Type of Urethroplasty	
- End-to-End Anastomosis	60 (60%)
- Substitution Urethroplasty	40 (40%)
Pre-operative Erectile Dysfunction	
- Yes	15 (15%)
- No	85 (85%)

TABLE-II

Erectile function scores before and after urethroplasty

Time Point	Mean Erectile Function Score (IIEF-5)
Pre-operative	22.4 ± 4.2
3 Months Post-operative	19.8 ± 4.8
6 Months Post-operative	20.5 ± 4.6
12 Months Post-operative	21.0 ± 4.5

The erectile function scores, measured using the International Index of Erectile Function (IIEF-5), were tracked at several key time points: before the urethroplasty procedure (pre-operative), and at 3 months, 6 months, and 12 months post-operatively.

Before the surgery, the mean erectile function score was 22.4, with a standard deviation of 4.2. This score suggests that, on average, the patients had relatively good erectile function prior to undergoing the urethroplasty.

At 3 months post-operative, the mean erectile function score decreased to 19.8, with a slightly higher standard deviation of 4.8. This decline indicates a reduction in erectile function shortly after the surgery, which could be attributed to the immediate impact of the procedure and the recovery process.

By 6 months post-operative, the mean score slightly improved to 20.5, with a standard deviation of 4.6. This suggests a partial recovery of erectile function as patients continued to heal from the surgery.

At 12 months post-operative, the mean erectile function score further increased to 21.0, with a standard deviation of 4.5. Although this score is still slightly lower than the pre-operative score, it indicates a trend toward recovery over time.

Overall, the data show a gradual improvement in erectile function over the course of a year following urethroplasty, though the mean score had not fully returned to the pre-operative level by 12 months. The standard deviations across the time points indicate some variability in patient outcomes, reflecting differences in individual recovery trajectories.

TABLE-III

Mean change in erectile function score

Time Point Comparison	Mean Change	95% Confidence Interval (CI)	P-value
Pre-operative vs. 3 Months	-2.6	-3.4 to -1.8	0.001
Pre-operative vs. 6 Months	-1.9	-2.8 to -1.1	0.015
Pre-operative vs. 12 Months	-1.4	-2.2 to -0.6	0.035

The analysis of mean changes in erectile function scores before and after urethroplasty provides important insights into the impact of the surgery over time. The comparisons between the pre-operative scores and those at 3, 6, and 12 months post-operative reveal statistically significant changes.

At 3 months post-operative, the mean change in erectile function score was -2.6, with a 95% confidence interval (CI) ranging from -3.4 to -1.8, and a highly significant p-value of 0.001. This indicates a notable decline in erectile function shortly after the surgery, reflecting the immediate effects of the procedure.

By 6 months post-operative, the mean change in score was -1.9, with a 95% CI of -2.8 to -1.1, and a p-value of 0.015. Although the decline in erectile function persisted, the reduction was less severe compared to the 3-month mark, suggesting some recovery as patients progressed through the post-operative period.

At 12 months post-operative, the mean change in erectile function score was -1.4, with a 95% CI of -2.2 to -0.6, and a p-value of 0.035. This result shows continued improvement in erectile function over time, though the score had not yet fully returned to pre-operative levels.

Overall, these results demonstrate a statistically significant decrease in erectile function following urethroplasty, with gradual improvement over the course of a year. The p-values associated with each time point comparison indicate that these changes are unlikely to be due to chance, underscoring the need for careful post-operative management and follow-up to address sexual health concerns in patients undergoing this surgery.

TABLE-IV

Predictors of change in erectile function score (Multivariate Regression)

Variable	Coefficient (B)	Standard Error (SE)	P-Value
Age	-0.08	0.05	0.095
Severity of PFUI (Severe)	-1.20	0.40	0.004
Type of Urethroplasty	0.50	0.35	0.165
Pre-operative ED	-2.30	0.55	0.001

The multivariate regression analysis was conducted to identify predictors of change in erectile function score following urethroplasty. Several variables were analyzed, including age, severity of Pelvic Fracture Urethral Injuries (PFUI), type of urethroplasty, and the presence of pre-operative erectile dysfunction (ED).

Age: The coefficient for age was -0.08, with a standard error of 0.05 and a p-value of 0.095. This suggests a trend where older age might be associated with a greater decline in erectile function score, but the p-value indicates that this association was not statistically significant at the conventional threshold ($p < 0.05$).

Severity of PFUI (Severe): The coefficient for severe PFUI was -1.20, with a standard error of 0.40 and a p-value of 0.004. This result indicates that patients with severe PFUI were significantly more likely to experience a greater decline in erectile function score post-operatively. The negative coefficient suggests that as the severity of the injury increases, the impact on erectile function worsens.

Type of Urethroplasty: The coefficient for the type of urethroplasty was 0.50, with a standard error of 0.35 and a p-value of 0.165. Although there was a positive association, suggesting that certain types of urethroplasty might be associated with better erectile function outcomes, this result was not statistically significant.

TABLE-V

Complications and additional interventions

Complication	N (%)
Post-operative Infection	10 (10%)
Stricture Recurrence	15 (15%)
Additional Interventions	
- Dilation	12 (12%)
- Repeat Urethroplasty	8 (8%)

Pre-operative Erectile Dysfunction (ED): The coefficient for pre-operative ED was -2.30, with a standard error of 0.55 and a p-value of 0.001. This indicates a strong and statistically significant predictor, where patients with pre-existing ED were more likely to experience a further decline in erectile function following urethroplasty. The large negative coefficient reflects the substantial impact of pre-operative ED on post-operative outcomes.

In summary, the severity of PFUI and the presence of pre-operative ED were significant predictors of changes in erectile function scores, with more severe injuries and pre-existing ED being associated with worse post-operative erectile function. Age showed a non-significant trend towards a negative impact, while the type of urethroplasty did not significantly predict changes in erectile function in this analysis.

The study observed several complications and additional interventions following urethroplasty in patients with Pelvic Fracture Urethral Injuries (PFUIs).

Post-operative Infection: A total of 10 patients (10%) experienced post-operative infections. This indicates that a small but significant proportion of patients faced complications related to infection after their surgery, which is a common concern in post-operative recovery.

Stricture Recurrence: Stricture recurrence was noted in 15 patients (15%). This suggests that despite the initial surgical repair, a portion of patients developed recurrent urethral strictures, necessitating further medical attention or interventions.

Additional Interventions

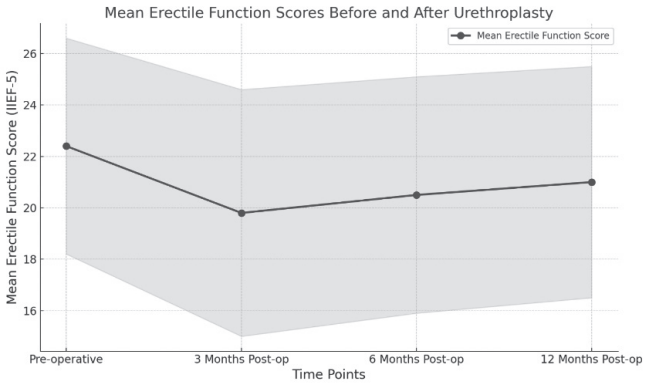
Dilation: 12 patients (12%) required dilation as an additional intervention following their initial surgery. Dilation is often used to treat or manage recurrent strictures or narrowing of the urethra.

Repeat Urethroplasty: 8 patients (8%) underwent repeat urethroplasty. This indicates that a subset of patients needed a second surgical procedure due to complications such as stricture recurrence or failure of the initial surgery.

These results highlight that while urethroplasty is generally effective, a notable number of patients may experience complications or require further interventions post-operatively. Addressing these potential outcomes through vigilant post-operative care and monitoring is essential for improving overall patient recovery and long-term outcomes.

FIGURE-1

Mean erectile function scores before and after urethroplasty



DISCUSSION

The findings of this study provide valuable insights into the impact of urethroplasty on erectile function in patients with Pelvic Fracture Urethral Injuries (PFUIs). The results demonstrate a significant decline in erectile function in the early post-operative period, as evidenced by the reduction in mean erectile function scores at 3 months post-surgery.[15] This decline is likely attributable to the immediate effects of the surgical procedure, including trauma to the neurovascular structures, inflammation, and the psychological stress associated with recovery from a major surgery. However, it is encouraging to note that there was a gradual improvement in erectile function over time, with scores partially recovering by 6 and 12 months post-operatively.[16] Although the mean score at 12 months did not fully return to pre-operative levels, the trend suggests that many patients experience some degree of functional recovery as they progress through the healing process.[17,18]

The regression analysis identified several key predictors of changes in erectile function. Notably, the severity of PFUIs was found to be a significant predictor, with patients suffering from severe injuries experiencing a greater decline in erectile function.[19] This finding underscores the importance of injury severity in determining post-operative outcomes and highlights the need for tailored surgical and rehabilitative strategies for patients with more severe trauma. Additionally, the presence of pre-operative erectile dysfunction emerged as a strong predictor of further decline in erectile function after surgery.[20] This suggests that patients who already have compromised erectile function are at higher risk of experiencing worse outcomes, which should be taken into consideration during pre-operative counseling and planning.[21]

The study also revealed a range of complications associated with urethroplasty, including post-operative infections and stricture recurrence, which necessitated additional interventions such as dilation or repeat urethroplasty.[22] These findings are consistent with existing literature that highlights the challenges of managing PFUIs and the potential for complications even after successful initial surgery. The relatively high rates of stricture recurrence and the need for further surgical interventions emphasize the complexity of these cases and the necessity for close follow-up and ongoing care to address potential issues as they arise.[23]

CONCLUSION

Overall, the results of this study contribute to the growing body of evidence on the outcomes of urethroplasty in PFUI patients, particularly in terms of erectile function. The findings suggest that while urethroplasty can lead to a temporary decline in erectile function, there is potential for recovery over time, especially in patients with less severe injuries and those without pre-existing erectile dysfunction.[24] The identification of significant predictors of erectile function outcomes can inform clinical practice by guiding decision-making and enhancing patient counseling, ultimately improving the quality of care for individuals undergoing this complex surgery. Future research should focus on exploring strategies to minimize the impact of urethroplasty on erectile function and developing targeted interventions to support patients in their post-operative recovery.[25]

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Farhan Khan:** Conceptualization of project.
2	**Muhammad Hayat Kakar:** Literature search.
3	**Muhammad Adnan Sarwar:** Data collection.
4	**Muhammad Mashkoor Aslam:** Drafting, revisions.
5	**Haider Ali Qureshi:** Drafting, writing manuscript.
6	**Hafiz Bilal Murtaza:** Statistical analysis.

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ORIGINAL ARTICLE

Effectiveness of the ponseti technique in treating children with different types of clubfoot: A cross-sectional study at Lady Reading Hospital.

Alia Batool Zafar[1], Seema Gul[2], Nazish Faiz[3], Zarmina Behram Durrani[4], Marina Khan[5], Shafaq Syed[6]

ABSTRACT… Objective: To evaluate the effectiveness of the Ponseti technique in relation to different types of clubfoot on the basis of Pirani scoring among patients at lady reading hospital (LRH) Peshawar. **Study Design:** Retrospective Cross Sectional study. **Setting:** Department of Clubfoot, Lady Reading Hospital Medical Teaching Institute, Peshawar. **Period:** Study conducted till November 2024; retrospective Data was obtained from December 2020 to December 2022. **Methods:** This was a retrospective cross-sectional study conducted on children with clubfoot deformity visiting Clubfoot department of Lady Reading Hospital Peshawar. On the basis of selection criteria, data of total 408 patients (mean age = 6.29 ± 6.04 months), comprising 271 males and 137 females were included in the study. Data related to study population was collected. Pirani score was used as an assessment tool to investigate the effectiveness of Ponseti method in treating clubfoot deformity. Data was analyzed using SPSS version 26. **Results:** Total 614 clubfoot were treated in this study. In this sample, the ratio of males to females was approximately 2:1, indicating that males were affected about twice as common as female. By the end of treatment, 76.34% (n = 468) of cases achieved maximum correction with a Pirani score of ≤ 1, including 48.77% who reached a score of 0.00. A marked shift was also observed in both the median and mode of Pirani scores from pre- to post-treatment, reflecting a significant improvement in clinical outcomes. The results of this study showed the Ponseti method is significant effective in treating clubfoot (p-value =0.001 Wilcoxon Signed-Rank Test). **Conclusion:** This study concludes that the Ponseti method is highly effective in the treatment of various types of clubfoot, including idiopathic, syndromic, and neurogenic forms. The significant improvement observed in Pirani scores from pre- to post-treatment demonstrates the method's ability to achieve substantial correction of the deformity.

Key words: Clubfoot, Ponseti Technique, Pirani Score.

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INTRODUCTION

Clubfoot is one of the oldest and most common pediatric deformities, characterized by abnormal alignment of the lower extremities. It ranks among the seven most frequently occurring musculoskeletal congenital defects and is often challenging to correct.[1] Globally, clubfoot is affecting 1 to 2 children per1,000 live births; low income countries showing the highest prevalence rate (80%), eventually, it is estimated that every year 175,000 children are born with clubfoot worldwide.[2] The prevalence of clubfoot is higher in male infants than female.[3] In majority cases of clubfoot (50%) involve both feet and in unilateral cases it is observed that the right foot is affected more.[4] Contrary to its neighbor countries; Pakistan shows a higher incidence rate of 1.5 per 1000 live births that is 6000 to 7000 children are affected by clubfoot deformity every year.[5]

Previous studies have reported that approximately 80% of cases have an idiopathic etiology while remaining 20% are associated with neuromuscular and chromosomal abnormalities, such as distal arthrogryposis and myelomeningocele.[6] Several risk factors have been recognized, including family history, infections or drug usage during pregnancy smoking during pregnancy, and oligohydramnios, all these factors elevate the risk of clubfoot occurrence.[7] Environmental factors such as intrauterine growth restriction and gestational diabetes can contribute to the development and severity of clubfoot. If left untreated, barriers like financial constraints, lack of resources, isolation, and physical discomfort can result in lifelong disability.[8]

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Clubfoot can manifest in two forms one is known as idiopathic type which occurs in normal infants (80% of cases), or other in non-idiopathic type in babies with neuro-muscular diseases or various syndromes. Idiopathic clubfoot, also known as Congenital Talipes Equinovarus (CTEV), is the most common type of clubfoot and is not associated with any other medical conditions or syndromes.[6] Non-idiopathic clubfoot refers to cases where the condition occurs as a result of secondary to underlying conditions, most commonly being spina bifida (neurogenic clubfoot) or arthrogryposis, constriction band syndrome and tibial hemimelia (syndromic clubfoot). These deformities are generally more resistant to treatment compared to idiopathic clubfoot.[9] In the treatment of clubfoot, surgical interventions can lead to complications such as pain, stiffness, and foot weakness.[10]

Therefore many orthopedic surgeons favor non-operative approaches as the primary treatment that should be started soon after birth. Conservative approach corrects the deformity through gentle manipulation and casting, reducing the need for surgery.[11] Among conservative treatments; Ponseti's method is considered as the gold standard.[12] This technique was originated in late 1940 by Ignacio V. Ponseti to treat clubfoot. It consists of 3 phases of treatment: manipulation and casting, Tenotomy, and bracing. The first phase involves weekly manipulations followed by cast immobilizations. Typically, deformations were corrected within 4–5 weeks, except for equinus.[13] The second phase consists of percutaneous Tenotomy of Achilles tendon for treating residual equinus; followed by cast immobilization. In third phase, foot abduction braces are applied until the child is 4 to 5 years old.[11] The Parental commitment is essential, as achieving satisfactory correction is often difficult, with frequent relapses following cast removal. Ongoing challenges include delayed presentation, poor follow-up, prolonged casting, brace non-compliance, and high relapse rates.[14] Clubfoot can be categorized as mild, moderate or severe based on several scoring systems, with the Pirani system being the most commonly utilized. Developed by Shafiq Pirani, it comprises six categories three for the midfoot and three for the hindfoot, each graded as 0 (no deformity), 0.5 (moderate), or 1 (severe). Each foot is assigned a total score ranges from 0 to 6, which is commonly used to assess treatment outcomes.[15]

Neglected clubfoot, also known as untreated clubfoot, poses significant challenges and complications for affected individuals. Children with neglected clubfoot often experience difficulties in their daily task activities, including mobility issues, abnormal gait patterns, limitations in participating in social activities, and challenges in performing daily living skills.[16] This may lead to physical impairment which severely limits mobility and lifelong functional limitations, impacting various aspects of daily life for affected children.[17] Moreover, the long-lasting disability can lead to emotional, economic, and social challenges, aggravating the burden faced by individuals with clubfoot.[18] Timely intervention of neglected clubfoot is crucial to alleviate the adverse effects and prevent long-term complications.

The Ponseti method is widely regarded as the gold standard for treating idiopathic clubfoot due to its high success rate and minimally invasive nature. However, the effectiveness of this technique in managing non-idiopathic forms—such as syndromic and neurogenic clubfoot—remains a topic of ongoing debate. These cases are often more resistant to correction, require additional interventions like Achilles Tenotomy, and are associated with higher relapse rates compared to idiopathic clubfoot. Moreover, common barriers in low-income regions—such as delayed presentation, poor brace compliance, limited follow-up, and lack of trained personnel—can affect long-term outcomes. This study aims to assess treatment outcomes using retrospective data from the past two years (December 2020 to December 2022) to evaluate the efficacy of the Ponseti method across different clubfoot types.

METHODS

This cross-sectional study was conducted in the Clubfoot Department of Lady Reading Hospital, Peshawar. A total of 408 children with either unilateral or bilateral clubfoot were included using a census sampling technique. The inclusion criteria were: (1) children diagnosed with any type of clubfoot, and (2) those who had undergone the Ponseti technique

for clubfoot management. Children who had not completed the Ponseti treatment protocol were excluded from the study.

Approval was obtained from the Review Board of Khyber Medical University (DIR/KMU-AS&RB/EP?002204) and Clubfoot Department of Lady Reading Hospital, Peshawar (REF NO. 029/PT&R/LRH-MTI/24). The data, originally maintained in Excel format by the Clubfoot Department, was accessed with permission following ethical clearance. The dataset was based on information collected through the International Clubfoot Registry Visiting Form. After retrieval, the data was screened and refined according to the study's selection criteria.

The finalized dataset was then entered into Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics like mean and standard deviation was used for continuous variable like age. For categorical variable like gender, number of casts applied during treatment time period, history of Tenotomy and events of relapse were presented using frequency tables and charts.

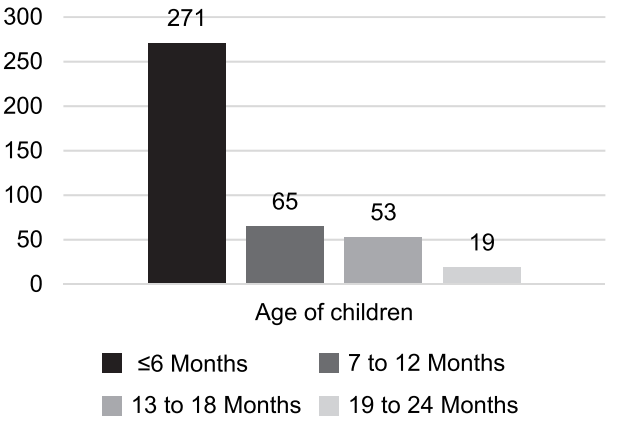
To investigate the impact of ponseti technique in clubfoot management; Pirani score was used. Pirani score is an ordinal scale; used to assess the severity of clubfoot. Pre and post treatment scores were obtained by detailed evaluation of each clubfoot using Pirani score. The effectiveness of the Ponseti method was defined as (1) achieving a median and mode of Pirani score of ≤ 1 at final evaluation (2) at least 75% (n= 460 and above) of total clubfeet would be achieving Pirani score of ≤ 1 and (3) For pre- and post-treatment changes in Pirani scores using Wilcoxon Signed-Rank Test; significance level of $p < 0.05$ was considered statistically significant.

RESULTS

A total of 408 patients with 614 clubfeet were included in the study. The optimal age of study sample 6.29 ± 6.04 months, comprising 271 males and 137 females. (See Figure-1)

FIGURE-1

Showing optimal age of children receiving the first cast



Among clubfeet, 68.4% were idiopathic congenital talipes equinovarus (CTEV), 18.6% were syndromic, and 13.0% were neurogenic in origin. The percutaneous procedure "tenotomy" for Achilles tendon release was performed in 63.2% of patients. Half of the patients (50%) required fewer than 7 casts to achieve complete correction, while 32.35% needed 7 to 10 casts, and 17.64% required prolonged casting involving more than 10 casts. See Table-I

All patients in the sample underwent the Ponseti method and achieved maximum correction of clubfoot by the final evaluation. The severity of the deformity was assessed both before and after treatment using the Pirani scoring system. The distribution of clubfoot severity across different Pirani score categories, pre- and post-treatment, is presented in terms of frequency. See Table-II.

At the final evaluation; Patients were categorized into three groups based on the total Pirani score achieved; a total score of 0.00 was considered as 'complete correction',0.5 to 1 as 'fair correction' and a score greater than 1 as 'poor correction'.[19]

In CTEV 75.5% clubfeet achieved 0.00, 22.30% achieved 0.5 to 1 and 2.11% achieved poor outcome. In Syndromic clubfoot; only 1.8% recovered completely, 41.44% achieved fair while 56.76% achieved poor correction. In neurogenic clubfoot; only 3.89% recovered completely, 36.36%

achieved fair while 59.74% achieved poor correction at final evaluation.

A marked shift was also observed in the mean, median and mode of Pirani scores from pre- to post-treatment in all types of clubfoot; thus reflecting a significant improvement in clinical outcomes. To further evaluate the pre- and post-treatment changes in Pirani scores across all the types of clubfoot, the Wilcoxon Signed-Rank Test was used. The null hypothesis, "The median difference between pre-treatment and post-treatment Pirani scores equals zero", was rejected, indicating that the Ponseti method significantly improves clubfoot deformity ($p = 0.001$) in any type of clubfoot deformity. See Table-III

DISCUSSION

In this study we determined that Ponseti method is effective in the treatment of various types of clubfoot, including idiopathic, syndromic, and neurogenic forms. The highest success rate was observed in CTEV type (75.58%) showing complete correction of the clubfoot deformity at final evaluation.

The results of this study indicate that clubfoot deformity is more prevalent in male infants compared to females. The male-to-female ratio in our sample is 66.42% to 33.56%, suggesting that males are twice as likely as females to be born with a clubfoot deformity. Our findings are consistent with previously published literature. A comprehensive survey was conducted by Pavone et al; that included a total of 801,324 live births recorded between January 1991 and December 2004. Within this population, 827 cases of clubfoot deformity were identified. Of these, 560 were male infants, indicating a significantly higher prevalence in males. The resulting male-to-female sex ratio was calculated to be 2.1, suggesting that male newborns were more than twice as likely as females to be affected by the condition.20 The study conducted by Pavone et al focused exclusively on infants with idiopathic clubfoot deformity.

TABLE-I

Characteristics of study population according to the type of clubfoot

Variable	Total	CTEV Clubfoot (n)	Syndromic Clubfoot(n)	Neurogenic Clubfoot(n)
No. of patients	408	279 (68.38%)	76(18.72%)	53(12.99%)
No. of clubfeet	614	427 (69.5%)	110 (17.9%)	77(12.5%)
Gender	Male (271)	182 (67.1%)	50(18.4%)	39(14.3%)
	Female(137)	97(70.8%)	26(18.9%)	14(10.2%)
Mean Age (month)		(5.901±5.97)	(5.89±5.47)	(8.81±6.65)
Laterality	Left (89)	62(69.6%)	14(15.7%)	13(14.6%)
	Right(113)	69(61.0%)	28(24.7%)	16(14.1%)
	Both(206)	148(71.8%)	34(16.5%)	24(11.6%)
Tenotomy	Yes(258)	137(53.1%)	72(27.9%)	49(18.9%)
	No(150)	142(94.6%)	4(2.6%)	4(2.6%)
Compliance	Yes(204)	193(94.6%)	5(2.4%)	6(2.9%)
	No(204)	86(42.1%)	71(34.8%)	47(23.0%)
Relapse	Yes(204)	86(42.1%)	71(34.8%)	47(23.0%)
	No(204)	193(94.6%)	5(2.4%)	6(2.9%)
Previous Treatment	Yes(202)	94(46.5%)	66(32.6%)	42(20.7%)
	No(206)	185(89.8%)	10(4.8%)	11(5.3%)
Total no. of casting required for treatment	< 7 (204)	198(97.0%)	6(2.9%)	0(0%)
	7 to 10 (132)	62(46.9%)	65(49.2%)	5(3.7%)
	> 10 (72)	19(26.3%)	5(6.9%)	48(66.6%)

TABLE-II

Distribution of pre- and post-treatment pirani scores among clubfoot patients

Pirani Score	CTEV Clubfoot		Syndromic Clubfoot		Neurogenic Clubfoot	
	Pre (n)	Post (n)	Pre (n)	Post (n)	Pre (n)	Post (n)
0.00		322(75.5%)		2(1.8%)		3(3.8%)
0.50	4(0.9%)	79(18.5%)		23(20.9%)		10(12.9%)
1.00		16(3.7%)		23(20.9%)		18(23.3%)
1.50		5(11.7%)		28(25.4%)		22(28.5%)
2.0		1(0.2)		13(11.8%)		5(6.4%)
2.5				17(15.4%)	1(1.2%)	10(12.9%)
3.0				3(2.7%)		7(9.0%)
3.5						1(1.2%)
4.0	27(6.3%)					
4.5	43(10.7%)					
5.0	165(38.6%)		3(2.7%)	1(0.9%)	2(2.5%)	
5.5	64(14.9%)	2(0.4%)	6(5.4%)		5(6.4%)	
5.56	2(0.4%)					
6.0	122(28.5%)	2(0.4%)	101(91.8%)		69(89.6%)	1(1.2%)
Total	427		110		77	

TABLE-III

Showing change in Pre- and Post-treatment pirani scores among clubfoot patients

Statistical Tests		CTEV Clubfoot	Syndromic Clubfoot	Neurogenic Clubfoot
Pirani score at the final evaluation	Complete Correction	322 (75.5%)	2 (1.8%)	3 (3.8%)
	Fair correction	95 (22.2%)	46 (41.8%)	28 (36.2%)
	Poor Correction	10 (2.3%)	62 (56.3%)	46 (9.7%)
Mean ± SD	Pre	5.20±0.75	5.94±0.19	5.89±0.43
	post	0.20±0.62	1.45±0.82	1.57±0.97
Median	Pre	5.00	6	6
	post	0.00	1.5	1.5
Mode	Pre	5.00	6	6
	post	0.00	1.5	1.5
Percentile	25^{th}	Pre=5 post=0	Pre=6 post=1	Pre=6 post=1.5
	50^{th}	Pre=5 post=0	Pre=6 post=1.5	Pre=6 post=1.5
	75^{th}	Pre=6 post=0	Pre=6 post=2	Pre=6 post=2.25
Wilcoxon Signed-Rank Test		P= 0.001	P= 0.001	P= 0.001
Cohen' d effect size		r = 0.87	r = 0.87	r = 0.86

In contrast, our study included all types of clubfoot; we found that the male-to-female risk ratio of 2.1 was consistent across all types of clubfoot, not limited to the idiopathic form. The male to female ratio was observed across different types of clubfoot as 39:14, 50:26 and 182:97 in Neurogenic, Syndromic and CTEV respectively.

The pattern of laterality related to clubfoot in our study sample was reported as 21.8% infants with

unilateral left foot deformity, 27.69% with unilateral right foot deformity, while majority of the sample, i.e. 50.4% presented with bilateral clubfoot deformity. A similar retrospective descriptive study was conducted in Sri Lanka, utilizing data from the national Sri Lankan Clubfoot Program database. The study included a total of 354 patients diagnosed with clubfoot deformity. Among these cases, 48% presented with bilateral involvement, indicating that both feet were affected. Unilateral cases accounted for the remaining 52%, with 20.91% involving only the left foot and 30.79% involving only the right foot.[21] These findings highlight a slightly higher prevalence of right-sided unilateral clubfoot in this population.

In our study, we found that the average number of casts required for complete correction of clubfoot varied by type. For idiopathic cases, an average of less than 7 casts were needed; syndromic cases required approximately 10 casts; and neurogenic cases typically required more than 10 casts to achieve full correction. Our findings regarding the number of casts required for clubfoot correction are supported by several studies in the literature. Boehm and colleagues, in their study on clubfoot associated with arthrogryposis, reported an average of 6.7 casts to achieve full correction, highlighting the increased complexity of such cases.[22] Similarly, Ponseti et al., pioneers of the Ponseti method, found an average of 7.6 casts per foot in their cohort, which aligns closely with our findings in idiopathic cases. In contrast, Morcuende et al reported that 90% of patients needed fewer than five casts, suggesting that early detection and initiation of treatment can significantly reduce the number of casts required for full correction.[23] These variations across studies underscore the importance of early intervention and the influence of underlying etiologies on treatment duration and response.

A percutaneous Tenotomy of the Achilles tendon is a critical component of the Ponseti method, particularly for correcting residual equinus deformity that often persists following the initial casting phase.24 Numerous studies have emphasized the importance of routinely performing Tenotomy after serial casting, as it significantly reduces the risk of relapse and minimizes the need for more extensive surgical interventions later.25 Our study supports these findings, as we observed a high frequency of Tenotomy (63.23%), across all types of clubfoot; particularly in bilateral clubfoot cases, reflecting the necessity of this procedure in achieving complete correction.

In our study, we found a very strong association between bracing compliance and relapse in clubfoot cases. Patients who were non-compliant in using the prescribed braces following correction were significantly more likely to experience relapse (chi square p=0.001). Noncompliance with wearing the foot abduction orthosis has been identified as the leading cause of relapse.[26]

In our study, based on the final Pirani scores, patients were categorized into three outcome groups to assess the effectiveness of treatment. A total score of 0.00 was classified as 'complete correction', scores ranging from 0.5 to 1.0 were labeled as 'fair correction', and scores greater than 1.0 were considered as 'poor correction'. This approach of assigning clinical meaning to the final Pirani scores has also been employed in previous studies, such as the one conducted by Jain et al., where Pirani score thresholds were similarly used to evaluate treatment outcomes and categorize levels of deformity correction.[19] On the basis of this, 75.5% idiopathic clubfeet achieved complete correction and 22.30% achieved fair correction of the deformity. In Syndromic clubfoot; only 1.8% recovered completely and 41.44% achieved fair correction. In neurogenic clubfoot; only 3.89% recovered completely and 36.36% achieved fair correction. Across all the types we observed that total 81.23% complete correction was reported at the final evaluation. These findings align with a systematic review conducted by Lopez et al; that the Ponseti method is effective with a success rate of 90% in correcting clubfoot deformity.[13] A marked shift was also observed in the mean, median and mode of Pirani scores from pre- to post-treatment in all types of clubfoot; thus reflecting a significant improvement in clinical outcomes. To further evaluate the pre- and post-treatment changes in Pirani scores across all the types of clubfoot, the Wilcoxon Signed-Rank Test was used. The null hypothesis, "The median difference between pre-

treatment and post-treatment Pirani scores equals zero", was rejected, indicating that the Ponseti method significantly improves clubfoot deformity (p = 0.001) in any type of clubfoot deformity. Effect size for improvement in clubfoot deformity was assessed; showing a large treatment effect size (r=0.8) in all types of clubfoot.

LIMITATION & RECOMMENDATION

This study is single-center design, which may limit the broader applicability of the findings. Additionally, being a retrospective study based on data from the previous years may impose potential selection bias. Despite these constraints, larger, multicenter, prospective studies are recommended for broader validation.

CONCLUSION

This study concludes that the Ponseti method is highly effective in the treatment of various types of clubfoot, including idiopathic, syndromic, and neurogenic forms. The significant improvement observed in Pirani scores from pre- to post-treatment demonstrates the method's ability to achieve substantial correction of the deformity

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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6	**Shafaq Syed:** Drafting, revising manuscript.

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ORIGINAL ARTICLE

Comparison of functional outcomes of dynamic hip screw and proximal femoral nail in elderly patients presenting with intertrochanteric femur fracture.

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ABSTRACT… Objective: To evaluate and compare the functional outcomes and perioperative metrics of Dynamic Hip Screw (DHS) and Proximal Femoral Nail (PFN) fixation in elderly individuals with intertrochanteric femoral fractures. **Study Design:** Prospective, Observational Comparative study. **Setting:** Department of Orthopaedic, Ziauddin Hospital, Karachi. **Period:** August 2022 and February 2023. **Methods:** One hundred patients aged 60 years or older with OTA/AO type 31-A1 and 31-A2 intertrochanteric fractures were enrolled and divided equally into DHS and PFN groups. Patients with pathological fractures, high-energy trauma, or severe cognitive impairment were excluded. Surgeries were performed within 72 hours using standardized operative protocols. The primary endpoint was functional recovery at 6 months, assessed using the Harris Hip Score (HHS). Secondary variables included intraoperative parameters, hospital stay duration, time to mobilization, fracture healing time, and postoperative complications. **Results:** The PFN group demonstrated a shorter operative time, reduced blood loss, and earlier mobilization ($p<0.001$). Mean HHS at 6 months was significantly higher in the PFN cohort (85.8 ± 6.6) compared to DHS (80.9 ± 6.9, $p<0.001$). Excellent outcomes were more frequent in PFN (32%) than DHS (12%). Screw cut-out was seen only in the DHS group (10%, $p = 0.022$). **Conclusion:** PFN fixation provides superior early functional results and fewer mechanical complications compared to DHS in elderly patients with intertrochanteric fractures.

Key words: Dynamic Hip Screw, Elderly Patients, Harris Hip Score, Intertrochanteric Fracture, Orthopedic Trauma, Proximal Femoral Nail.

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INTRODUCTION

Hip fractures are a major public health issue in the elderly, causing disability, mortality, and rising costs. Global incidence has climbed in recent decades, driven by aging populations.[1,2] In GBD studies estimate annual hip fractures will approach 2.6 million by 2025 and over 4 million by 2050.[3,4] Older women are disproportionately affected due to osteoporosis, with lifetime hip fracture risks up to 15 after age 50.[1,5,6] By 2050, Asia is expected to account for nearly half of all osteoporotic hip fractures.[4]

Intertrochanteric femur fractures are among the most common injuries in the geriatric population, largely attributed to osteoporosis and low-energy falls. With a globally aging population, the incidence of such fractures is projected to rise substantially, increasing the burden on healthcare systems.[4,5] Surgical stabilization remains the preferred treatment to enable early mobilization, reduce morbidity, and lower mortality.[1]

"Two of the most frequently employed fixation methods are the Dynamic Hip Screw (DHS) and the Proximal Femoral Nail (PFN).[4] The DHS (introduced in the 1970s) is an extramedullary 135° screw-plate device that stabilizes the femur via a sliding lag screw.[7] It provides dynamic compression but can fail (e.g. screw cut-out or plate pull-off), especially in unstable patterns.[4] Intramedullary nails (PFNs) were introduced in the 1990s as a less-invasive alternative. Biomechanically, PFNs have a shorter lever arm and smaller bending moment compared to DHS.[3] The intramedullary position better resists varus collapse and may improve stability, particularly in unstable fractures.[3,4,8]

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Despite these biomechanical differences, clinical studies have reported inconsistent results comparing DHS and PFN. A recent systematic reviews report that PFN often reduces operative time and blood loss but does not significantly change union or complication rates.[4,9] Backman et al. found slightly higher Harris Hip and Parker mobility scores with nails (mean differences<1point)[9], but these small gains may lack clinical significance. Large randomized trials, including the international INSITE trial, have likewise shown equivalent outcomes: INSITE (n=850) found no difference in 1-year HHS or quality-of-life between a gamma nail and sliding hip screw.[10] Registry data are similarly mixed, with some series showing lower reoperation rates or mortality with nails in unstable fractures, while others show no survival advantage.[10,11] Hence, there is no clear consensus on which implant yields better functional recovery.

Given this uncertainty, especially in our local practice environment, we conducted an observational study comparing PFN and DHS fixation in elderly patients with intertrochanteric femur fractures. We hypothesized that PFN would provide at least equivalent, and possibly improved, 6-month Harris Hip Score (HHS) versus DHS, aligning clinical results with its theoretical biomechanical benefits."

METHODS

A prospective observational study was conducted at the Department of Orthopaedic Surgery, Ziauddin Hospital, Karachi, over a six-month period from August 2022 to February 2023. The study protocol received approval from the institutional ethics committee (06-07-25), and informed consent was obtained from all participants or their legal representatives.

"We performed an a priori sample size calculation to ensure sufficient power to detect a clinically meaningful difference in the primary outcome i.e. the HHS at 6 months. A minimally clinically important difference of 10 points on the HHS was selected based on prior literature demonstrating that such a difference reflects meaningful functional improvement in hip fracture patients.[12] Assuming a two-sided α=0.05 and power (1 –β)=0.80, with a standard deviation (SD) of approximately 7 derived from previously published scores in elderly hip fracture cohorts[12], the required sample size per group was estimated as 40. Allowing for a 20% rate of potential attrition or incomplete follow-up, the final sample size target was increased to 50 patients per group (total n=100).

Patients aged 60 years or older presenting with low-energy intertrochanteric femoral fractures, classified as OTA/AO types 31-A1 and 31-A2, were eligible for inclusion. Exclusion criteria were pathological fractures, polytrauma, prior surgery on the affected limb, cognitive disorders (e.g., dementia) affecting consent or compliance, and any contraindication to follow-up.

Eligible patients were allocated into two equal groups (1:1) to undergo either DHS or PFN fixation. Group assignment was based on the attending surgeon's routine practice pattern rather than randomization, maintaining an observational design with prospective follow-up. All procedures were performed by experienced orthopedic consultants within 72 hours of admission using standardized surgical techniques. The DHS group had a standard 135° sliding hip screw and side plate; the PFN group had a cephalomedullary nail (AO/ASIF type) with lag screw/antirotation screw. Both procedures followed standard surgical techniques, aiming for anatomic fracture reduction. All patients received similar perioperative antibiotics and thromboprophylaxis, and were encouraged to bear weight as tolerated postoperatively.

Patients were clinically and radiographically assessed at 6 months postoperatively. The primary outcome was functional recovery at 6 months, assessed using the HHS, a validated instrument ranging from 0 to 100, with higher scores indicating better function. included: Secondary outcomes: time to full weight bearing, time to radiological union (defined as bridging callus on three cortices on standard ap and lateral radiographs), duration of surgery, estimated intraoperative blood loss, length of hospital stay, and complications such as surgical site infection, screw cut-out, need for revision surgery, and thromboembolic events (DVT/PE).

Data were analyzed using SPSS version 25.

Continuous variables were expressed as mean±standard deviation and compared using independent samples t-tests. Categorical variables were presented as frequencies and percentages and compared using chi-square or Fisher's exact tests as appropriate. A p-value <0.05 was considered statistically significant."

RESULTS

A total of 100 elderly patients with intertrochanteric femur fractures were enrolled, with 50 patients randomized to the DHS group and 50 to the PFN group. The mean age in the PFN group was significantly higher than in the DHS group (p=0.003). The gender distribution was comparable between the groups, with females constituting 50% of the DHS group and 58% of the PFN group (p=0.422). Notably, diabetes mellitus was significantly more prevalent in the DHS group (48%) than in the PFN group (26%; p=0.023). There were no statistically significant differences in hypertension status (p=0.159) or ASA classification (p=0.500). (Table-I)

The PFN group demonstrated statistically significant advantages in all perioperative metrics (Table-II). Mean duration of surgery was shorter in the PFN group (59.75 ± 11.03 minutes) compared to the DHS group (p=0.001). PFN fixation was also associated with significantly less intraoperative blood loss (p=0.001). Postoperatively, the PFN group had shorter hospital stays (p=0.001) and achieved earlier weight bearing (p=0.001). Additionally, the mean union time was significantly faster in the PFN group (p=0.008), respectively.

At 6-month follow-up, functional outcomes assessed via HHS favored the PFN group (Table-III). The mean HHS was significantly higher in patients treated with PFN compared to DHS (p=0.001). Categorically, a greater proportion of patients in the PFN group achieved excellent functional scores (p=0.045). While good outcomes were nearly equivalent between groups, the DHS group had more patients in the fair and poor categories.

Complication rates were generally low across both groups (Table-IV). The incidence of superficial infection was slightly higher in the DHS group compared to the PFN group, but this was not statistically significant (p=0.695). Notably, screw cut-out occurred exclusively in the DHS group (p=0.022). Revision surgery was required for one patient in the DHS group and none in the PFN group (p=0.315). Conversely, two cases of deep vein thrombosis or pulmonary embolism were observed in the PFN group, while none occurred in the DHS group (p=0.153), though this difference was not statistically significant.

TABLE-I

Baseline characteristics of study participants (n=100)

Variable	DHS Group (n=50)	PFN Group (n=50)	P-Value
Age (years)	72.53±6.06	75.90±5.16	0.003*
Gender (Female)	25 (50)	29 (58)	0.422
Diabetes (Yes)	24 (48)	13 (26)	0.023*
Hypertension (Yes)	19 (38)	26 (52)	0.159
ASA Class I	10 (20)	5 (10)	0.500
ASA Class II	11 (22)	10 (20)	
ASA Class III	16 (32)	18 (36)	
ASA Class IV	13 (26)	17 (34)	

Data presented as mean±SD or n (%)
*p-value<0.05

TABLE-II

Operative and postoperative parameters (n=100)

Variable	DHS Group (n=50)	PFN Group (n=50)	P-Value
Duration of Surgery (min)	75.15±12.63	59.75±11.03	0.001*
Blood Loss (ml)	304.17±41.57	211.04±37.80	0.001*
Hospital Stay (days)	7.30 ± 1.27	6.47 ± 0.99	0.001*
Time to Weight Bearing (days)	5.68 ± 1.44	3.70 ± 0.96	0.001*
Union Time (weeks)	11.11 ± 1.11	10.56 ± 0.93	0.008*

Data presented as mean±SD
*p-value<0.05

TABLE-III			
Functional outcome (Harris Hip Score) at 6 Months (n=100)			
HHS Category	**DHS Group (n=50)**	**PFN Group (n=50)**	**P-Value**
Excellent (90–100)	6 (12.0)	16 (32.0)	0.045*
Good (80–89)	26 (52.0)	25 (50.0)	
Fair (70–79)	17 (34.0)	9 (18.0)	
Poor (<70)	1 (2.0)	0 (0.0)	
Mean HHS ± SD	80.89 ± 6.93	85.83±6.56	0.001*
Data presented as n (%) *p-value<0.05			

TABLE-IV			
Postoperative complications by treatment group (n=100)			
Complication	**DHS Group (n=50)**	**PFN Group (n=50)**	**P-Value**
Infection	4 (8.0%)	3 (6.0%)	0.695
Screw Cut-out	5 (10.0%)	0 (0.0%)	0.022*
Revision Surgery	1 (2.0%)	0 (0.0%)	0.315
DVT/PE	0 (0.0%)	2 (4.0%)	0.153
Data presented as n (%) *p-value<0.05			

DISCUSSION

In this prospective comparative study of elderly patients with intertrochanteric femur fractures, proximal femoral nail (PFN) fixation yielded notable advantages in perioperative outcomes, early functional recovery, and mechanical failure rates compared to dynamic hip screw (DHS) fixation over a six-month period. At 6 months, the PFN group demonstrated superior functional outcomes with a mean Harris Hip Score (HHS) of 85.8 versus 80.9 in the DHS group ($p < 0.001$), and a significantly higher proportion of "excellent" outcomes (32% vs 12%; $p = 0.045$). These results align with findings from Prakash et al., who reported significantly higher 6-month HHS values (89.3 vs 84.3) favoring PFN in an elderly cohort of 46 patients ($p = 0.023$).[13] Moreover, a comparative Indian study involving 60 patients also found higher HHS at 6 months in the PFN group, though differences ceased by 12 months. Given that clinically significant differences in HHS are defined in the 4–8 point range[14], our 5-point advantage likely represents a meaningful improvement for patients, especially during early recovery.

Our study found substantial perioperative benefits with PFN: shorter operative time (59.8 vs 75.2 minutes), reduced blood loss (211 vs 304 mL), shorter hospital stay, and earlier weight-bearing; all significant at $p=0.001$. These findings echo those of Xu et al. in a meta-analysis, confirming operative time and blood loss reductions with PFN, although they found no significant difference in long-term complications.[3] Another RCT meta-analysis of 12 studies reaffirmed shorter surgical duration and reduced intraoperative blood loss in PFN-treated patients, although DHS required less fluoroscopy.[4] These efficiencies may translate into shorter hospitalizations and reduced perioperative morbidity in elderly populations.

Notably, screw cut-out occurred in 10% of DHS patients but none in the PFN group ($p = 0.022$). This aligns with Zhang C et al. findings favoring PFN in cut-out rates and implant stability in unstable fractures.[15] While overall complication rates did not significantly differ, the significant mechanical failure disparity underscores the structural advantage of intramedullary support, particularly in osteoporotic bone where PFN better resists Varus collapse and rotational forces.

Contrary to our early functional advantages, large-scale RCTs and meta-analyses report no significant differences in 12-month HHS between PFN and DHS.[15,16] A 2024 meta-analysis examining multiple RCTs found comparable 6-month HHS outcomes (MD –3.28; 95% CI, –7.66 to 1.09; $p = 0.14$), suggesting that while PFN may enable faster early recovery, long-term results converge.[16] These findings support the notion that PFN primarily accelerates early functional recovery, but that DHS can achieve equivalent outcomes by 12 months; particularly in less frail patients or stable fracture patterns.

From a clinical standpoint, PFN offers clear benefits in early mobilization, reduced blood loss, and mechanical reliability, critical factors in elderly patients at high risk for immobility-related complications.[17] However, PFN implants come with higher costs, greater demands for surgical expertise, and increased radiation exposure during fluoroscopy.[16,18,19] In resource-limited settings where

surgical infrastructure is constrained, DHS may still represent an acceptable, cost-effective option, especially for stable fractures.[20,21]

Strengths of this study include prospective design, consistent implant use, and six-month follow-up with no patient attrition. However, several limitations merit attention. This single-center, observational design lacks randomization, which may introduce selection bias. Although baseline demographics were similar, the PFN group was slightly older, which could have attenuated the observed functional benefits. Fracture stability was not stratified, limiting applicability to unstable versus stable patterns. Also, the follow-up period captures early outcomes but cannot address longer-term concerns such as implant longevity, post-traumatic arthritis, or mortality. Future research should include larger, randomized multicenter trials with stratification based on fracture stability, incorporation of quality-of-life instruments, cost-effectiveness analyses, and follow-up beyond one year.

CONCLUSION

Proximal femoral nailing offers a statistically significant early functional advantage, reduced operative morbidity, and improved mechanical reliability over dynamic hip screw fixation for elderly patients with intertrochanteric femur fractures. These benefits, while most evident within the first six months, must be weighed against implant cost and surgical resource demands. Long-term outcomes appear similar between the two methods, suggesting implant selection should be driven by individual patient factors, fracture stability, and resource availability. High-quality RCTs with longer follow-up are necessary to refine practice guidelines and optimize outcomes across diverse settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Asim Aziz:** Principal investigator; Study conception and design, patient recruitment, surgical procedures, data supervision, and manuscript final review.
2	**Naseem Munshi:** Study conception, surgical supervision, critical analysis of data, literature review, and manuscript editing
3	**Arham Azizi:** Data collection, operative data management, statistical analysis, and drafting of results section.
4	**Uzma Azmatullah:** Radiological evaluation, interpretation of imaging data, and contribution to discussion on union outcomes.
5	**Muhammad Hassam:** Follow-up coordination, clinical examination at follow-up visits, data entry, and formatting of tables.
6	**Muhammad Ahmad:** Literature search, referencing, figures preparation, and preparation of initial manuscript draft.

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ORIGINAL ARTICLE

The effect of proximal cortical screw length of volar locking plates on clinical outcomes in distal radius fractures.

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ABSTRACT… Objective: To evaluate the impact of proximal cortical screw length in volar locking plates (VLPs) on clinical outcomes in patients with distal radius fractures (DRFs). **Study Design:** Prospective observational study. **Setting:** Department of Orthopedic Surgery, Nishtar Hospital, Multan, Pakistan. **Period:** June 2024 to April 2025. **Methods:** We enrolled 104 patients aged ≥18 years with DRFs treated with VLPs, followed for at least 12 months. Exclusion criteria included prior limb injuries, open fractures, non-VLP interventions, and extensor soreness from distal screws. Clinical outcomes, including grip strength (Jamar dynamometer), range of motion (ROM), Quick Disabilities of the Arm, Shoulder, and Hand (QDASH) scores, and extensor tendon complications, were assessed. Radiological evaluations measured dorsal cortical screw prominence (>1.2 mm) using postoperative X-rays. Surgical procedures used a Colar Henry incision and Acu-Loc VLP with unicortical distal and bicortical proximal screws. Data were analyzed using SPSS 26.0, with Mann-Whitney U and chi-square tests for non-normally distributed continuous and categorical variables, respectively. **Results:** Of 104 patients (63 males, 60.6%; mean age 49.13 years), 61 (58.7%) had right-sided fractures, primarily caused by road traffic accidents. Extensor sensitivity occurred in 36 (34.6%) cases. Proximal screw prominence >1.2 mm was significantly associated with extensor synovitis ($p<0.05$), but not with grip strength, ROM, or QDASH scores. Patient satisfaction was 50.96% (53/104). **Conclusion:** Proximal cortical screw prominence >1.2 mm in VLPs significantly increases extensor tendon irritation in DRFs, emphasizing the need for precise screw length to optimize clinical outcomes and patient satisfaction.

Key words: Dorsal Cortex Protrusion, Radius Fracture, Screw Prominence, Volar Locking Plate, Wrist.

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INTRODUCTION

Distal radius fractures (DRFs) are described as the most common type of fractures in the adult population and may increase in occurrence as adults continue to become more active in old age.[1,2] These are the difficult fractures that present meaningful challenges to the clinical setting because it can often need surgical measures to restore the functionality, as well as, to avoid long-term disability. The introduction of the volar locking plates (VLPs) transformed the way of managing DRFs and came with its complications because the technique also offers stable fixation. One of the complications that may occur after VLPs is irritation of extensor tendons that may cause tenosynovitis, rupture of tendons, and patient dissatisfaction. These complications have the risk of undermining functional outcome of an otherwise successful surgical procedure and hence the need to shed light on risk factors involved in VLP fixation and reducing these risk factors.

According to the current literature, extensor tendon complications, such as extensor pollicis longus (EPL) or extensor digitorum communis ruptures are also linked to the usage of VLPs and the incidence rates are reported to be less than 1 or more than 12.5 percent.[3-6] These problems are frequently caused by iatrogenic damages of drill penetration or dorsally prominent screws when using bicortical fixer, which can injure tendons around the dorsal cortex.[8,10] Even though, the biomechanical investigations indicate that unicortical distal screws with lengths more than 75 percent of the radar thickness can have similar stiffness to the bicortical fixation, such results are not fully replicable in the case of intra-articular DRFs.[7]

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Remarkably, most studies have been done on distal screw insertion and little was aimed at the role played by the proximal cortical prominence screw over the radial shaft.[9,10]

This particular study seeks to examine whether conspicuous proximal cortical screw insertion in VLPs is linked to extensor tendon friction or business break or pinch removal in patients getting surgical decontamination of DRFs. The assessment of these outcomes will allow the study to evidence the properties of surgical techniques, leading to the enhancement of clinical outcomes.

METHODS

It was a prospective observation study aimed at assessing clinical and radiological outcomes of distal rhythm fractures in cases operated with volar locking plates (VLP) conducted at Nishtar Hospital, Multan, Pakistan, within the Department of Orthopedic Surgery from June 2024 to April 2025.

A total of 104 patients with distal radius fractures treated with VLP were enrolled in the study.

A non-probability consecutive sampling technique was employed to recruit eligible patients presenting at the hospital during the study period.

Inclusion Criteria

Patients were included if they were at least 18 years old, had a distal radius fracture treated with VLP, and had a minimum follow-up period of 12 months.

Exclusion Criteria

Patients were excluded when they had previous break in the same limb, an open fracture, non-VLP surgical treatment (e.g., percutaneously pinning or external fixation), had plates and screws taken out because of intra-articular distal screw position or excessively long screws stuck in a joint, and did not attend their last follow-up visit. Also patients with a soreness of the extenders with the distal screws (those who experienced pain during the active extension of hand above Lister tubercle or palpation on the extensor compartments) and those who had the plates removed owing to the intra-articular screws were excluded.

At the last follow-up, clinical outcomes were evaluated, such as grip strength, tourniquet time, range of motion (ROM) extensor tendon rupture, complication, extensor tenosynovitis, and reoperation. Both the fractured and the healthy sides were used to measure the grip strength using the Jamar hand dynamometer (Asimow Engineering, Los Angeles, CA, USA) with the difference being noted. ROM was identified through the difference in measurements between the fractured side and the healthy one. A questionnaire known as Quick Disabilities of the Arm, Shoulder and Hand (QDASH) was administered to assess the pain, functional capacity in daily living activities and level of disturbance of the symptoms. The anamnesis and palpation revealed extensor tenosynovitis, during which discomfort was present during extension either at the radial shaft or Lister tubercle or both. Those patients who complained of pain around or at Listers tubercle were excluded.

Radiological evaluation was done on digital radiographs (PACS). Both the lateral and posterior X-rays were taken preoperatively and postoperatively to determine the radial height, ulnar variance, volar tilt and radial inclination. Dorsal cortical prominence was measured by using immediate postoperative radiographs, where the most prominent proximal cortical screw was identified and its measurement was obtained by finding an outer dorsal cortex to the tip. Radiological assessments were performed by two orthopedic surgeons with the help of PACS computerized tools to accurately measure the angles and distances.

Surgical procedures were performed under infraclavicular block anesthesia. Patients were positioned supine, and a pneumatic tourniquet was applied at 250 mmHg for 90 minutes. A Colar Henry incision was used to access the fracture, which was reduced and fixed with an Acu-Loc volar distal radius plate (Acumed, Hillsboro, OR, USA) secured with 2.7 mm and 3.5 mm screws. Distal locking screws were placed in a single cortical, while proximal screws engaged a second cortex. After hemostasis, the skin was closed, and a short arm splint was applied. Finger motion was initiated immediately, the splint was removed after two weeks to begin wrist movements, and strengthening exercises

commenced after six weeks of fracture healing.

The data were analysed using an IBM SPSS Version 26 (IBM Corp., Armonk, NY, USA). Continuous variables normality was determined using a Shapiro-Wilk test and was shown not to be normally distributed. They were hence quoted as medians and interquartile interval (IQR, 25 75). The comparison of Groups in continuous variables was performed with the help of Mann-Whitney U. Variables expressed as categories were presented in frequencies and as percentages, yet the distribution of the latter was analyzed with the help of the chi-square test.

The study was approved by the Institutional Review Board of Nishtar Hospital, Multan, under reference number 002/IRB/TCH/N-II. Informed consent was obtained from all participants.

RESULTS

We found 63 (60.6%) males and 41 (39.4%) females among all cases. The mean age was 49.13 years. Right side was the most common fracture side found in 61 (58.7%). RTA was the most common cause followed by fallen and sports. (Table-I)

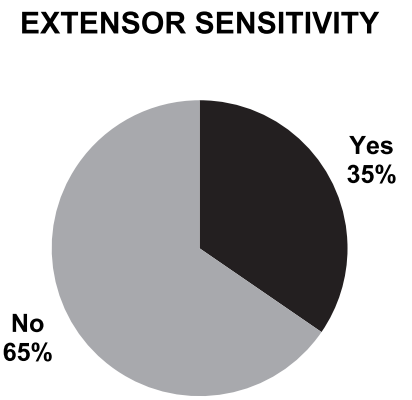
Patients detailed baseline information

Variables	No./%age
Average age (years)	49.13
Gender	
Men	63 (60.6%)
Women	41 (39.4%)
Affected Side	
Right	61 (58.7%)
Left	43 (41.3%)
Cause of fracture	
RTA	47 (45.2%)
Fallen	38 (36.5%)
Sports	29 (27.9%)

Frequency of extensor sensitivity was found in 36 (34.6%) cases. (Figure-1)

FIGURE-1

Association of extensor sensitivity



For extensor synovitis, a proximal screw prominence greater than 1.2 mm was shown to be statistically significant ($p<0.05$). Factors such as grip strength, range of motion, QDASH, and other variables were not linked to extensor tenosynovitis. (Table-II)

TABLE-II

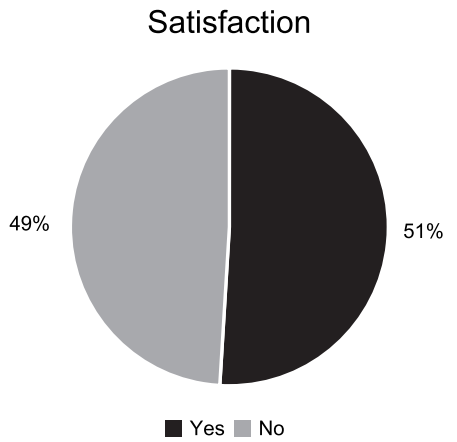
Association of variables with extensor tenosynovitis

Variables	Median [IQR] (36)	P Value
Length of Proximal Screw		
>1.2 mm	30 (83.3%)	<0.001
<1.2 mm	6 (16.7%)	
Frequency of proximal screw		
2 screws	5 (13.9%)	<0.002
2-3 screws	31 (76.1%)	
Mean QDASH	9.6 (2.2-30)	0.421
Radial inclination		
Pre-operative	15 (16-25)	0.354
Post-operative	20 (15-28)	
Radial Height		
Pre-operative	9 (2-12)	0.698
Post-operative	10 (7-15)	
Volar Tilt		
Pre-operative	-12 (-18 to -12)	0.594
Post-operative	9 (3-15)	

Frequency of satisfaction among all cases were 53 (50.96%). Figure-2

FIGURE-2

Post-operative satisfaction among all cases



DISCUSSION

This study identifies a significant association between proximal cortical screw prominence greater than 1.2 mm in volar locking plates (VLPs) and extensor tenosynovitis in distal radius fractures (DRFs), a finding that underscores the importance of proximal screw length. Unlike prior studies that often conflate the effects of proximal and distal screws when discussing extensor tendon irritation [11–14], our research specifically isolates the impact of proximal screw prominence in the radial shaft. This focus revealed that dorsal cortical protrusion exceeding 1.2 mm significantly increases the risk of extensor tenosynovitis ($p<0.05$), a novel threshold that contrasts with the broader focus on distal screws in existing literature. By excluding patients with distal screw-related irritation, we ensured a more precise evaluation of proximal screw effects, highlighting a previously underemphasized risk factor in VLP fixation.

Comparisons with biomechanical and clinical studies further contextualize our findings. Wall et al.[15] demonstrated that unicortical screws achieving 75% of radial thickness provide comparable rigidity to bicortical screws, suggesting that bicortical fixation may not always be necessary. However, our study diverges from Pulos et al.[11] who found proximal screw prominence clinically insignificant, possibly due to their inclusion of patients with implant removal for varied reasons. In contrast, White et al.[16] and Hong et al.[17] reported that dorsal prominence ≥2 mm increases tendinopathy and rupture risk, a higher threshold than our 1.2 mm finding. Our lower threshold suggests that even minor proximal screw prominence can compromise outcomes, advocating for meticulous screw length control to minimize complications.

Another critical aspect of our study is the influence of intraoperative techniques on screw prominence. Eng et al.[18] found that adjusting forearm supination-pronation by 10 degrees during proximal screw placement reduces prominence and associated complications. Our prospective study could not standardize intraoperative fluoroscopy for supination-pronation due to its observational design, relying instead on the most accurate postoperative radiographs to measure prominence. This limitation highlights the need for precise intraoperative imaging to optimize screw placement. We propose that maintaining proximal screw protrusion below 1.2 mm or using unicortical fixation could mitigate extensor tendon issues, offering a practical guideline for surgeons to enhance patient outcomes.

Despite its contributions, this study has limitations. The single-center design and sample size of 104 patients may limit generalizability. The prospective observational methodology precluded standardized intraoperative radiographs to assess supination-pronation angles, relying instead on postoperative X-rays, which may introduce measurement variability. Additionally, the assessment of extensor tendon irritation depended on subjective palpation data, potentially affecting reliability. Future multicenter studies with larger cohorts, standardized imaging protocols, and objective tendon irritation measures are needed to validate and expand upon these findings.

CONCLUSION

The surgeon's focus on the proximal cortical screws is just as important as the reduction quality, distal screw position and length, and overall success rate of using VLP in DRFs. Patients may experience extensor tendon soreness and dissatisfaction due to lengthy proximal cortical screws, even after a successful operation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Kamran Shafi:** Conceptualization, writing, formal analysis.
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3	**Mukhtar Ahmad Tariq:** Inestigation, resources.
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ORIGINAL ARTICLE

Autonomy in family planning decision-making and its predictors among married women: A cross-sectional study at maternal and child health Centre, Nawabshah.

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ABSTRACT... Objective: To investigate the factors influencing family planning use among married women by assessing their decision-making autonomy regarding family planning, identifying household predictors of this autonomy, and determining the association between reproductive health services and decision-making power. **Study Design:** Analytical cross-sectional study. **Setting:** MCH and Family Planning Centre at Nawabshah Sindh. **Period:** January 2025 to March 2025. **Methods:** A total of 345 married women who visited were selected who visited MCH and Family Planning Centre at Nawabshah Sindh. The selection of the sample was done by using a consecutive sampling technique. Researchers collected data using structured and a structured, pre-tested questionnaire through Google Forms. Binary logistic regression and multiple logistic regression analysis were used to identify the associated factors and the oodds ratios with 95% confidence intervals were computed to assess the strength of the association. **Results:** Overall, only 19.4% of married women were found to have decision-making power in family planning. Women of graduate level of education [AOR: 7.156, 95% CI: (1.11 – 48.37)], husband's secondary education [AOR: 0.220, 95% CI: (0.05 – 0.76)], husbands who were shopkeepers [AOR: 4.891, 95% CI: (1.57 – 15.87)], monthly income >100,000 [AOR: 32.06, 95% CI: (1.94 – 1498)] were significantly associated with women's decision-making power in family planning. **Conclusion:** In this study, women had low decision-making power in family planning use. Women's and their husbands' formal education, and husbands' occupational status, and monthly income had effects on women's decision-making power.

Key words: Autonomy, Decision-making Power, Family Planning, Maternal Health, Reproductive Health.

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INTRODUCTION

Women's autonomy contributes significantly to many health advantages for both mothers and their children. Women's autonomy is defined as the ability of women to act independently regarding their health, their children's health, freedom of movement, and control over finances without seeking permission from anyone.[1] In developing nations, women are crucial to family well-being, primarily seen as mothers and homemakers. Their ability to participate in family decisions significantly impacts the overall welfare of the household, and their involvement is essential for achieving equality and harmony. However, in countries like Bangladesh and Pakistan, women's decision-making power is often restricted. They frequently lack autonomy, especially regarding personal movement, family planning, and their children's education.[2] Factors like household structure and size, the joint family system, and the husband's characteristics may influence a woman's use of contraception and ability to realize her reproductive rights.[3] Pakistan has the lowest prevalence of contraceptive use in the South Asian region, but the highest discontinuation rate, possibly due to concerns about side effects of modern contraceptives and intra-family dynamics where husbands and mothers-in-law influence contraception decisions.[4] In previous studies, researchers identified factors affecting women's autonomy in decision-making regarding contraceptive choices at both the individual and community levels, such as place of residence, age, wealth index, women's education and occupation, number of living children, desire to have children, media exposure, and whether they visited a health facility in the last 12 months.[5]

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In many developing countries like Ethiopia, economic, social, and environmental constraints frequently inhibit women from fully exercising their reproductive rights. According to the results of a 2017 Ethiopian study, 52% of the participants demonstrated high decision-making power regarding modern family planning methods.[6] The study conducted across 11 East African countries revealed a significant proportion of women 68.37% possessed autonomy in healthcare decision-making.[7] In 2023, the prevalence of women who independently decided to use family planning was 65.47% in Guinea, on the other hand only 25.1% of Nepalese women had autonomy in making reproductive health decisions.[8,9] The issue of women's empowerment in urban Pakistan, particularly in metropolitan areas like Lahore, is a complex and multifaceted challenge that has garnered increasing attention in recent years. In 2020, 75% of women felt their participation in household decision-making was minimal, reflecting the long-standing patriarchal norms that dominate their socio-cultural context.[10] In Pakistan, where teen pregnancy rates are high and family planning use is low, women's limited control over reproductive choices remains a major concern. This lack of autonomy often leads to larger families than desired, straining household resources and affecting maternal and child health. Despite government efforts to improve maternal care, contraceptive use remains low, especially in rural areas. This study aims to investigate the factors influencing family planning use among married women by assessing their autonomy of decision-making regarding family planning, identifying household predictors of this autonomy, and determining the association between reproductive health services and decision-making power.

METHODS

This analytical cross-sectional study was conducted over three months from January 2025 to March 2025, at the Gynae ward, Gynae OPD, and Family Planning Centre of the Maternal and Child Health (MCH) Centre, PUMHSW, Nawabshah. The study population comprised married women aged 18-49 seeking services at the centre. Ethical approval (PUMHSW/SBA/IPH-601) was obtained before collecting the data from the participants. Non-probability consecutive sampling technique was employed, with a sample size of 345 participants. The sample size was determined using a 66% prevalence of autonomy from previous research[11], a 95% confidence level, and a 5% margin of error.

Married women of reproductive age visiting MCH centre were included in the study. Due to the sensitivity of the topic and the presence of husbands or mothers-in-law, which could influence participants' responses, privacy was carefully maintained. Women who consented to participate were respectfully guided to a separate, quiet area where they could respond freely without external pressure or observation. Exclusion criteria were women with comorbidities, pregnancy, previous sterilization, severe cognitive or mental health issues, or inability to provide informed consent. Data were collected through a structured, pre-tested questionnaire covering socio-demographic characteristics, previous reproductive history, decision-making autonomy, and decision-making power. Prior approval was obtained from hospital authorities and informed written consent was secured from all participants.

Data analysis was performed using SPSS v25.0 and GraphPad Prism v9.5. Descriptive statistics were used for categorical data, while chi-square tests examined related frequencies between decision-making autonomy and independent variables. Variables with significant associations were further analyzed using binary and multiple logistic regression to identify predictors and adjust for potential confounders such as income, education, and employment status. A p-value of <0.05 was considered statistically significant, with results presented through tables, charts, and graphs.

RESULTS

The majority were aged between 18–33 years, with 32.8% in the 18–25 age group and 33% in the 26–33 age group. Most participants (90.4%) had a monthly income of less than 50,000 PKR. Over half of the women (55.1%) were illiterate, while only 4.1% had attained graduation-level education. Similarly, 46.1% of the participants' husbands were illiterate. The most common occupation among husbands was labour (46.7%) (Table-I).

Most (46.7%) had a parity of 2–4. Antenatal care (ANC) visits were reported by 75.9% of women, with 58% having fewer than four follow-up visits. Husbands were involved in delivery care in 69.9% of cases. Only 42.3% of women had household decision-making power, and a mere 19.4% had autonomy in family planning decisions (Table-II).

Family planning decision-making was significantly associated with participants' education ($p < 0.001$), husband's education ($p = 0.003$), and husband's occupation ($p = 0.002$). Higher household income was strongly linked to increased decision-making power ($p < 0.001$). Additionally, involvement in financial decisions ($p = 0.001$), household decisions ($p < 0.001$), and greater freedom of movement ($p < 0.001$) were all positively associated with family planning decision-making power (Table-III).

TABLE-I

Participants characteristics:

Study Variables	Total Participants n=345	N (%)
Age (Years)	18-25	113 (32.8%)
	26-33	114(33%)
	34-41	94(27.2%)
	42-49	24(7%)
Monthly Income	<50,000	321(90.4%)
	50,000 - 100,000	27(7.8%)
	>100,000	6(1.7%)
Participant's Education	Illiterate	190(55.1%)
	Primary	64(18.6%)
	Secondary	47(13.6%)
	Higher	30(8.7%)
	Graduation	14(4.1%)
Husband's Education	Illiterate	159(46.1%)
	Primary	67(19.4%)
	Secondary	62(18%)
	Higher	34(9.9%)
	Graduation	23(6.7%)
Husband's Occupation	Labour	161(46.7%)
	Farmer	37(10.7%)
	Shopkeeper	46(13.3%)
	Others	101(29.3%)
Desired Family Size	< 3	65(18.8%)
	3-5	204(59.1%)
	>5	76(22%)

TABLE-II

Reproductive history and utilization of healthcare services:

Study Variables	Total Participants n=345	N (%)
Parity	1	70(20.3%)
	2-4	161(46.7%)
	>4	114(33%)
Had ANC visits	Yes	262(75.9%)
	No	83(24.1%)
Number of ANC Follow-Up (N=281)	< 4	163(58%)
	> 4	118 (42%)
HAD PNC Visits	Yes	100(29%)
	No	245(71%)
Number of PNC Follow-Up (N=100)	< 3	73(73%)
	> 3	27(27%)
Place of Delivery	Government	149(42.2%)
	Health Center	50(14.5%)
	Private	79(22.9%)
	At home	67(19.4%)
Birth Assisted By	Health Professional	279(80.9%)
	TBA	66(19.1%)
Husband's Involvement in Delivery Car	Yes	241(69.9%)
	No	104(30.1%)
Household Decision Power	Yes	146(42.3%)
	No	199(57.7%)
Family Planning Decision Power	Yes	67(19.4%)
	No	278(80.6%)

Women with graduation-level education had 7 times higher odds of having family planning decision-making power compared to those who were illiterate (AOR: 7.15; CI: 1.11–48.7; $p = 0.039$). Similarly, women whose husbands had secondary education were significantly less likely to have decision-making power compared to those whose husbands were illiterate (AOR: 0.22; 95% CI: 0.05–0.76; $p = 0.023$). Women whose husbands were shopkeepers had nearly 5 times higher odds of autonomy compared to those whose husbands were labourers (AOR: 4.89; CI: 1.57–15.8; $p = 0.006$). Additionally, participants with a monthly income exceeding 100,000 PKR had 32 times higher odds of having decision-making power than those earning less than 50,000 PKR (AOR: 32.0; CI: 1.94–1498; $p = 0.035$) (Table-IV).

TABLE-III

Frequency of decision making power of family planning with participants characteristics and household decisions

Study Variables	Categories	Yes	No	P-value <0.05
		N (%)	N(%)	
Age (Years)	18-25	22(32.8%)	91(32.7%)	0.814
	26-33	23(34.3%)	91(32.7%)	
	34-41	19(28.3%)	75(26.9%)	
	42-49	3(4.4%)	21(7.5%)	
Participant's Education	Illiterate	24 (43.6%)	166 (59.7%)	<0.001*
	Primary	12 (21.81%)	52 (18.7%)	
	Secondary	13 (23.63%)	34 (12.2%)	
	Higher	11 (20%)	19 (6.83%)	
	Graduation	7 (12.7%)	7 (2.51%)	
Participant's Husband Education	Illiterate	24 (35.8%)	135 (48.5%)	0.003
	Primary	15 (22.3%)	52 (18.7%)	
	Secondary	7 (10.4%)	55 (19.7%)	
	Higher	12 (17.9%)	22 (7.91%)	
	Graduation	9 (13.4%)	14 (5.0%)	
Husband's Occupation	Labour	23 (34.3%)	138 (49.6%)	0.002
	Farmer	3 (4.47%)	34 (12.2%)	
	Shopkeeper	16 (23.8%)	30 (10.7%)	
	Others	25 (37.3%)	76 (27.3%)	
Household Income	<50,000	56 (73.6%)	256 (92.0%)	<0.001*
	50,000 - 100,000	6 (7.89%)	21 (7.5%)	
	>100,000	5 (6.57%)	1 (0.35%)	
ANC Visits	Yes	61 (91.0%)	201 (72.3%)	<0.001*
	No	6 (8.95%)	77 (27.6%)	
Number of ANC Visit	> 4	28 (44.4%)	90 (41.2%)	<0.011
	<4	35 (55.5%)	128 (58.7%)	
Financial Decisions	Yes	53 (79.1%)	130 (46.7%)	<0.001*
	No	14 (20.89%)	148 (53.2%)	
Household Decisions	Yes	54 (80.59%)	136 (48.9%)	<0.001*
	No	13 (19.4%)	142 (51%)	
Freedom of Movement	Yes	30 (44.7%)	53 (19%)	<0.001*
	No	37 (55.2%)	225 (80.9%)	

DISCUSSION

This study investigates the autonomy of decision-making power in family planning among married women of reproductive age. It aims to understand how factors influence women's reproductive health choices and assess the extent of women's decision-making autonomy in family planning. Overall, 19.4% had decision-making power, aligning with a study from Senegal (17.9%).[12] However, this is lower than findings from South Ethiopia (67.2%), Addis Ketema (73.3%), and Dinsho Woreda (52%).[13,14,6] These differences may be attributed to variations in socioeconomic and demographic factors, study design, and sample sizes.

Women's participation in household decision-making in the study area was 42.3%, which is lower than southern Ethiopia (56%)[15], but lower than East Africa (68.37%) and Ghana (75.26%).[7,16] These differences may stem from study settings, as the referenced studies focused on rural areas, while this study included both rural and urban communities in Nawabshah. Data on women's household decision-making shows limited autonomy, particularly in finances and mobility. While 64% had free access to money similar to a North Indian city (60%)[17] this was lower than in Lahore (77%)[10], likely due to differences in population settings. In this study, 72.5% of women had autonomy in small decisions, 53.9% in major ones, and 63.8% required permission to leave home. Restrictions on movement were reported by 58.6%.

TABLE-IV

Predictors of family planning decision-making power

Covariates & Ref: Category	Categories	Odds ratio	CI (95%) (Lower-upper)	P-Value	AOR	CI (95%) (Lower-Upper)	P-Value <0.05
Participants' Education Ref: Illiterate	Primary	1.596	0.72 - 3.36	0.227	1.58	0.56-4.32	0.368
	Secondary	2.64	1.20 - 5.65	0.013	3.09	0.98-9.83	0.053
	Higher	4.00	1.66 - 9.37	0.001	1.51	0.36-5.99	0.557
	Graduation	6.917	2.19	21.92	7.15	1.11-48.7	0.039
Husband's Education Ref: Illiterate	Primary	1.623	0.77 - 3.31	0.187	1.46	0.56 - 3.76	0.427
	Secondary	0.715	0.27 - 1.68	0.465	0.22	0.05 - 0.76	0.023
	Higher	3.06	1.31 - 6.97	0.007	1.20	0.31 - 4. 78	0.746
	Graduation	3.61	1.37 - 9.22	0.007	0.62	0.11 - 3.03	0.563
Husband's Occupation Ref: Labour	Farmer	0.529	0.12 - 1.63	0.322	0.58	0.11 - 2.30	0.475
	Shopkeeper	3.200	1.49 - 6.77	0.002	4.89	1.57 - 15.8	0.006
	Others	1.974	1.04 - 3.73	0.034	1.35	0.51 - 3.53	0.554
Monthly Income Ref: <50,000	50,000 - 100,000	1.306	0.46 - 3.20	0.582	0.91	0.22 – 3.42	0.893
	>100,000	22.86	3.59 - 442.2	0.004	32.0	1.94 - 1498	0.035
Living Children Ref: 1	2-4	1.116	0.58 - 2.20	0.746	1.20	0.45 – 3.28	0.704
	>4	0.360	0.15 - 0.82	0.016	0.51	0.14 – 1.82	0.307
Control Over Finance Ref: Yes	No	0.232	0.11 - 0.42	0.000	0.58	0.22 – 1.45	0.253
Decision-Making Power Ref: Yes	No	0.230	0.11 - 0.42	0.000	0.42	0.16 – 1.02	0.060
Freedom of Movement Ref: Yes	No	0.290	0.16 - 0.51	0.000	0.59	0.23 – 1.47	0.263

These figures are lower than in a North Indian city, where 81% made small decisions, 92% could go out alone, and 58% could visit parents.[17] Differences may be due to socio-cultural norms, religious views, and economic development.

In our study, 33% of women were aged 26–33, 32% were 18–25, 27% were 34–41, and only 7% were 42–49. No association was found between age and family planning decision-making autonomy. In contrast, studies from Malawi, East Africa, and Senegal reported a positive link between older age and autonomy.[18,7,12] This discrepancy may be due to the smaller proportion of older women in our sample. 55.1% of women were illiterate, while only 4.1% were graduates, among whom 50% had decision-making autonomy. Women with secondary or higher education (27.7% and 36.7%) showed greater autonomy compared to those with no (12.6%) or primary education (18.8%). A significant association was found between education and decision-making power. This aligns with findings from East African countries and Ghana[7,16], possibly because education improves women's understanding of health issues of health issues and their ability to make informed decisions. Our study found a significant association between the husband's education and women's decision-making power in family planning. Autonomy increased from 15.1% with illiterate husbands to 39.1% with graduate husbands, suggesting higher male education supports women's empowerment. This aligns with findings from Senegal.[12]

Women whose husbands are shopkeepers reported the highest decision-making power (34.8%), while those with farmer husbands had the lowest (8.1%). Overall autonomy remained low at 19.4%, reflecting ongoing socio-cultural barriers. These findings align with studies from East African countries.[7] Our study found that women with a monthly household income >100,000 (83.3%) have greater autonomy in decision-making compared to those with <50,000 (17.9%). A similar study in the Bale zone also showed that women with higher socioeconomic status had better access to decision-making autonomy over their health.[19]

Women with 2-4 children showed greater participation in decision-making (26.8%) than those with >4 children (9.6%). However, these figures are lower than those in a similar study in Zambia[49], possibly due to differences in socio-cultural contexts or data collection methods, as the Zambian study used previous demographic survey data.

The binary logistic analysis reveals that women's household decision-making power in Nawabshah is influenced by education, economic status, healthcare access, and husband's involvement. Women's education is a key predictor, with secondary education (OR=2.64) and graduation-level education (OR=6.91) significantly increasing decision-making power. Husband's education also positively impacts decision-making, with graduates showing (OR=3.61) higher odds of their wives participating in decisions. Occupational and economic factors are crucial; with women whose husbands are shopkeepers having (OR=3.20) higher odds of decision-making power. Households earning above 100,000 show (OR=22.86) higher odds compared to those earning below 50,000. Healthcare access also influences autonomy, with women attending >4 antenatal care visits showing (OR=1.138) higher odds of decision-making power. Several variables, including control over finance (OR=0.232, P-value 0.000), decision-making power (OR=0.230, P-value 0.000), freedom of movement (OR=0.290, P-value 0.000), and household decision-making autonomy (OR=0.235, P-value 0.000), show positive associations.

In our analysis, we compared the results of binary logistic regression (BLR) and multiple logistic regression (MLR) to understand the factors associated with women's decision-making power in family planning. While both models identified several significant predictors, the MLR revealed variations and changes in the strength and significance of these associations when controlling for other variables.

After adjusting for variables, women's education remained a significant predictor of decision-making power, with higher education levels, particularly graduation, showing increased odds (AOR=7.15). This suggests the impact of education is amplified when controlling for other factors. A notable change was observed in the effect of the husband's education. The BLR showed a positive association for higher education (OR=3.06), but the adjusted model revealed a negative association (AOR=0.220), indicating women with highly educated husbands were less likely to have decision-making power when accounting for other variables. This underscores the importance of considering confounding factors. Both models consistently identified the husband's occupation as a significant predictor. Women whose husbands were shopkeepers had higher odds of decision-making power, with the adjusted model showing a slightly higher odds ratio (AOR=4.89) compared to the BLR (OR=3.20). A strong positive association was also found between monthly income and decision-making power, especially for households earning above 100,000. After adjustment, this association strengthened (AOR=32.06) compared to the (OR=22.86). Having more than four living children was associated with lower odds of decision-making power, but this was not statistically significant in either model. Variables related to women's autonomy, such as control over finance, decision-making power, and freedom of movement, remained non-significant after adjustment, though their association strength varied slightly compared to the BLR. Variables related to women's autonomy, such as control over finance, decision-making power and freedom of movement, remained non-significant predictors after adjustment. However, the strength of these associations varied slightly compared to the BLR.

There are several limitations to this study, Primarily, it only surveyed women, neglecting the views of their spouses, this restricts how widely the findings can be applied to the general population. Additionally, while various demographic factors were considered, the study had relatively small numbers of older women, educated women, and high-income families, which could distort the results.

CONCLUSION

The magnitude of women's decision-making power in family planning among married women was found to be low (19.4%) in our study. Factors such as women's and husbands' secondary-level education and above, monthly income, and occupational status of husbands were found to be statistically significant by controlling the effect of all other variables related

to the decision-making power. While women were autonomous in some areas of decision-making, in other domains, like control over finance, decision-making in small and large household decisions, and freedom of movement, they had limited autonomy. This study suggests a multifaceted approach to improve women's decision-making power in family planning. Economic empowerment initiatives, such as income-generating opportunities such as skill-enhancement programs, market access, and financial support, can help women build on their existing talents and skills and can also enhance women's autonomy.

ETHICAL APPROVAL

This study was reviewed and approved by the ethical research committee of the Institute of Public Health, Faculty of Community Health Sciences under reference number (PUMHSW/SBA/IPH 601). The study adhered to the Helsinki Declaration, as well as national, international, and institutional ethical standards at all stages, given the involvement of human participants.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Hanna Khair Tunio:** Concept of research, revisions.
2	**Aisha Choudhry:** Writing of manuscript, revisions, final draft.
3	**Syeda Khadija Zehra:** Initial writing, data analysis.
4	**Kiran Iqra:** Interpretation of results.
5	**Aliza Chandio:** Data collection, analysis, proofreading.
6	**Lareb Nawaz:** Data collection, analysis.

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ORIGINAL ARTICLE

Comparing cone beam computed tomography with panoramic radiography for prediction of implant planning and size.

Bakhtawar Tahir[1], Mustafa Sajid[2], Amara Nazir[3], Hira Anmol[4], Mehwish Munawar[5], Amira Shahid[6]

ABSTRACT… Objective: To compare the accuracy and effectiveness of CBCT and panoramic radiography for determining implant size and placement in patients requiring dental implants. **Study Design:** Cross-sectional study. **Setting:** Department of Operative Dentistry, Bakhtawar Amin Dental Hospital, Multan. **Period:** Jan 2025 to Oct 2025. **Methods:** Data were collected using a consecutive non-probability sampling technique, with a sample size of 97 edentulous sites from adult patients (18-55 years) who were candidates for dental implants. Both CBCT and panoramic radiography were used to measure implant length and width. **Results:** The results showed that CBCT provided more accurate measurements for both implant length (mean = 10.3 mm, SD = 1.4) and width (mean = 4.6 mm, SD = 0.6) compared to panoramic radiography (length: mean = 10.1 mm, SD = 1.5; width: mean = 4.5 mm, SD = 0.7). The correlation coefficient for implant length between CBCT and panoramic radiography was 0.92 ($p < 0.01$), while for implant width, it was 0.84 ($p < 0.01$). CBCT also demonstrated a higher success rate in implant planning (91.8%) compared to panoramic radiography (78.4%). **Conclusion:** It is concluded that CBCT provides superior accuracy and precision in implant planning compared to panoramic radiography, particularly for implant length and width. CBCT should be considered the preferred imaging modality for complex implant planning, especially when high precision is required.

Key words: Cone Beam Computed Tomography, Implant, Panoramic Radiograph, Size and Shape.

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INTRODUCTION

Dental implants are prosthetic devices made from alloplastic material that's implanted into the oral tissues and they are considered a superb alternative for the rehabilitation of teeth. The osseointegration of dental implants is a fundamental prerequisite and a dental implant is considered to be osseointegrated when "direct functional and structural connection between living bone and the surface of an implant under load" is reached.[1] Before the 1980s, conventional radiographic techniques like intra-oral, cephalometric and panoramic images were accepted as standard methods. It is observed that preoperative diagnosis and planning for implants based on two-dimensional (2D) imaging results in potential risk to vital structures.[2] This 2D imaging does not give information for implant site width, stent for implant positioning and thus causing a greater risk of injury to adjacent anatomical structures such as floor of maxillary sinus or the inferior alveolar nerve.[3]

The recent introduction of cone-beam computed tomography (CBCT) in dentistry has opened up a new horizon in providing a comprehensive preoperative implant size assessment and sophisticated surgical guide in dental implantology. CBCT-3D (Cone Beam Computed Tomography) is an advanced radiographic imaging technology that is currently being developed and utilized in dentistry, with the advantages of accurately depicting three-dimensional (3D) tissue structures, minimal distortion, and low radiation doses.[4] In the evaluation of hard tissues, CBCT is superior to conventional CT and panoramic scans due to the voxel size.[5] The most common uses of CBCT include identifying the 3D anatomy, identifying potential risks of intrusion into vital structures including nerves and blood vessels, assessing bone qualityincluding facial & lingual cortical plates and assessing potential sites for implant.[6] Thus, CBCT can be considered as an appropriate diagnostic tool for 3D preoperative planning.

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Consecutive patients referred from the outpatient department for implant treatment were submitted to clinical examination, panoramic (PAN) radiography and a final CBCT exam.[7] Previous studies suggest that the implant sizes estimated by CBCT images are narrower and shorter than those obtained from panoramic radiographs suggesting that CBCT exams lead to a safer decision.[8] Many studies have confirmed superiority of CBCT over panoramic radiography for detecting anatomical structures and for planning the insertion of dental implants in the mandible and the maxilla and owing to its unique advantages, dental practitioners consider CBCT as an essential tool in performing the preoperative phase of implant surgery, identifying potential bone augmentations and in avoiding perioperative complications.[9] The American Academy of Oral and Maxillofacial Radiology (AAOMR) recently recommended CBCT as the best option for implant planning and also for the prediction of implant size (length, width). Successful implant treatment depends on efficient planning and this should include information on height, width, morphology and density of the bone, as well as identification and location of anatomical landmarks in imaging exams. Implant diameter and bone quality are two major factors that influences the biomechanics of an implant supported prostheses.[10]

A retrospective cross-sectional study was done by Ludmila et al.[3], conducted a study on the impact of cone-beam computed tomography on implant planning and prediction of implant size at Department of Prevention and Oral Rehabilitation, Brazil. This study comprised of 95 implants in 27 patients. Agreement in implant length between initial and final planning was 50.5%. Agreement in implant width between initial and final planning was 69.5%.[11] Maria et al.[4], evaluated the retrospective cross-sectional preoperative implant planning considering alveolar bone grafting needs and complication prediction using panoramic versus CBCT images, the specialist selected one hundred and five partially edentulous patients (77 males, 28 females, mean age: 46 years, range: 26-67 years) seeking oral implant rehabilitation were referred for pre-surgical imaging, imaging consisted of panoramic and CBCT imaging. Agreement between panoramic and CBCT on implant length was 92.1% (n=570) of cases. There was 88.5% (n=548) agreement between panoramic and CBCT for implant width. The rationale of the current research is to basically based on accurate implant planning requires precise measurement of bone dimensions. Panoramic radiographs, though commonly used, may lead to errors due to distortion and magnification. CBCT offers 3D imaging and more accurate assessment of implant length and width and resolve pre and post complications. This study aims to compare implant dimensions planned using panoramic images versus CBCT. The findings will help determine the reliability of each method in clinical implant planning

To determine the agreement between CBCT vs panoramic images for implant length and width in Out Patient Department in Bakhtawar Amin Dental Hospital.

METHODS

This Cross-sectional study was conducted at Department of Operative Dentistry, Bakhtawar Amin Dental Hospital, Multan during Jan-Oct 2025. Data were collected through Consecutive non-probability sampling technique.

Sample size was calculated using the findings of Ludmila et al., who reported initial and final implant planning. Sample size was calculated by using the WHO Sample size calculator. The confidence level of study was kept at 95%, margin of error was 10% to calculate the sample size. This gives the sample size of 97. The inclusion criteria for this study comprised adult patients, both male and female, aged between 18 and 55 years, presenting with single or multiple edentulous spaces in the mandible or maxilla. Conversely, the exclusion criteria eliminated patients with conditions that could potentially compromise the outcomes, including confirmed pregnancy (verified by ultrasound), local bone diseases such as osteoporosis or osteomyelitis, and uncontrolled diabetes mellitus (blood glucose levels exceeding 125 mg/dl). Additionally, individuals who smoked more than 10 cigarettes per day, those selected for bone grafting procedures, and patients on bisphosphonate therapy were also excluded from the study.

Ethical approval for the study was obtained from

the institutional ethical review board of Bakhtawar Amin Medical and Dental College, Multan (Ref. No. 419/22) prior to data collection. The study included 97 edentulous sites from patients visiting the Operative Dentistry Department of Bakhtawar Amin Dental Hospital, Multan. Demographic details (age, gender), implant location, panoramic scans, and CBCT images were collected. After obtaining informed consent from the participants (Attached Annexure A), CBCT images were acquired using a CBCT scanner (Carestream DENTAL 9600), with a field of view of 50 x 37 mm and voxel size of 75µm. The operating parameters for the scan were set to 120kVp and 6.3mA with a scanning time of 15 seconds. Measurements for CBCT and panoramic images were evaluated using the Carestream Dental Imaging Software 3D Module v2.4 (Carestream Health, Inc). The obtained data, including the anterior and posterior edentulous areas, were recorded on a performa (attached).

Data were entered and analyzed using SPSS version 27 for Windows. Descriptive statistics, including means and standard deviations, were calculated for age, implant length, and width as measured on CBCT and panoramic images. Frequencies and percentages were calculated for gender, implant location, and agreement between CBCT and panoramic images. Data were stratified according to age groups, gender, and implant location to assess their impact on the agreement between CBCT and panoramic imaging. Post-stratification chi-square tests were applied, with a significance level set at $p<0.05$.

RESULTS

Data were collected from 97 patients, with a mean age of 42.5 ± 4.56 years, and participants ranged from 18 to 55 years. The sample consisted of 45 males (46.4%) and 52 females (53.6%). Implant locations were distributed across both arches, with 45 sites (46.4%) in the mandibular arch and 52 sites (53.6%) in the maxillary arch, indicating a balanced representation of both gender and implant locations.

The mean implant length measured by CBCT was 10.3 mm (SD = 1.4), while panoramic radiography yielded a mean length of 10.1 mm (SD = 1.5). For implant width, CBCT measured a mean of 4.6 mm (SD = 0.6), while panoramic radiography showed a mean of 4.5 mm (SD = 0.7).

TABLE-I

Demographic and baseline values of study participants

Demographic/ Baseline Characteristic	Value
Mean Age	42.5±4.56 years
Age Range	18 - 55 years
Gender	
Male	45 (46.4%)
Female	52 (53.6%)
Implant Location	
Mandibular Arch	45 sites (46.4%)
Maxillary Arch	52 sites (53.6%)

TABLE-II

Implant measurement data (CBCT vs. Panoramic)

Type of Imaging	Implant Measurement	Mean (mm)	Standard Deviation (mm)
CBCT	Length	10.3	1.4
	Width	4.6	0.6
Panoramic view	Length	10.1	1.5
	Width	4.5	0.7

The correlation for implant length was very strong at 0.92 ($p < 0.01$), while for implant width, it was moderate at 0.84 ($p < 0.01$), indicating a statistically significant agreement between the two imaging modalities. When analyzed by gender, the agreement was higher in males ($r = 0.91$ for length, $r = 0.80$ for width) compared to females ($r = 0.89$ for length, $r = 0.78$ for width). Regarding implant location, stronger agreement was observed in the mandibular arch ($r = 0.94$ for length, $r = 0.87$ for width) compared to the maxillary arch ($r = 0.89$ for length, $r = 0.81$ for width).

For implant length, the majority of measurements in both CBCT and panoramic radiography fell within the "Medium" category (10-12 mm), with 53 sites (54.6%) for CBCT and 48 sites (49.5%) for panoramic radiography. In the "Short" (<10 mm) category, CBCT recorded 28 sites (28.9%) compared to 31 sites (32.0%) for panoramic radiography. For the "Long" (>12 mm) category, CBCT showed 16 sites (16.5%) and panoramic radiography showed

18 sites (18.6%).For implant width, the majority of measurements were categorized as "Medium" (4-6 mm), with 64 sites (66.0%) in CBCT and 59 sites (60.8%) in panoramic radiography. The "Narrow" (<4 mm) category accounted for 20 sites (20.6%) in CBCT and 22 sites (22.7%) in panoramic radiography. The "Wide" (>6 mm) category was the least common, with 13 sites (13.4%) in CBCT and 16 sites (16.5%) in panoramic radiography.

TABLE-III

Agreement between CBCT and panoramic imaging

Implant Measurement	Correlation Coefficient (r)	P-Value
Length	0.92	<0.01
Width	0.84	<0.01
Gender		
Male	0.91	0.80
Female	0.89	0.78
Implant Location		
Mandibular Arch	0.94	0.87
Maxillary Arch	0.89	0.81

TABLE-IV

Frequency of implant length and width categorization based on imaging modalities

Implant Measurement	Category	CBCT Frequency (%)	Panoramic Frequency (%)
Length	Short (<10 mm)	28 (28.9%)	31 (32.0%)
	Medium (10-12 mm)	53 (54.6%)	48 (49.5%)
	Long (>12 mm)	16 (16.5%)	18 (18.6%)
Width	Narrow (<4 mm)	20 (20.6%)	22 (22.7%)
	Medium (4-6 mm)	64 (66.0%)	59 (60.8%)
	Wide (>6 mm)	13 (13.4%)	16 (16.5%)

CBCT demonstrated a higher overall success rate, with 89 sites (91.8%) achieving complete success, where the predicted implant size accurately matched the ideal implant dimensions. In contrast, panoramic radiography had a lower success rate, with 76 sites (78.4%) achieving complete success. For moderate success, where the implant size was close but not ideal, CBCT showed 6 sites (6.2%) while panoramic radiography had 16 sites (16.5%). Failure, where the implant size was incorrectly predicted, occurred in 2 sites (2.1%) for CBCT and 5 sites (5.2%) for panoramic radiography.

FIGURE-1

Implant Length Categories Comparison between CBCT and Panoramic Radiography

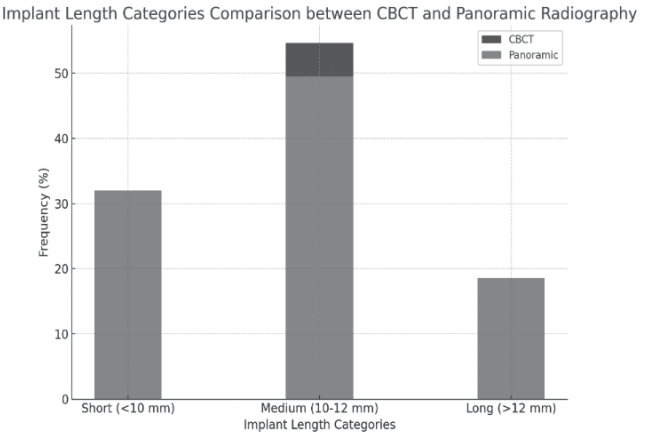


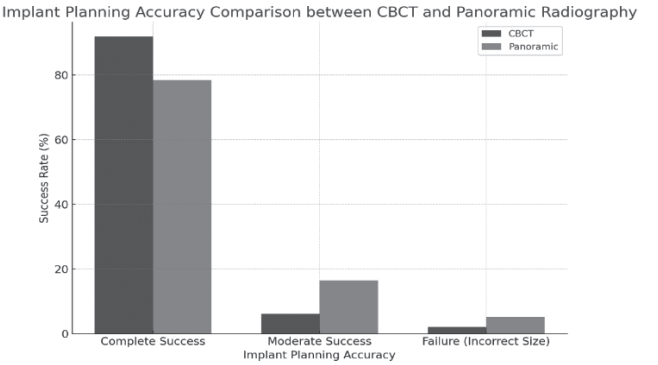
TABLE-V

Comparison of implant planning success rate using CBCT and panoramic imaging

Implant Planning Accuracy	CBCT Success Rate (%)	Panoramic Success Rate (%)
Complete Success	89 (91.8%)	76 (78.4%)
Moderate Success	6 (6.2%)	16 (16.5%)
Failure (Incorrect Size)	2 (2.1%)	5 (5.2%)
Total	97 (100%)	97 (100%)

FIGURE-2

Implant Planning Accuracy Comparison between CBCT and Panoramic Radiography



DISCUSSION

The present study aimed to compare the efficacy of Cone Beam Computed Tomography (CBCT) and panoramic radiography in implant planning, with a focus on predicting implant size and placement accuracy. The results demonstrated that CBCT significantly outperforms panoramic radiography,

offering higher precision in determining both implant length and width. This aligns with findings from previous studies that have shown CBCT to be superior in providing three-dimensional imaging, which is essential for accurate implant placement. The results of the implant measurements, including mean lengths and widths, revealed that CBCT provided more accurate dimensions compared to panoramic radiography. For implant length, CBCT showed a mean of 10.3 mm (SD = 1.4), while panoramic radiography showed a mean of 10.1 mm (SD = 1.5).[12] Although the differences between the two imaging modalities were minimal, the agreement between the measurements was stronger for CBCT, with a correlation coefficient of 0.92 ($p < 0.01$). This high degree of agreement emphasizes CBCT's ability to offer a more detailed and precise assessment of implant size, particularly when compared to panoramic radiography, which often suffers from distortions and superimposition of anatomical structures.[13]

The moderate agreement in implant width measurements between CBCT (r = 0.84) and panoramic radiography further suggests that while panoramic radiography can offer valuable preliminary information, CBCT provides a more reliable assessment, especially in cases where implant width is critical for achieving proper osseointegration and avoiding damage to adjacent structures. The data supports the growing use of CBCT in dental practices, particularly for complex cases that require a higher degree of precision. Stratification by gender and implant location revealed subtle variations in the agreement between the two imaging modalities.[14] While both male and female groups showed high levels of agreement for implant length, males had slightly higher correlation coefficients for both length (r = 0.91) and width (r = 0.80). This may be attributed to anatomical differences in bone structure, which could affect the accuracy of panoramic radiography. Additionally, implant location played a role in the agreement between CBCT and panoramic radiography. A comparable analysis of vertical bone height measurements demonstrated a strong correlation between CBCT and panoramic radiography (r = 0.87), reinforcing the diagnostic value of panoramic imaging in initial treatment planning. However, CBCT showed superior accuracy in detecting anatomical variations such as sinus floor contours and alveolar crest resorption, which are critical for precise implant placement and grafting procedures. This advantage becomes particularly relevant in posterior maxillary regions, where overlapping anatomical structures can obscure details in panoramic images. Stratified analysis by jaw region revealed that correlation coefficients were higher in the mandible (r = 0.89) than in the maxilla (r = 0.82), possibly due to the greater density and less anatomical complexity of mandibular bone. These findings support the complementary use of CBCT, especially in cases involving compromised or variable bone morphology, and underscore its growing importance in advanced implant diagnostics. The mandibular arch showed stronger agreement for both length (r = 0.94) and width (r = 0.87) compared to the maxillary arch. The maxilla's complex anatomy, including the presence of sinus cavities and the less predictable bone density, may contribute to the lower accuracy of panoramic radiographs.[15] The study also examined the success rate of implant planning based on the accuracy of predicted implant sizes.

A significant difference was observed between CBCT and panoramic radiography, with CBCT achieving a higher success rate of 91.8%, compared to 78.4% for panoramic radiography. These findings highlight the critical importance of accurate imaging in the success of implant procedures.[16] In the CBCT group, the majority of cases (89%) resulted in complete success, where the predicted implant size matched the ideal implant dimensions. In contrast, panoramic radiography had a higher incidence of moderate success (16.5%) and failure (5.2%), suggesting that panoramic radiographs are more prone to errors in implant size estimation. The superior accuracy of CBCT in predicting implant size and placement has significant clinical implications. CBCT allows for comprehensive 3D visualization of the bone structure, including bone density, volume, and proximity to vital anatomical structures such as nerves and blood vessels.[17] This enhances the clinician's ability to make more informed decisions, reducing the risk of complications during implant surgery.

Although panoramic radiography remains a useful

tool for initial screening and evaluation, CBCT provides a more reliable and detailed assessment, particularly in complex cases or when precise measurements are critical for the success of the implant.[18] Despite the advantages of CBCT, it is important to acknowledge its limitations. CBCT is associated with higher radiation doses compared to conventional panoramic radiography, although the dose is still relatively low compared to medical CT scans.[19] Additionally, CBCT requires more advanced equipment and technical expertise, which may not be available in all clinical settings. Future studies should aim to explore the cost-effectiveness of CBCT in different clinical scenarios and investigate the long-term outcomes of implant success by using small voxel size imaging techniques, modern algorithms and interactive reconstruction techniques.

CONCLUSION

It is concluded that Cone Beam Computed Tomography (CBCT) significantly outperforms panoramic radiography in terms of accuracy and precision for implant planning. The study demonstrated a strong agreement between CBCT and panoramic radiography for implant length measurements, with CBCT providing more reliable results overall. While panoramic radiography remains a useful tool for initial screening, CBCT offers superior 3D imaging that is critical for detailed implant placement, particularly in complex cases. The higher success rate in implant planning using CBCT further supports its role as the preferred imaging modality for dental implant procedures.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Risk factors, microbiology and clinical outcomes of puerperal sepsis.

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ABSTRACT… Objective: To determine the factors leading to the development puerperal sepsis. A secondary objective was to determine the pattern of bacterial spectrum in-hospital mortality to puerperal sepsis in our local population. **Study Design:** Descriptive Cross-sectional study. **Setting:** A Tertiary Care Hospital Department of Gynaecology and Obstetrics, Unit 3, Civil Hospital Karachi. **Period:** 4th March 2022 to 22nd September 2022. **Methods:** The study recruited post-delivery women with clinical diagnosis of puerperal sepsis. Socio-demographic, clinical and obstetric information, factors leading of termination of pregnancy and in-hospital mortality were collected. **Results:** 177 Puerperal sepsis patients presenting with fever, lower abdominal pain, and foul-smelling lochia were analysed. The average age of the patients was 30.2 (± 7.4) years, ranging between 20-45 years. Mean gestational age was 37.9 (± 3.4) weeks. Majority (85%) were delivered after 36 weeks. Risk factors for puerperal sepsis included caesarean section in 137 (77.4%), anaemia in 105(59.3%) and diabetes in 4 (7.9%). A total of 108 (61.1%) blood cultures were positive. The most common organism was staphylococci aureus (32.2%) followed by E. coli (14.7%), klebsiella pneumonia (7.9%) and streptococcus pyogenes (1.1%). Both pseudomonas and proteus were observed in 2.8% cases. It has observed that 16 (9%) died during hospital stay. **Conclusion:** Caesarean delivery, anaemia and diabetes were associated with high risk of puerperal sepsis. Most of the bacterial infection was found to be caused by Staphylococcus Aureus which accounted for 57 [32.2%].

Key words: Antimicrobial Susceptibility, Blood Culture, Bacterial Spectrum, In-hospital Mortality, Puerperal Sepsis, Termination of Pregnancy, World Health Organization (WHO).

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INTRODUCTION

The World Health Organization (WHO) defines puerperal sepsis as an infection of the genital tract that occurs during labour or within 42 days following childbirth.[1] It is a highly preventable and treatable condition, occurring in 1-8% of all deliveries, associated with significant morbidity and mortality. Half of the maternal deaths related to childbirth during the 18th and 19th century, were due to puerperal sepsis and it was the single most common cause of maternal mortality. Puerperal Sepsis was the most common cause of maternal mortality (30.9%), followed by obstetric haemorrhage and hypertensive disorders of pregnancy according to a study conducted in a tertiary care hospital of Uganda.[2] According to the WHO, 15% of the 358,000 maternal deaths occurring during labour and childbirth were attributed to sepsis.[3] Now when we are in the 21st century, it is still one of the main obstetric clinical complications in developed and developing countries both, despite the availability of low-cost antibiotics and the application of standard aseptic techniques. Home deliveries in unhygienic conditions, low socioeconomic status, poor nutrition, primiparity, anaemia, prolong rupture of membranes, multiple vaginal examinations and caesarean sections are key predisposing factors that contribute to the development of sepsis.[4] Delivery by an untrained traditional birth attendant/ Dai, traditional practices such as insertion of foreign objects and substances into vagina, delay in reaching appropriate level of health facility due to lack of transportation and resources, cultural factors which delay care seeking behaviour also contribute to this major public health problem and posing a significant challenge to overburdened health care system. Puerperal sepsis is caused by a variety of different aerobic and anaerobia microorganisms and is frequently a polymicrobial infection. Escherichia Coli is commonly reported as a major cause of severe maternal sepsis originating from the genital tract.[5,6]

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Additionally, Group A Streptococcus, Staphylococcus aureus, Streptococcus spp., Klebsiella species, Pseudomonas spp. and anaerobes are implicated in the majority of cases.[6] Among these group A streptococci is the most feared pathogen.[7] Puerperal infections delay postpartum restoration, requires women to be hospitalized for prolonged period and interfere with the bonding between mother and newborn.

In Pakistan, specially in rural areas still a big proportion of women are delivering at home by untrained personnel in unhygienic environment resulting in an increased incidence of puerperal sepsis accounting for about 16.3% of maternal mortalities.[8] According to a study conducted in Civil Hospital Karachi Gynae unit III in 2005-2008, 6.7% maternal mortalities were due to puerperal sepsis.[9] It causes a considerable impact on the neonate, with 1 million neonatal deaths attributed to maternal infection or sepsis annually.[10] Incidence and mortality rate varies among different studies conducted in different regions of Pakistan as many cases go undiagnosed and unreported. Kajeguka et al evaluated patients presenting with puerperal sepsis and factors leading to its development (postpartum haemorrhage 57.1%, caesarean delivery 66.7%, vaginal delivery 33.7%, diabetes mellitus type II 4.8% and anaemia 66.7%).[10] Tamboli et al study showed klebsiella pneumonia (28.26%), staphylococci aureus (21.73%), pseudomonas aeruginosa (19.5%), proteus (10.8%), E. Coli (8.69%) and streptococcus (6.52) isolated in patients with puerperal sepsis.[11] Khaskheli et al found in-hospital mortality in puerperal sepsis to be 8.52%.[12] Among the leading causes of preventable maternal morbidity and mortality in developing countries are maternal infection or sepsis. The progression of sepsis is lethal hence early identification may help reduce further complications.

Very few research has been conducted locally, particularly on bacterial aetiology relating to puerperal sepsis. It is widely recognized that bacterial infection patterns and their antimicrobial resistance are constantly evolving, making regular surveillance of this critical issue essential in all healthcare settings. Hence in this study patients presenting with puerperal sepsis will be analysed so the findings of this study may help to plan implementation of preventive measures and early recognition of this complication that would remarkably reduce the morbidity and mortality associated with it.

OBJECTIVES

1. To determine the factors leading to the development of puerperal sepsis at Civil Hospital Karachi, Sindh.
2. To determine the pattern of bacterial spectrum in patient presenting with puerperal sepsis.
3. To determine the in-hospital mortality in patient presenting with puerperal sepsis.

METHODS

A descriptive, observational, cross-sectional study was conducted at the Department of Gynaecology and Obstetrics, Unit 3, Civil Hospital Karachi from March 4, 2022, to September 22, 2022.

A total of 176 patients were included in the study. The sample size was determined using a Prevalence rate of vaginal delivery of 33.7%[10], a margin of error of 7% and a confidence level (C.I) of 95%. The WHO sample size calculator was employed to compute the required sample size.

- **Inclusion Criteria**

Patients presenting with fever, lower abdominal pain, and foul-smelling lochia after delivery were included in the study after receiving a valid informed consent from the patients.

- **Exclusion Criteria**

Patients who presented with fever either during pregnancy, after delivery or following a miscarriage and whose symptoms persisted for more than 42 days were excluded from the study. Additionally, patients presenting with fever due to other medical conditions such as Malaria, Dengue, Typhoid, wound infection (other than episiotomy and C/S), mastitis, UTI or thrombophlebitis were also excluded from the study.

Data Collection Procedure

This study was carried out after seeking a formal approval from the College of Physicians and Surgeons Pakistan (CPCP/REU/OBG-2019-183-9591-30-10-23). Patients presenting to department

of Obstetrics and Gynaecology, Civil Hospital Karachi who met the inclusion criteria and not having the conditions specified in exclusion criteria were enrolled in the study. An informed verbal consent was taken after explaining the purpose of the study. Brief history including demographic data was taken. Patients developing puerperal sepsis were evaluated by the researcher for factors leading to its development (postpartum haemorrhage, caesarean delivery, vaginal delivery, diabetes mellitus type II and anaemia) after confirming on history and medical records at the time of delivery. Specimens for culture were obtained by the researcher. The swabs were sent to microbiology laboratory after being immersed in transport medium. These samples were stored in steriled containers before being transported to the microbiology laboratory after being stored in sterile containers. Suspected positive cultures were sub-cultured to MacConkey agar, Bile Esculin Agar, Mannitol salt Agar, Blood Agar and Chocolate Agar which were incubated for 48 hours at 37 °C in 5 % CO2. Plates which showed growth were considered positive, while those with no growth were classified as negative, as reported by the same microbiologist. Using routine microbiological methods positive growths were subsequently identified. The names of the organisms identified, and the pattern of growth were included in the laboratory data and were indicated by the number of colonies forming units on the culture for each organism, by the microbiologist and reported to the researcher. All patients were followed during stay in hospital and till 2 weeks after discharge. The findings were entered in a pre-designed proforma by the researcher.

Data Analysis

The data were analysed using SPSS Version 20. Mean and standard deviations were calculated for the quantitative variables like maternal age, length of hospital stay, and gestational age. For quantitative variables normally distributed mean and standard deviation was reported while median (IQR) was reported for the non-normality distributed quantitative variables. For the qualitative variables, including residence status, parity, gravida, antenatal care status, rupture of membrane, prolonged labour, family monthly income, educational status, occupational status, factors leading to the development puerperal sepsis, pattern of bacterial spectrum and in-hospital mortality frequencies and percentages were calculated. Effect modifiers including maternal age, residence status, parity, gravida, antenatal care status, rupture of membrane, prolonged labour, family monthly income, educational status and occupational status were controlled through stratification to see the effect of these on outcome variables. P-value of ≤ 0.05 was taken as statistically significant and applied on post stratification chi square test/Fischer test.

RESULTS

177 patients who were diagnosed clinically as Puerperal sepsis presenting with fever, lower abdominal pain, and foul-smelling lochia after delivery, having parity ≥ 1 and women aged between 20 and 45 were part of the study. The average age of the patients was 30.2 (± 7.4) years, ranging between 20-45 years, with median age was 28 years. Most of the patients are aged 20-30 years, accounting for 105 (59%). The average stay of women in the hospital was 7.8 (± 2.3) days, and 151(85.3%) had stayed >= seven days. The mean gestational age of women was 37.9 (± 3.4), and 151(85%) women belonged to gestational age more than 36 weeks. Almost 118(66.7%) women came from urban residential areas. Antenatal Care observed in 57 (32.2%) of the total women. 92 (52%) of women had gravida less than 3. 118(66.7%) women were multiparous, and the remaining 59 (33.3%) were primigravida. 132 (74.6%) women had membranes ruptured for <24 hours, and 135 (76.3%) had labour for <12 hours.

FIGURE-1

Duration of rupture of membranes in women presenting with puerperal sepsis.

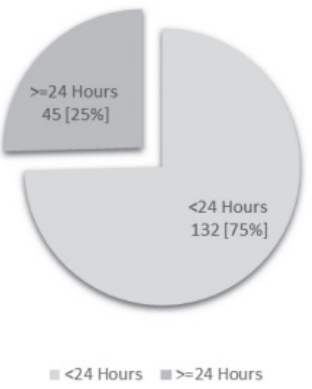


FIGURE-2

Prolonged labour in patients presenting with puerperal sepsis.

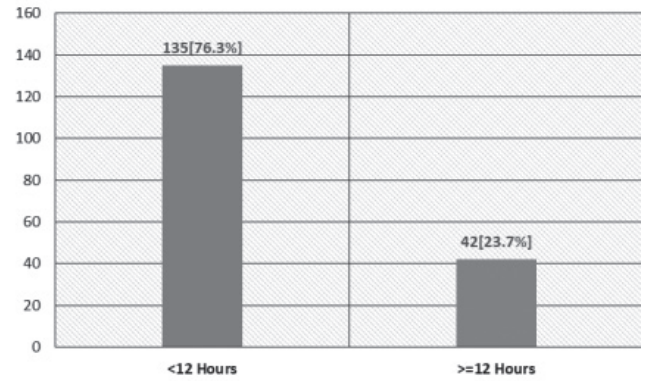
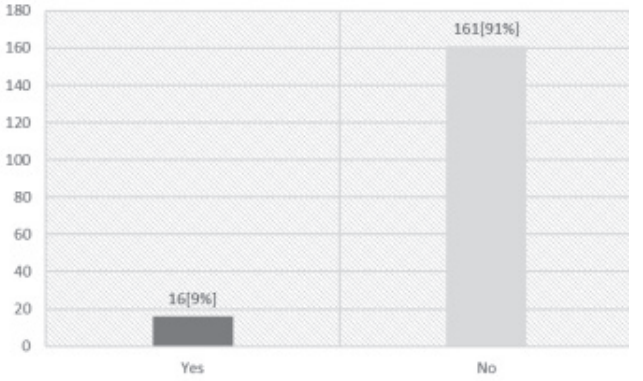


FIGURE-3

Maternal mortality in patients presenting with puerperal sepsis.



Almost all women with a family monthly income had < 50000 PKR, accounting for 176 (99.4%). Majorities were housewives, 176 (99.4%), and one woman was found to be employed. The most common risk factor was caesarean section in 37(77.4%) and anaemia in 105(59.3%) was the second most common factor. Other risk factors included prolonged rupture of membranes (25%), prolonged labour (23.7%), PPH (8.5%) and diabetes (2.3%). A total of 108 (61.1%) blood cultures were positive, with Staphylococci Aureus (32.2%) the most predominant bacteria, followed by 26[14.7%] E-coli, 7.9% were Klebsiella Pneumonia and 1.1% were Streptococcus pyogenes. In comparison, Pseudomonas aeruginosa and Proteus each accounted for 2.8%. 16 (9%) died during hospital stay due to severe sepsis.

TABLE-I

Frequency of Bacterial Spectrum in patients presenting with puerperal sepsis

Bacterial Spectrum	Yes	No
Klebsiella Pneumonia	14 [7.9%]	163 [92.1%]
Staphylococcus Aureus	57 [32.2%]	120 [67.8%]
Pseudomonas Aeruginosa	4 [2.3%]	173 [97.7%]
Proteus Mirabilis	5 [2.8%]	172 [97.2%]
Escherichia Coli	26 [14.7%]	151 [85.3%]
Streptococcus Pyogenes	2 [1.1%]	175 [98.9%]

The comparison of maternal mortality among all demographics and clinical characteristics observed that parity, prolonged duration of labour, family monthly income, and occupation status were significantly associated with maternal outcome.

In contrast diabetes mellitus does not associate with any confounding parameters. It has been observed that anaemia was statistically significantly associated with almost all study parameters. Bacterial infections were compared among all confounding of the parameters.

DISCUSSION

Globally, puerperal sepsis has been proved to be one of the primary contributors to maternal morbidity and mortality. The World Health Organization (WHO) defines puerperal sepsis as an infection of the genital tract that occurs during labour or within 42 days after childbirth. Common symptoms of puerperal sepsis/pyrexia include fever, pelvic pain, foul-smelling vaginal discharge, and delayed uterine involution.[13] In underdeveloped countries, this group of women faces significant challenges due to infective morbidities worldwide. It has several reasons such as due to poverty, illiteracy, or malnutrition. Poor nutritional status and low resistance to the infection during pregnancy leads to increased risk and these women often do not seek antenatal checkups or contraception guidance.

TABLE-II

Comparison of maternal mortality among demographics and clinical characteristics in patients presenting with puerperal sepsis

	Total	Maternal Mortality		P- Value
		Yes	No	
Total	**177**	**16**	**161**	-
Age Groups				
20-30 years	105 [59.3%]	11 [68.8%]	94 [58.4%]	0.421
31-45 years	72 [40.7%]	5 [31.3%]	67 [41.6%]	
Gestational Age (weeks)				
≤ 36 weeks	26 [14.7%]	2 [12.5%]	24 [14.9%]	0.795
≥ 36 weeks	151 [85.3%]	14 [87.5%]	137 [85.1%]	
Length of Hospital Stay				
≤ 7 days	168 [94.9%]	15 [93.8%]	153 [95%]	
≥ 7 days	9 [5.1%]	1 [6.3%]	8 [5%]	0.824
Residence Status				
Urban	118 [66.7%]	12 [75%]	106 [65.8%]	0.458
Rural	59 [33.3%]	4 [25%]	55 [34.2%]	
Antenatal Care Status				
Booked	57 [32.2%]	2 [12.5%]	55 [34.2%]	0.077
Unbooked	120 [67.8%]	14 [87.5%]	106 [65.8%]	
Gravida				
≤ 3	92 [52%]	12 [75%]	80 [49.7%]	0.053
≥ 3	85 [48%]	4 [25%]	81 [50.3%]	
Parity				
Primigravida	59 [33.3%]	9 [56.3%]	50 [31.1%]	0.041*
Multigravida	118 [66.7%]	7 [43.8%]	111 [68.9%]	
Rupture of Membranes				
≤ 24 hours	132 [74.6%]	11 [68.8%]	121 [75.2%]	0.575
≥ 24 hours	45 [25.4%]	5 [31.3%]	40 [24.8%]	
Prolonged Labour				
≤ 12 hours	135 [76.3%]	8 [50%]	127 [78.9%]	0.01*
≥ 12 hours	42 [23.7%]	8 [50%]	34 [21.1%]	
Family monthly income				
≤ 5000 PKR	176 [99.4%]	15 [93.8%]	161 [100%]	0.001*
≥ 5000 PKR	1 [0.6%]	1 [6.3%]	0 [0%]	
Occupational Status				
Employed	1 [0.6%]	1 [6.3%]	0 [0%]	0.001*
Unemployed	176 [99.4%]	15 [93.8%]	161 [100%]	
Educational Status				
Illiterate (never went to school)	132 [74.6%]	13 [81.3%]	119 [73.9%]	
Primary (Class 1-5)	35 [19.8%]	3 [18.8%]	32 [19.9%]	0.775
Secondary (Class 6-Matric)	6 [3.4%]	0 [0%]	6 [3.7%]	
Higher (Intermediate Graduate)	4 [2.3%]	0 [0%]	4 [2.5%]	

Majority of the cases included in this study, were referrals delivered in other health facilities 176 (99.4%) and had undergone induction of labour 37 (20.9%), with inadequate sterilization and lack of aseptic techniques by unskilled personnel. This can lead to significant infective morbidities. Most of the women in our study, 135 (76.3%), had rupture of membranes with duration of less than 12 hours upon admission. In these women, a prolonged second stage of labour led to a higher rate of interventions, including emergency Caesarean section 137 (77.4%) and instrumental vaginal deliveries 22 (17.05%). Similar findings were reported by Shamshad et al.[14], Seale AC et al.[15] and Hussein J et al.[16] who emphasized that specific interventions for the prevention and treatment of infection should include proper hand hygiene, the use of antiseptic solutions and appropriate antibiotic coverage. Proper education, development of national and local guidelines and various technologies are required to control and reduce the rate of infection.[17]

The mortality rate was 16 (9%), as reported by other national studies.[18] According to a study conducted in CHK Gynae unit III in 2005-2008, 6.7% maternal mortalities were due to puerperal sepsis.[9] Maternal infection or puerperal sepsis results in a considerable impact on the neonate, leading to 1 million neonatal deaths annually.[10] Incidence and mortality rate varies among different studies conducted in different areas of Pakistan as many cases go undiagnosed and unreported. Kajeguka et al evaluated patients presenting with puerperal sepsis and factors leading to its development (postpartum haemorrhage 57.1%, caesarean delivery 66.7%, vaginal delivery 33.7%, diabetes mellitus type II 4.8% and anaemia 66.7%).[10] Tamboli et al study showed klebsiella pneumonia (28.26%), staphylococci aureus (21.73%), pseudomonas aeruginosa (19.5%), proteus (10.8%), E. Coli (8.69%) and streptococcus (6.52) isolated in patients with puerperal sepsis.[11] Khaskheli et al found in-hospital mortality in puerperal sepsis to be 8.52%. (12) Managers' roles are not well specified, contributing to poor service quality.[19,20] Prophylactic antibiotics during surgery reduce the risk of endometritis by 66-75% and minimizes the rate of wound infection.[21] In this region of the world, proper education, infection prevention and control trainings regarding antiseptic techniques, and proper antibiotic cover need to be improved significantly. Prolonged rupture of membranes[22] and prolonged labour[23] are significant risk factors that contribute to infection around the time of delivery as prolonged opening of the cervix, and the impairment of natural barriers that prevent ascending infections from the vagina.[14] Multiple vaginal examinations[38] and using unclean material to control the flow of lochia[24] are significant risk factors and should be avoided during labour and delivery. Intrapartum bleeding, perineal tears, and stillbirth are other determinants during labour and delivery.[25] The low socioeconomic status of mothers[24], which may be linked to illiteracy, limited access to antenatal care, poor hygiene, and overall health[14-16,19,20,22,24], represents key community level risk factors for puerperal sepsis.

Many traditional practices have been observed to result in poor hygiene, such as not taking a bath in the postpartum period, and this highlights the need to focus on the socio-cultural reasons which might be facilitating puerperal infection. These observations align with the findings from the reviews conducted in developing countries and sub-Saharan Africa.[15] However, the relative importance of risk factors may vary depending on the region and setting. Caesarean section has been identified as a key factor contributing to puerperal infection in several reviews.[13-26]

This might explain the increasing rates of puerperal sepsis in healthcare facilities, driven by the rising trend of assisted deliveries particularly caesarean sections. In this systematic review, risk factors for puerperal sepsis were identified from the studies where it was a secondary objective and therefore the investigation was not comprehensive. Mortality from puerperal sepsis which is an essential indicator of the magnitude of this condition was not investigated as an outcome in this review. Puerperal sepsis, if not diagnosed and managed timely, can rapidly worsen resulting in significant morbidity[22], leading to severe septicaemia and ultimately death. The highest proportion of global maternal deaths in South Asia results from sepsis at 13.7%, resulting in 107,000 maternal deaths between 2003 and 2009[26] and approximately 9,400 deaths in 2013.[27] Hence, puerperal sepsis remains a significant

problem in South Asia, despite of having a relatively low estimated prevalence, due to potentially severe sequelae and its impact on maternal mortality. The most common microorganisms causing puerperal sepsis include Escherichia coli, staphylococcus aureus, and Streptococcus species. Other organisms include Klebsiella, Clostridium sordellii, Mycoplasma, Chlamydia, and coliform bacteria.[28] In a prospective cohort study involving 151 women with puerperal sepsis, the authors discovered that the most common bacterial isolates were E. coli (30.6%) and Klebsiella pneumoniae (15.3%), followed by coagulase-negative staphylococci and S. aureus.[29] This study observed that primiparity, lack of antenatal care, and caesarean delivery were significant factors for developing puerperal sepsis. In addition, it was observed that maternal anaemia, prolonged labour, and prolonged rupture of membranes was associated with a significantly higher risk of developing puerperal sepsis compared to other factors, as highlighted in a study by Maharaj D et al.[30] Burrows LJ et al. found that primary caesarean delivery with the trial of labour resulted in 21.2-fold increased risk of endometritis compared to spontaneous vaginal delivery. Women who underwent primary caesarean section, even without undergoing a trial of labour, were 10.3 times more likely to develop endometritis as compared to those who had spontaneous vaginal delivery.[31] This risk persisted even after prophylactic antibiotics were administered to all cases undergoing caesarean section, as recommended by the RCOG green top guidelines. Therefore, it is necessary to review our antibiotic policy and asses their effectiveness. Additionally, as the rates of caesarean sections are rising in developed as well as developing countries, it is suggested the incidence of puerperal pyrexia is expected to rise in the coming years. In a study conducted by Bako B et al., the most isolated microorganism were Staphylococcus aureus and Escherichia coli.[32] Several factors, including the mode of delivery (caesarean section), postpartum haemorrhage, moderate to severe anaemia, and prolonged labour were statistically associated with puerperal sepsis in both this study, and previous research. Puerperal sepsis was specifically correlated with the mode of delivery. Some data suggest that mothers who gave birth via spontaneous vaginal delivery were more likely to develop puerperal sepsis compared to those who had a caesarean section. These findings contrast with studies conducted in Ethiopia and Nigeria.[32] Additionally, this differs from a study in Uganda, which identified caesarean delivery was an independent risk factor for puerperal sepsis.[33]

In contrast to a study conducted in Ethiopia, which found that women who underwent caesarean sections had a lower risk of developing puerperal sepsis compared those who had a spontaneous vaginal delivery.[34] This study found that prolonged labour was strongly associated with an increased risk of puerperal sepsis. According to a study by Demisse et al.[33,35], participants with labours lasting 12 to 24 hours or longer than 25 hours had 3.1 and 4.7 times, respectively, the risk of developing puerperal sepsis compared to those with labours lasting less than 12 hours. The current study also identified anaemia as a major risk factor for puerperal sepsis. A study conducted in Kenya similarly found that anaemia is indirectly associated with both maternal mortality and puerperal sepsis.[36] To understand how anaemia contributes to puerperal sepsis more research is required. This study provides valuable insights for designing effective Reproductive Health Control Plans aimed at reducing the prevalence of puerperal sepsis and its associated morbidity among postnatal women receiving hospital care. This study also found that multiple vaginal examinations were associated with puerperal sepsis, with 77(51%) cases having undergone more than five vaginal examinations. This is consistent with a study conducted in Egypt, which found that having more than five vaginal examinations increased the risk of developing puerperal sepsis.

Similarly, a systematic review in South Asia demonstrated that frequent vaginal examination with unwashed hands significantly raised the risk of puerperal sepsis.[37] A study in Kenya reported that women who underwent two or more vaginal examinations were 3.95 times more prone to develop puerperal sepsis.[14-17,27,29,37,38] Recurrent manipulation of the genital tract increases the risk of transferring microorganisms from the lower genital tract, thereby increasing the likelihood of developing puerperal sepsis. In this study, 74 mothers (49.3%) with puerperal sepsis had prolonged labour lasting

more then 12 hours. Research from Kenya[39], Nepal[38], and Tanzania[39] summarized that the duration of labour contributes to the risk of puerperal sepsis, prolonged labour often leads to multiple and frequent vaginal examinations. Maternal sepsis is associated with significant morbidity and mortality which can be prevented by increasing awareness among antenatal women to seek regular antenatal care and visit for antenatal check-up as per the recommended schedule, identification of risk factors, and delivery in an aseptic and sterilized environment by trained healthcare personnel.

CONCLUSION

The mode of delivery, postpartum haemorrhage, prolonged labour, and anaemia are significant risk factors linked to puerperal sepsis. Majority of the bacterial infections were found to be due to Staphylococci Aureus which accounted for 57 [32.2%] of cases. However, it is recommended that to draw a firm and concrete conclusion further study with larger sample sizes may be conducted at local, regional and national levels. It is recommended that a surveillance system should be developed by the Pakistan Health Service to establish a monthly reporting system for reporting cases of puerperal sepsis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Faryal Rasheed:** Research proposal, data collection.
2	**Falak Naz Baloch:** Data analysis, manuscript writing.
3	**Rumsha Mallick:** Data collection.
4	**Atrooba Ismail:** Data collection.
5	**Zakir Ali Punar:** Data analysis, final editing.

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ORIGINAL ARTICLE

Age estimation from iliac crest epiphyseal fusion by conventional radiographic techniques.

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ABSTRACT… Objective: To determine the correlation between radiological age estimation from iliac crest fusion and actual chronological age. **Study Design:** Cross sectional study. **Setting:** Forensic Medicine & Toxicology Department, King Edward Medical University, Lahore and Radiology Department, Mayo Hospital, Lahore. **Period:** 01-08-2023 to 31-01-2024. **Methods:** Data collection & analysis: Digital X-rays of the pelvis of 80 individuals showing iliac crest in antero-posterior view were taken. The radiographic age was estimated. Then actual age of patients was noted from national identity card, form B, birth certificate of the municipal committee or hospital, school certificate and driving license. Demographic data (name, gender, ethnicity, occupation) was also recorded. Data was entered and analyzed in SPSS Version 20. **Results:** There were 51(63.7%) males and 29(36.25%) females. The mean estimated age on X-ray was 20.10+2.19 years. The correlation coefficient (r) value of estimated age (years) on X-ray was 0.964 which indicates very strong positive correlation with actual age and was significant ($p<0.0001$). Males showed stronger positive correlation($r=0.976$, $p<0.0001$) with estimated age (years) on x-ray as compared to females. **Conclusion:** It can be concluded from the study that mean age observed on X-ray was almost same as actual age, among all the individuals. There is strong correlation coefficient (r) of estimated age (years) on X-ray with actual age, and p value was significant.

Key words: Actual Age, Correlation, Ethnicity, Estimated Age, Iliac Crest Fusion, Occupation, X-ray.

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INTRODUCTION

Identification is required both in the living and the dead. Of the various parameters for establishment of personal identity, age determination is of paramount importance. The reliability of various regions of the skeleton to determine age differs at different age groups such as fetus, children, adolescence, adult, and elderly. Hence, expertise of forensic expert is required to determine the age in such cases.[1-3]

Besides physical examination, radiography of various bones and joints is used for determination of age. Lot of work has been done in this field and many studies have been conducted on estimation of age from examination of human bones by anatomists and anthropologists. Almost every bone has been used for this purpose.[4-8] The epiphyseal union at different sites in body occurs at different ages, thus allowing wide range of age estimation. Estimation of age from examination of almost every part of human skeleton to establish identity of the deceased has been done.[4-8]

In previous studies, age is estimated from iliac bone by using X-Rays, ultrasonography, computed tomography and magnetic resonance imaging. However, these studies have been conducted using various methods but there is no standard method yet documented. Among these age determinant methods, radiography of the bony skeleton focusing on appearance and union of ossification centers is regarded as having greater accuracy and reliability by the legal and medical authorities as the epiphyseal union of every bone takes place at a specific age.[9-11]

Since iliac crest ossifies relatively late, it is of use to estimate age after attaining age of majority. Estimation of age from radiological examination of iliac crest can be of use in medicolegal cases such as establishment of identity, age of majority, valid age of marriage for both sexes, criminal responsibility, right to cast vote in elections, eligibility for contesting elections, consent for participation in sports with risk to life.[11]

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A study reported that on radiological examination of pelvic bone, the correlation between estimated age and actual age was r=0.964 (R^2 =0.9688) while another study showed a positive significant correlation between age and iliac crest ossification (males: right side, r= 0.719; P=0.0001, left side r-0.716; P=0.0001, girls: right side, 0.724, left side, r=0.700; P=0.0001).[12,13]

Use of pelvic bone for assessment of age of an individual for medicolegal purpose can be highly reliable due to very strong positive correlation observed. However, local evidence is lacking in our region so this study is conducted.

METHODS

This Cross sectional study was conducted at Forensic Medicine & Toxicology Department, King Edward Medical University, Lahore and Radiology Department, Mayo Hospital, Lahore for Six months from 01-08-2023 to 31-01-2024. The sample size of 80 cases is calculated with 5% type I error, 10% type II error and value of correlation coefficient between chronological age and estimated age on X-ray i.e. r=0.964.[12] Sampling technique was Non Probability, Consecutive sampling.

Inclusion Criteria

Healthy alive candidates of age 17-25 years, both genders were included presenting to Forensic medicine department for medicolegal purposes.

Exclusion Criteria

Patients with fracture or surgery of hip joint (on medical record), patients with tuberculosis, carcinoma or metastasis (on medical record), osteomalacia, muscular or skeletal dystrophy, cerebral palsy, Down's syndrome, rheumatoid arthritis.

Eighty healthy alive candidates of both genders between 17-25 years of age were enrolled in the study. They were referred to Radiology Department, Mayo hospital Lahore after taking written informed consent. Demographic data (name, gender, ethnicity, occupation) was noted. Then patient underwent X-ray by a single radiologist having 4 years experience in radiology. Digital X-rays (antero-posterior view) of the pelvis showing iliac crest was taken. Stage of epiphyseal union of iliac crest was noted on the X-ray film. The radiographic age was estimated. Then actual age of patients was noted from national identity card, form B, birth certificate of the municipal committee or hospital, school certificate, driving license. All the data was noted on a specially designed proforma.

Data entry and analysis was done through SPSS version 20. Quantitative data like estimated age on radiograph and actual age was presented as mean and SD. Frequency and percentage were calculated for gender, ethnicity and occupation. Pearson's correlation coefficient was calculated to measure correlation between estimated age on radiograph and actual age. p-value ≤0.05 was taken as significant. Data was stratified for gender, ethnicity and occupation. Post-stratification, Pearson's correlation coefficient was calculated to measure correlation between estimated age on radiograph and actual age for each stratum. p-value ≤0.05 was taken as significant.

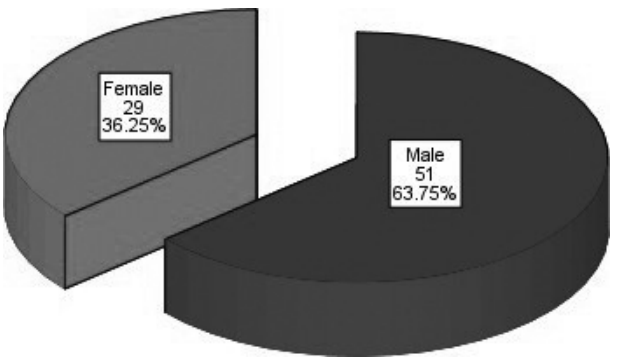
Ethical approval was obtained from institutional review board vide letter ref. no. 489/2023 dated 13-07-2023.

RESULTS

Of the 80 individuals, there were 51(63.7%) males and 29(36.25%) females. Figure-1

FIGURE-1

Gender distribution

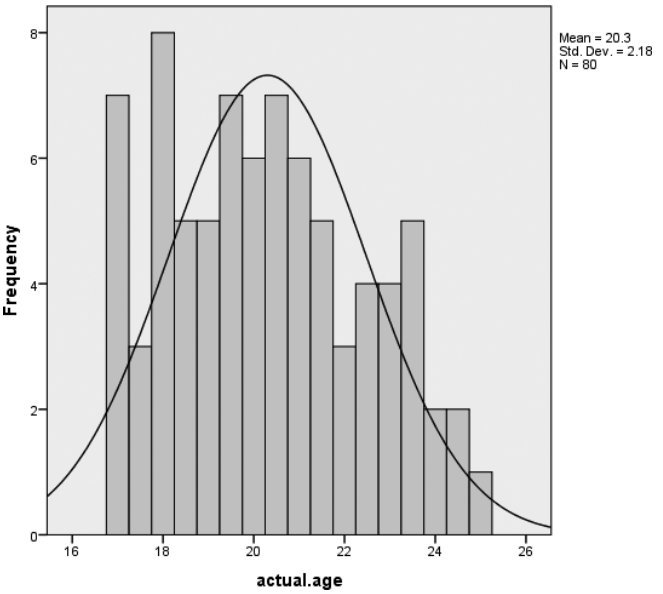


The mean age estimated on X-ray was 20.10±2.19 years with minimum and maximum value 17.0 and 24.0 while the mean actual age was 20.30 ± 2.18

years with minimum and maximum value 17.0 and 25.0. (Figure-2)

FIGURE-2

Descriptive Analysis of Estimated Age on X-ray and Actual age



The correlation coefficient (r) value of estimated age (years) on x-ray was 0.964 which indicates a strong positive significant correlation between them (p<0.0001).Table-I, Figure-3

TABLE-I

Correlation between estimated age (years) on X-ray with actual age

		Age (years)
EAO_X-Ray	Pearson Correlation	0.964
	Sig.(2-tailed)	0.000
	N	80

According to gender, male had strong positive correlation (r=0.976, P<0.0001) with estimated age (years) on x-ray as compared to female showing moderate positive correlation (r=0.932, P<0.0001). Table-II

As in occupation, for prediction of employee age, strong positive correlation was observed i.e. r = 0.950 (p<0.0001). In laborers and nursing students, correlation was highest i.e. r>0.999, (P <0.0001) whereas moderate positive significant correlation was seen in students (r=0.960, P< 0.01) and workers (r=0.971, P<0.01) respectively. (Table-III)

FIGURE-3

Descriptive Analysis of Estimated Age on X-ray and Actual age

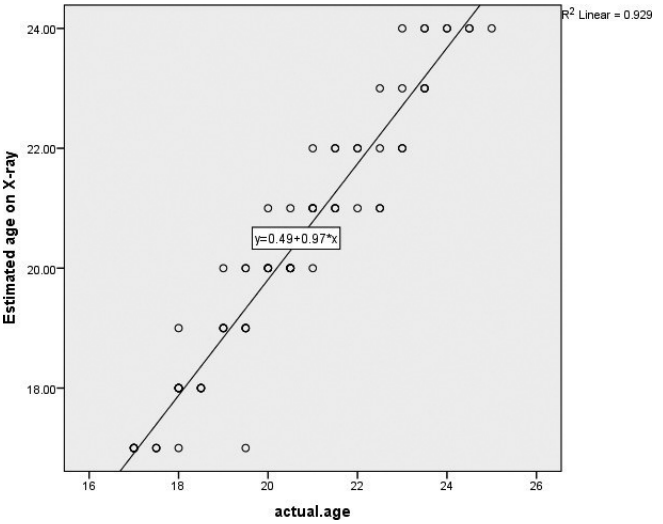


TABLE-II

Correlation between estimated age on X-ray with gender

Gender			Age(years)
Male	EAO_X-Ray	Pearson Correlation	0.976
		Sig.(2-tailed)	0.000
		N	51
Female	EAO_X-ray	Pearson Correlation	0.932
		Sig.(2-tailed)	0.000
		N	29

On the variable of ethnicity, strong positive correlation was observed in Punjabis (r=0.976, p<0.01) followed by Pathans and Urdu speaking (r=0.963 & 0.951, p<0.01) with estimated age on X-ray respectively. (Table-IV)

The relation between actual age and iliac crest fusion in males showed that complete fusion of iliac crest (stage V) occurred at 21.91 ±1.64 years. (Table-V)

The relation between actual age and iliac crest fusion in females revealed that complete fusion (stage V) occurred at 20.98 ±1.52 years. (Table-VI)

TABLE-III

Correlation of estimated age on X-ray with occupation

Occupation	Estimated age on X-ray	Actual Age
Auto mechanic	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Butcher	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Chef	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Car business	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Doctor	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Employee	Pearson Correlation	.950**
	Sig.(2-tailed)	.000
	N	17
Laborer	Pearson Correlation	1.000**
	Sig.(2-tailed)	.000
	N	5
Maid	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Medical student	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Nursing student	Pearson Correlation	1.000**
	Sig.(2-tailed)	.000
	N	3
Property dealer	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Student	Pearson Correlation	.960**
	Sig.(2-tailed)	.000
	N	39
Sweeper	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Worker	Pearson Correlation	.971**
	Sig.(2-tailed)	.001
	N	6

TABLE-IV

Correlation of estimated age on X-ray with ethnicity

Ethnicity	Estimated age on X-ray	Actual Age
Hindkoh	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Pathan	Pearson Correlation	.963**
	Sig.(2-tailed)	.008
	N	5
Punjabi	Pearson Correlation	.976**
	Sig.(2-tailed)	.000
	N	39
Saraiki	Pearson Correlation	a
	Sig.(2-tailed)	.
	N	1
Urdu speaking	Pearson Correlation	.951**
	Sig.(2-tailed)	.000
	N	34

TABLE-V

Frequency of stage of fusion of iliac crest among males

Male		Iliac Crest Stage on X-ray				Total
		II	III	IV	V	
Actual age	17.0	7	0	0	0	7
	17.5	2	0	0	0	2
	18.0	0	4	1	0	5
	18.5	0	4	0	0	4
	19.0	0	0	2	1	3
	19.5	0	0	1	1	2
	20.0	0	0	0	2	2
	20.5	0	0	0	5	5
	21.0	0	0	1	3	4
	21.5	0	0	0	3	3
	22.0	0	0	0	2	2
	22.5	0	0	0	2	2
	23.0	0	0	0	2	2
	23.5	0	0	0	4	4
	24.0	0	0	0	1	1
	24.5	0	0	0	2	2
	25.0	0	0	0	1	1
Total		9	8	5	29	51
Mean		17.11	18.25	19.30	21.91	20.24
Median		17.00	18.25	19.00	21.50	20.25
SD		0.22	0.27	1.10	1.64	2.39

TABLE-VI

Frequency of stage of fusion of iliac crest among females

Female		Iliac crest stage on X-ray				Total
		II	III	IV	V	
Actual age	17.5	0	1	0	0	1
	18.0	0	1	2	0	3
	18.5	0	0	1	0	1
	19.0	0	0	0	2	2
	19.5	0	1	0	4	5
	20.0	0	0	0	4	4
	20.5	0	0	0	2	2
	21.0	0	0	0	2	2
	21.5	0	0	0	2	2
	22.0	0	0	0	1	1
	22.5	0	0	0	2	2
	23.0	0	0	0	2	2
	23.5	0	0	0	1	1
	24.0	0	0	0	1	1
Total		0	3	3	23	29
Mean		NA	18.33	18.17	20.98	20.41
Median		NA	18.00	18.00	20.50	20.00
SD		NA	1.04	0.29	1.52	1.78

DISCUSSION

Expert opinion of forensic experts is many times needed in situations having significant implications for the individuals targeted by the decision. The cases of age estimation of individuals to determine whether the estimated age is actually the age claimed by him/her is undoubtedly one of these scenarios.

Of the various parameters of identification, age is of fundamental importance as it is a primary characteristic of biometric profiling. According to Maples (1989), age estimation is an art rather than science. According to Osborne et al (2004), it is the greatest challenge faced by the forensic experts.[14] However, the need to conduct studies to determine age in the living have caught attention of the forensic experts only recently because of its increasing medicolegal importance in both civil and criminal cases. Forensic age assessment is, therefore, of great significance because of the serious implications of inaccurate age estimation, particularly in cases of unaccompanied minors considered as adults when applying for asylum. Another important situation chiefly encountered in developing countries like Pakistan is lack of maintenance of birth records especially in rural areas due to illiteracy.[1] According to United Nations Children's Fund (UNICEF), only 50% of births are registered in developing countries.[15]

Different bones are used to determine age at various age groups. Age ranging from 14 to 22 years is critical in judicial and non-judicial proceedings in many countries.[15] Forensic experts are summoned to determine age in such cases. Amongst all the parameters of age determination, radiological examination to assess the extent of epiphyseal union has been found to be reliable by medicolegal experts.

In this study, among 80 individuals, the mean estimated age on X-ray was 20.10±2.19 years. The mean actual age was 20.3±2.18 years. Maqsood et al.[16] conducted a similar study including 200 individuals of both gender of age group 17- 25 years at Shalamar Hospital, Lahore. In his study, the mean actual age was 20.41± 2.55 years which is in agreement with our study.

According to the present study, the correlation coefficient (r) value of estimated age (years) on X-ray was 0.964 indicating a strong positive correlation between them (P<0.0001). In a prospective study by Pandey et al.[17] age was determined by radiological methods (X-ray and ultrasonography) of 240 individuals of ages between 12-21 years. A strong positive correlation was observed between the estimated mean age and the actual age on X-ray (p=0.0001) among all the individuals of both genders.[17] This is in accordance with our findings.

Males had strong positive correlation (r=0.976, P<0.0001) with estimated age (years) on X-ray as compared to females showing moderate positive correlation (r=0.932, P<0.0001). Our finding is in agreement with that of Hosmoni et al.[18] who reported a greater degree of correlation between the estimated age and chronological age in males than in females.[18]

As in occupation, for prediction of employee age, strong positive correlation was observed i.e. r=0.950 (p<0.0001). In laborer and nursing students, correlation was highest i.e. r>0.999,

(P<0.0001) whereas moderate positive significant correlation was seen in students (r=0.960, P< 0.01) and workers (r=0.971, P<0.01). The correlation of occupation with the prediction of age was studied, based on the assumption that strenuous physical activity leading to higher metabolic rate in heavy weight lifters may affect the rate of skeletal maturity. Our study was supported by study of Theintz[19] who evaluated the impact of intensive physical training in adolescent female swimmers and gymnastics. He observed delay in fusion of epiphysis relative to the adult height and chronological age in gymnastics. The underlying mechanism was thought to be exercise, in association with or due to metabolic effects of dieting. Saini[20] also studied relationship between estimated skeletal age and sports and exercise. He found estimated age was more than the chronological age. This is congruent with our study. However, occupation did not have significant impact on the age of union of iliac crest as the p value was not significant (0.123) in study by Maqsood et al.[16]

In the present study, on the variable of ethnicity, Punjabis had a strong positive correlation (r=0.976, P<0.01). Pathans and Urdu speaking (r=0.963 & 0.951, P <0.01) also showed strong positive correlation with estimated age on x-ray. Cole at al.(2015)[21] studied the role of ethnicity and gender in skeletal maturation in 607 boys and girls of black and white ethnic groups between ages 9 and 20 years in South Africa. Girls, both black and white, attained skeletal maturation 1.9 years before boys. However, black boys, showed a delay of 7 months as compared to white boys. These findings indicated that skeletal maturation varied differentially by sex and ethnicity.[21] This is in line with our findings. The delayed maturity of black boys, but not black girls, indicates that boys are affected more from environmental stressors than girls. However, Maqsood et al.[16] reported that there is no significant role of ethnicity on ossification of the iliac crest (p value > 0.751) in his study.[16] This is contrary to our findings.

In our study, stage V of the complete union of the iliac crest on radiographic examination was found to be 21.91 years in males and 20.98 years in females. One hundred and fifty seven pelvic radiographs were studied to assess age from ossification stage of iliac crest by Chowdhuri et al.[22] who found 20.85 years in males and 20.43 years in females as age of complete union of iliac crest respectively. This is in agreement with our study. In study by Bhise[23], epiphyseal union of iliac crest was seen at 21 - 22 years in males and 20-21 years in females also supporting our findings. Maqsood et al.[16] reported complete union among 93 (70.45%) males in the age group of 21-25 years as compared to 40 (58.83%) females between 20-25 years of age which is comparable with our findings.[16] The findings of our study are also in agreement with the study done by Coqueugniot and Weaver[24] on 137 Portuguese skeletal remains of ages 7–29 years. They observed that complete fusion of the iliac crest occurred at 20 years of age in males and 22 years in females. However, Memon[25] in a study on heterogeneous population of Hyderabad city and vicinity in Pakistan observed complete union of iliac crest at earlier age i.e.17 years and 10 months in females and 18 years and 10 months in males. This may be because rate of skeletal maturity varies in response to various factors like dietary habits, socioeconomic status, health, gender, ethnicity etc.

In our study females showed ossification of iliac crest approximately one year earlier than males which has also been reported in literature.[16,23,25]

CONCLUSION

It can be concluded from the study that mean age observed on X-ray was almost same as actual age, among all the individuals. There is strong correlation coefficient (r) of estimated age (years) on X-ray with actual age, and p value was significant.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Mariam Arif:** Data collection, compilation, manuscript writing.
2	**Syed Rayyan Hamad:** Data collection.
3	**Syed Hamad Rasool:** Data entry, analysis.

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ORIGINAL ARTICLE

Seeing beyond vision: A comparative study of intelligence, academics, and lifestyle in myopic and non-myopic medical students.

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ABSTRACT… Objective: To compare intelligence (IQ), academic performance, and lifestyle factors between myopic and non-myopic undergraduate medical students, while also evaluating demographic, familial, and environmental risk factors associated with myopia. **Study Design:** Cross-sectional study. **Setting:** CMH Lahore Medical College Lahore. **Period:** February to April 2025. **Methods:** Involving 302 undergraduate students (180 myopic, 120 non-myopic) from medical, dental, nursing, and allied health programs in medical college, Lahore, Pakistan. Participants were selected via non-probability convenience sampling. Data were collected on eyesight status, academic grades (matriculation, intermediate, and GPA), IQ levels, lifestyle habits (screen time, outdoor activities, posture), and familial myopia history. Statistical analyses included chi-square tests and independent sample t-tests, with a significance threshold of $p < 0.05$. **Results:** No significant differences were found between myopic and non-myopic students in IQ levels (myopic: 94.3 ± 23.1 vs. non-myopic: 96.2 ± 24.0; $p = 0.419$) or academic performance (GPA: 3.30 ± 0.50 vs. 3.29 ± 0.51; $p = 0.864$). Lifestyle factors, including screen time, study hours, and outdoor activities, also showed no significant associations ($p > 0.05$). A weak positive correlation was observed between myopia and paternal eyesight weakness ($p = 0.048$), but maternal myopia and family history of hypertension were not significant. Poor posture during studying was more prevalent among myopic students, though statistically insignificant ($p = 0.174$). **Conclusion:** Myopia prevalence was high (60%) among students, but no significant links were found with IQ, academics, or most lifestyle factors. The study highlights the need for awareness about eye health and debunks stereotypes linking myopia with intelligence.

Key words: Academic Performance, Intelligence (IQ), Lifestyle Factors, Myopia, Medical Students, Refractive Error.

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INTRODUCTION

Myopia, commonly known as short-sightedness, is a refractive issue where light rays converge in front of the retina due to an elongated eyeball or a cornea that is too curved.[1] In the year 2020, approximately 46.1% of the population aged 10 to 39 in South-East Asia was affected by myopia, while in Pakistan, about 36.5% of the population is myopic.[2] Myopia, the most common type of refractive error, not only affects vision but also imposes a considerable financial burden on individuals due to the high costs associated with spectacles, lenses, and other ocular correction methods.[3]

While the exact mechanisms behind the onset and progression of myopia remain unclear, it has been linked to genetic, environmental, and lifestyle influences. It occurs more frequently in girls than in boys. Those with one or two myopic parents are 2-3 times more likely to develop myopia compared to those without myopic parents.[4] Various environmental factors have been investigated for their role in causing myopia, including prolonged exposure to low lighting, insufficient outdoor activities, and digital eye strain stemming from the use of smartphones, tablets, computers, televisions, or other screens.[5]

Studies suggest that students with myopia tend to have higher Intelligence Quotients (IQ) than their non-myopic peers, indicating a possible connection between the genetic inheritance of intelligence and myopia.[6] Intelligence is considered a broad mental ability encompassing reasoning, problem-solving, and learning, which require mental perception, focus, memory, language skills, and planning.

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IQ is assessed through a combination of various tests that involve answering questions based on accessible information, thereby evaluating an individual's reasoning, knowledge, vocabulary, visual spatial skills, working memory, and perceptual abilities. The IQ test results are represented as scores ranging from 0 to 190, where scores of 0-39 indicate severe impairment and those of 145 or more signify genius-level intelligence.[7]

Additionally, research has established a correlation between myopia and educational attainment. There is a positive relationship between the number of years of education an individual receives and the likelihood of developing myopia.[8] Typically, higher academic performance is associated with a more rapid progression of myopia. Academic grades and results from achievement tests are often viewed as indicators of cognitive ability, reflecting a student's overall academic skills and intelligence, typically measured on a four-point scale.[9]

Some previous studies show comparisons between IQ and academic success suggest that these two factors do not have a strong relationship and that a student's diligence can offset a lack of intelligence to achieve better grades. While some research indicates a connection between the two, their relationship with myopia remains ambiguous.[5,10]

The aim of our research was to evaluate and compare IQ scores and academic performance among undergraduate students based on their myopic status within our population. Additionally, it sought to examine different demographic, familial, social, and academic aspects between myopic and non-myopic students. The study also aimed to raise awareness of the risk factors associated with myopia and to promote early detection and management strategies.

METHODS

We recruited undergraduate students from the medical, dental, nursing and allied health fields for this cross-sectional study design. Through non-probability convenience sampling, which was based on voluntary participation, both male and female students between the ages of 19 and 25 were included. The study eliminated participants with uncorrected refractive defects, those who had already undergone corrective surgery for myopia, those who gave insufficient information, and those who failed to give informed consent.

A sample size of 300 people was enrolled, above the previously determined criterion of 270, in order to guarantee solid results. With a 95% confidence interval and a design effect of 1.0, the sample size was calculated using the OpenEpi software, an online sample size calculator. The computation was predicated on a prior study that found 84% of medical students had myopia.

The study was conducted from February 2025 to April 2025 at several institutions connected to Avicenna Medical & Dental College in Lahore, Pakistan, with institutional ethical approval (684/ERC/CMH/LMC).

RESULTS

The demographic data of participants are shown in Table-I as frequency (N) and percentages (%). The age at which myopia was diagnosed varied among different groups with the majority falling between 11 to 15 years (21.2%), followed by 16 to 20 years (18.2%). The distribution of current dioptre measurements among the myopic reveals that 9.9% had less than 1 dioptre, and 26.5% fell within the 1 to 3 dioptre range. Additionally, 13.9% ranged between 3.1- 5 dioptres.

The comparison between myopic and non-myopic individuals with respect to gender showed no statistical significance (p-value 0.210), as indicated in Figure-1.

FIGURE-1

Gender comparison between myopic and non-myopic

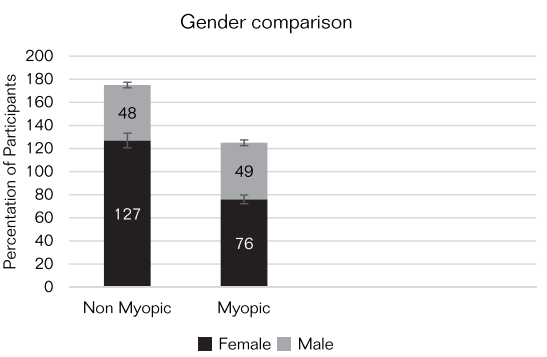

Table-II shows the comparison of various risk factors and their p-values among myopic and non-myopic individuals, the majority being insignificant. Table-III shows the comparative analysis of time distribution related to lifestyle factors in myopic and non-myopic individuals, which is again non-significant. Table-IV shows the insignificant difference between academic grades in matriculation and intermediate examination of myopic and non-myopic students. Table-IV shows the insignificant difference between GPA and IQ levels between myopic and non-myopic students.

Table-III shows the comparative analysis of time distribution related to lifestyle factors in myopic and non-myopic, which is again non-significant.

Table-IV shows the insignificant difference between academic grades in matriculation and intermediate examination of myopic and non-myopic students. Table-V shows the insignificant difference between GPA and IQ levels between myopic and non-myopic students.

TABLE-I

Demographic characteristics of study participants

Variables		Frequency (N)	Percentage (%)
Total Participants		300	(100%)
Eyesight Status	Myopic	180	60%
	Non Myopic	120	40%
Gender	Male	97	32.3%
	Female	203	67.6%
Enrollment Program	MBBS	97	32,3%
	BDS	47	15.6%
	Nursing	75	25%
	Allied Sciences	81	27%
Age Distribution	19-21 years	242	80.6%
	22-25 years	58	19.3%

TABLE-II

Comparison of risk factors and lifestyle factors between myopic and non-myopic

Variables	Groups				
	Myopic		Non-Myopic		*P-Value/ Likelihood ratio
	No N (%)	Yes N (%)	No N (%)	Yes N (%)	
Vitamin A intake	57 (19%)	113 (37.6%)	32 (10.6%)	98 (32.6%)	0.110
Maternal Eyesight Weakness	69 (23%)	104 (34.6%)	52 (17.3%)	75 (25%)	0.166
Paternal sight weakness	57 (19%)	113 (37.6%)	50 (16.6%)	77 (25.6%)	0.084/0.048*
Family History of Diabetes	86 (28.6%)	82 (27.2%)	77 (25.6%)	53 (17.6%)	0.574
Family History of Hypertension	75 (25%)	104 (34.6%)	57 (19.5%)	64 (23.2%)	0.389
Take rest after 30 minutes continuous reading	77 (25.6%)	95 (31.6%)	40 (13.3%)	88 (29.3%)	0.250
Bad Posture while studying/reading	37 (12.3%)	130 (43.4%)	42 (14%)	91 (30.1%)	0.174
Smoking	169 (56.3%)	10 (3.3%)	112 (37.3%)	67 (22.3%)	0.453
Awareness about eye exercise protocol	98 (32.6%)	75 (25%)	75 (25%)	52 (17.3%)	0.221
Perform Eye exercise	130 (43.4%)	26 (8.6%)	121 (40.3%)	23 (7.6%)	0.243

*Pearson Chi-Square test of independence

TABLE-III

Comparative analysis of time distribution and lifestyle factors in myopic and non-myopic

		1-4 Hrs.	5-8 Hrs.	9-12 Hrs.	13-16 Hrs.	P-Value*
Groups		N (%)				
Time given to studies / 24 hrs.	Myopic	103 (34.1%)	55 (18.2%)	13 (4.3%)	2 (0.7%)	0.904
	Non Myopic	82 (27.2%)	37 (12.3%)	9 (3.0%)	1 (0.3%)	
Time spent on computer/24 hrs.	Myopic	134 (44.4%)	30 (9.9%)	4 (1.3%)	5 (1.7%)	0.127
	Non Myopic	100 (33.1%)	19 (6.3%)	9 (3.0%)	1 (0.3%)	
Time spent on mobile/24 hr.	Myopic	83 (27.5%)	62 (20.5%)	23 (7.6%)	5 (1.7%)	0.802
	Non Myopic	62 (20.5%)	47 (15.6%)	14 (4.6%)	6 (2.0%)	
Time spent outdoors/24 hrs.	Myopic	87 (28.8%)	63 (20.9%)	18 (6.0%)	5 (1.7%)	0.778
	Non Myopic	63 (20.9%)	47 (15.6%)	17 (5.6%)	2 (0.7%)	
Sleeping hrs. / 24 hrs.	Myopic	17 (5.6%)	124 (41.1%)	29 (9.6%)	3 (1.0%)	0.673
	Non Myopic	9 (3.0%)	99 (32.8%)	20 (6.6%).	1 (0.3%)	

*Pearson Chi-Square test of independence

TABLE-IV

Comparison of academic grades between myopic and non-myopic individuals

		Academic Grades				
		A+	A	B	C	
Groups		N (%)				P-Value*
Matric Result	Myopic	103 (34.1%)	55 (18.2%)	9 (3.0%)	2 (0.7%)	0.688
	Non Myopic	85 (28.2%)	36 (12%)	9 (3%)	1 (0.3%)	
Intermediate Result	Myopic	91 (30.1%)	60 (19.9%)	19 (6.3%)	1 (0.3%)	0.418
	Non Myopic	79 (26.2%)	36 (12%)	14 (4.6%)	1(0.3%)	

*Pearson Chi-Square test of independence

TABLE-V

Comparison of IQ Level and cGPA between myopic and non-myopic

Groups	N	IQ Level Mean ± SD	Std. Error Mean	95% C.I Difference (Lower-Upper)	P-Value*	GP Mean ± SD	Std. Error Mean	95% C.I Difference (Lower-Upper)	P-Value*
Myopic	180	94.3 ± 23.1	1.76	90.8 - 97.7	0.419	3.30 ± 0.50	0.03	3.2-3.3	0.864
Non-Myopic	120	96.2 ± 24.0	2.11	92.3-100.7		3.29 ± 0.51	0.04	3.2-3.3	

*Independent Sample test

DISCUSSION

The statement "People who wear glasses are smarter" implies that there is a direct relationship between myopia and intelligence, meaning that people who need corrective eyewear are more intelligent. We must stress again, though, that this is a stereotype and that there is no scientific proof for it. Only physical appearance or traits like wearing spectacles or having bad eyesight can be used to measure intelligence because it is a complex and multidimensional feature.[11] According to our study, 57% were myopic. We discovered a non-significantly greater frequency of myopic females, which is counter to previous findings that suggest males are more myopic and consistent with others.[6]

We discovered a weak positive correlation and relationship between myopia and paternal eyesight deficiency. Maternal myopia was more common in myopic people than in non-myopic people, despite the fact that there was no statistically significant difference. This suggests that there is a genetic link between parental myopia and the chance that their children will also have myopia.[2]

Similarly, people with a family history of hypertension were more likely to have myopia than people without the condition, but this difference was not statistically significant. There is currently no evidence linking diabetes-related myopia to a family history of hypertension. Nonetheless, research has looked into associated medical issues that could aggravate eye disorders.[12] While research has looked at how passive smoking affects myopia, no study has assessed the direct link between smoking and myopia. However, the majority of individuals in our study did not smoke, therefore the difference between the myopic and non-myopic groups was negligible.[13]

Regarding awareness of eye training procedures, there was no difference between the two groups. Due to ignorance, most students did not engage in any kind of eye exercise, which resulted in a negligible difference between the groups. This is somewhat consistent with research that indicates eye exercises for myopia are ineffective at controlling or delaying the condition's progression.[14] People who are myopic were more likely to adopt bad posture, albeit this difference was not statistically significant. This supports the study's conclusions that higher myopia levels are linked to more improper upper body posture, like slouching or forward head posture.[15]

Regarding the average amount of time spent on computers, mobile devices, studying, outdoor activities, and sleep over a 24-hour period, we did not find any significant variations between the two groups. The association between screen time and the development of myopia has been the subject of conflicting research, with the majority of studies finding no discernible link.[16] Spending time outside, however, may help lower the incidence of myopia and halt the advancement of axial length changes, according to research. Increased exposure to natural light, which may control eye growth, and the ability to see at a distance, which lessens eye strain from extended near work, are thought to be the causes of this impact.[8,9]

Our primary goal was to determine whether myopic and non-myopic kids differed in any way in their academic performance, IQ, or GPA, but this difference was sadly negligible. This contradicts other research that demonstrates a favorable correlation and is consistent with others that found no meaningful difference.[17,18] Additionally, we wanted to inform students about the various lifestyle choices that can lead to the onset and progression of myopia. By raising awareness, we intend to promote healthy lifestyle choices and preventative actions that can lower the incidence of myopia. This entails encouraging proper eye care habits, cutting back on screen time, making sure there is enough light for learning, and stressing the value of routine eye exams and exercises.[14]

The results of our study indicate that among college students, myopia is not a major predictor of cognitive capacity or academic achievement. The majority of students did not engage in any kind of eye exercise, and there was no difference in their awareness of the protocols. On the other hand, myopic people were more likely to adopt bad posture. People with a family history of hypertension were more likely to have myopia than people without the condition.[6]

This study's importance stems from its thorough assessment of the risk factors and drivers of myopia in undergraduate students. Additionally, it is the first study to examine the relationships between IQ, academic standing, and lifestyle characteristics in undergraduate students in Lahore, Pakistan.

CONCLUSION

Our analysis showed statistically insignificant differences between myopic and non-myopic individuals in terms of gender distribution, blood groups, myopic risk factors, time distribution, lifestyle factors, academic grades, GPA, and IQ levels, despite the fact that myopia is more common among undergraduate university students. These results imply that although myopia is common,

there is no significant correlation between it and the evaluated lifestyle, academic, and demographic characteristics of this group. Nonetheless, the study raised awareness of eye exercises and healthy living choices.

LIMITATION

The cross-sectional design, non-probability sampling, student self-reported data, and single university selection are some of the study's drawbacks. Furthermore, using non-specialized measurement tools may have hampered the accuracy of myopia classification, and removing myopic patients who have undergone corrective surgery may ignore pertinent data. Longitudinal designs, wider sample, and sophisticated diagnostic techniques should all be incorporated into future research.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
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ORIGINAL ARTICLE

Cutting costs, not quality: A cost minimization analysis of diabetes care at Northwest General Hospital and Research Center.

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ABSTRACT… Objective: To conduct a pharmacoeconomic evaluation and cost-minimization analysis of commonly used anti-diabetic medications, specifically comparing the costs of branded and generic versions of Empagliflozin and Metformin prescribed at Northwest General Hospital, Peshawar. **Study Design:** Cross-sectional, Retrospective Cost Minimization Analysis (CMA). **Setting:** The Northwest School of Medicine, Peshawar. **Period:** 3rd June 2024 to 3rd Jan 2025. **Methods:** This CMA was conducted by analyzing 202 prescriptions from 105 patients receiving anti-diabetic therapy. Retail prices of both branded and generic drug formulations were collected from local pharmacies. To ensure therapeutic equivalence, a UV spectrophotometric assay was used to compare active pharmaceutical ingredient concentrations between branded and generic products. **Results:** Metformin 500 mg and Empagliflozin 10 mg were the most commonly prescribed drugs. Generic versions demonstrated comparable bioavailability to branded counterparts. However, substantial cost differences were observed, with generic formulations offering significant savings. The average cost burden per patient was notably lower with generics, suggesting they are a viable and cost-effective alternative. **Conclusion:** Generic anti-diabetic medications, when bioequivalent, provide a cost-effective alternative to branded drugs without compromising efficacy. Promoting the use of generics in clinical practice can help reduce the financial burden on patients and improve access to essential diabetes care in resource-limited settings.

Key words: Branded Drugs, Cost-Minimization Analysis, Generic Drugs, Pharmacoeconomics, Type 2 Diabetes Mellitus.

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INTRODUCTION

Cost-minimization in healthcare

Health economics is the science of scarcity and choice, a fundamental concept that applies to all aspects of life, including healthcare. It specifically focuses on applying economic principles to healthcare systems, helping policymakers make informed decisions about resource allocation and treatment choices. This field:

- Analyzes the supply and demand for healthcare services.
- Provides a structured approach to evaluating decisions and their consequences.[1]

Pharmacoeconomics extends these principles to pharmaceutical interventions, measuring whether the additional benefits of a specific treatment justify its costs. It is defined as "the description and analysis of the cost of drug therapy to healthcare systems and society"[2], aiming to compare and quantify the economic and clinical impacts of pharmaceutical products and services. Economic evaluation in pharmacoeconomics follows a systematic and objective framework to assist decision-makers in optimizing resource allocation.[3]

There are four primary types of health economic evaluation studies, each differing in the measurement of costs and health outcomes. These include:

a) Cost-Minimization Analysis (CMA) = Assumes equivalent health outcomes and compares only the costs.
b) Cost-Effectiveness Analysis (CEA) = Measures health outcomes in natural units (e.g., life years gained, blood pressure reduction).
c) Cost-Benefit Analysis (CBA) = Converts both costs and health outcomes into monetary terms.
d) Cost-Utility Analysis (CUA) = Measures outcomes in Quality-Adjusted Life Years (QALYs) or similar utility-based metrics.[4]

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CMA is the simplest and most relevant for this study, as it focuses only on cost comparisons while assuming identical health outcomes. A classic example is the substitution of a generic drug for a brand-name drug, ensuring cost savings without compromising therapeutic efficacy.[5] For a generic drug to be approved, manufacturers must demonstrate bioequivalence to the original branded medication, reinforcing CMA as a critical tool for assessing affordability in treatment choices.[6]

While some debates exist regarding whether CMA qualifies as a full pharmacoeconomic evaluation since it does not measure clinical outcomes, many researchers categorize it as a cost-effectiveness approach due to the assumed equivalence in health benefits. Proper application of CMA requires caution to ensure that comparisons are valid and that cost reductions do not compromise patient care.

Diabetes Mellitus and its Economic Burden

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by insulin deficiency, resistance, or both, leading to hyperglycemia and associated complications in lipid and protein metabolism. It is not a single disease but a syndrome encompassing various subtypes, including Type 1, Type 2, and Gestational Diabetes Mellitus (GDM).

Diabetes Mellitus (DM) is a chronic metabolic disorder that is becoming increasingly prevalent worldwide, including in Pakistan.[7] According to the International Diabetes Federation (IDF), the economic burden of diabetes globally was estimated at $132 billion in 2002, and this figure continues to rise annually.[8] The most recent IDF Atlas estimated that 33 million people are living with type 2 diabetes in Pakistan, the third largest diabetes population globally. An additional 11 million adults in Pakistan have impaired glucose tolerance, while approximately 8·9 million people with diabetes remain undiagnosed. Data on long-term complications among people with diabetes in Pakistan are limited.[9]

The management of diabetes typically involves multiple drug therapies, with oral hypoglycemic agents (OHAs) such as Metformin, Glipizide, and Vildagliptin being among the most commonly prescribed medications.[10] However, the price variability between different brands of the same drug has raised concerns regarding the affordability of treatment, particularly in resource-constrained settings.

From a pharmacoeconomic perspective, diabetes represents one of the most expensive chronic conditions, imposing significant financial strain on both patients and healthcare systems. In developing countries like Pakistan, where healthcare expenses are predominantly out-of-pocket, the affordability of anti-diabetic therapy is a major concern.[11]

The Millennium Development Goal (MDG) 7 emphasizes equitable access to essential medicines, yet one-third of the global population lacks access to life-saving drugs. High drug prices remain a key barrier, particularly in regions where healthcare financing is inadequate. In Pakistan, many patients bear the full cost of medications, necessitating the adoption of cost-minimization strategies to improve treatment affordability and accessibility.[12]

This research aimed to conduct a Pharmacoeconomic Evaluation using Cost-Minimization Analysis (CMA) of anti-diabetic therapies prescribed to patients at Northwest General Hospital, Peshawar, Khyber Pakhtunkhwa. By comparing the costs of generic and brand-name oral hypoglycemic medications, our study provides insights into the financial burden on patients and potential strategies for cost-effective diabetes management.

MATERIALS & METHODS

Study Design and Setting

This study was a cost-minimization analysis conducted in the Northwest School of Medicine Peshawar, from 3rd June 24 to 3rd Jan 25, to evaluate the price variations among different brands of anti-diabetic medications available in the market. The study focused on two commonly prescribed drugs: Empagliflozin and Metformin, assessing their cost differences across various brands. The analysis was conducted in a pharmacoeconomic setting, utilizing data from local pharmacies and drug pricing databases.

The ethical approval No. 125/RC/NWSM/2024 was obtained from the institutional review board of

Northwest School of Medicine on 6/6/2024.

Data Collection

A comprehensive survey of anti-diabetic medications was performed by collecting data from multiple pharmacies and online pharmaceutical pricing sources. The selection criteria for drugs included:

1. **Active Ingredient:** The study included only brands containing Empagliflozin and Metformin.
2. **Dosage Strength:** Standard therapeutic doses were considered (Empagliflozin 10 mg and Metformin 500 mg).
3. **Market Availability:** Only brands widely available in the region were included.
4. **Price Information:** The retail price (cost per tablet) was recorded for each brand.

Spectrophotometric Assay for Drug Content Validation

To ensure the bioequivalence of different brands, the UV spectrophotometric assay findings were obtained from the literature, where the drug content of Empagliflozin and Metformin in different brands had been analyzed by measuring their absorbance at specific wavelengths.

Cost-Minimization Analysis

A cost-minimization approach was applied, assuming that all brands contained the same active pharmaceutical ingredient (API) and had comparable efficacy and safety profiles, as validated by the spectrophotometric assay. The analysis involved:

- **Comparing Brand Prices:** The cost per tablet was recorded and analyzed for price differences among brands.
- **Identifying the Least Expensive Option:** The lowest-priced brand was considered the most cost-effective choice.
- **Potential Cost Savings:** The percentage cost reduction was calculated by comparing the highest-priced and lowest-priced brands for each drug.

The collected price data were analyzed using descriptive statistics to summarize cost variations. The percentage differences between the highest and lowest-priced brands were computed. The results were presented in tabular form to illustrate pricing disparities.

RESULTS

A total of 105 patients were included in the study. The majority of patients (30%) were between the ages of 51–60 years, followed by 41–50 years (23.8%), and 61–70 years (19.0%). The smallest age group was 81–90 years (4.8%). (Table-I)

TABLE-I

Subject characteristics:

Age group and frequency of patients.

Age Group (years)	Frequency
18-40	15
41-50	25
51-60	30
61-70	20
71-80	10
81-90	5
Total	105

A total of 202 prescriptions were analyzed. Insulin was the most frequently prescribed therapy, accounting for 120 prescriptions, followed by Metformin (18), Empagliflozin (15), and Sitagliptin (9). Other frequently prescribed oral hypoglycemic agents included Glimepiride (7), Pioglitazone (5), and Glipizide (6). (Table-II)

TABLE-II

Most frequently prescribed drug molecule:

The frequency of each drug prescribed

Name of Drug	Number of Times Prescribed
Metformin (500, 750, 1000 mg)	18 (Glucophage, Neodipar, Comet)
Glimepiride (1, 2 mg)	7
Pioglitazone (7.5, 15 mg)	5 (Piozer, generic brands)
Voglibose	4
Insulin	120 (Basagine, Insuget R, etc.)
Glipizide	6
Empagliflozin	15 (Erliplus XR, Elzanor, etc.)
Sitagliptin	9 (Sitamet, Janumet, etc.)
Glibenclamide	5
Vildagliptin	3 (Viglip, other brands)
Acarbose	4
Gliclazide	6
Total	202

The costliest drug prescribed was Empagliflozin, having a cost of 31.50 PKR per tablet. The cheapest drug prescribed was Metformin having the cost of 3.88 PKR per tablet. The order of costliest to cheapest drug prescribed is as below:

Empagliflozin > Sitagliptin > Vildagliptine > Voglibose > Acarbose > Glibenclamide > Pioglitazone > Gliclazide > Glipizide > Glimepiride > Metformin. (Table-III)

TABLE-III

Cost of Drug molecules prescribed.

Name of Drug	Cost per Tablet (PKR)
Empagliflozin	31.50 (Costliest)
Sitagliptin	28.00
Vildagliptin	25.00
Voglibose	22.00
Acarbose	21.50
Glibenclamide	18.00
Pioglitazone	15.00
Gliclazide	12.50
Glipizide	11.00
Glimepiride	9.50
Metformin	3.88 (Cheapest)

The methodology for drug estimation, as outlined in the Pharmacopoeia, was used to analyze three brands each of Metformin and Empagliflozin. These brands were chosen based on their cost categories: the highest-priced, mid-range-priced, and the most affordable options. Please refer to the table provided for detailed pricing information for each drug brand.

UV spectrophotometric analysis confirmed that all tested brands of Empagliflozin and Metformin contained 100% of the labeled drug content, ensuring bioequivalence.

TABLE-IV

Assay of Sitagliptin and Metformin: The absorbance of samples of drugs by the UV-Spectrophotometric method.

Sample	Absorbance (nm)
Empaa	0.435
Emsyn	0.410
Diajard	0.420
Metfor	0.190
Glucophage	0.180
Comet	0.185

The slope equation for drugs to calculate drug content/concentration in each brand:

The slope equation for Empagliflozin is:

$A=0.065C+0.001$

The slope equation for Metformin is:

$A=0.018C+0.002$

The cost analysis of anti-diabetic medications revealed significant price variations among different brands of Empagliflozin and Metformin. Among the Empagliflozin brands, Emsvn was the most expensive at PKR 321.31 per tablet, followed by Empaa at PKR 220, while Diajard was the least costly at PKR 184.75. This variation indicates that opting for Diajard instead of Emsvn could result in a 42.5% cost reduction, emphasizing the economic impact of brand selection. Similarly, for Metformin, Glucophage was priced highest at PKR 33.48 per tablet, whereas Comet and Metfor were comparatively lower at PKR 12.2 and PKR 10.8, respectively. The substantial difference in costs highlights the potential for significant savings through the use of lower-priced yet bioequivalent alternatives, which could improve the affordability of diabetes management.

Price variations

$$\text{Price Variation} = \left(\frac{\text{Price of most expensive brand} - \text{Price of least expensive brand}}{\text{Price of least expensive brand}}\right) \times 100$$

Range of costs of other drugs prescribed to patients

When drugs are prescribed as mono, dual, or multiple therapies, the price of drugs varies, and the ranges of lowest cost to highest cost are given below Table 5:

DISCUSSION

This study conducted a cost-minimization analysis of commonly prescribed anti-diabetic medications, including Empagliflozin and Metformin, highlighting significant price variations among different brands. The findings revealed that Empagliflozin was the most expensive oral anti-diabetic drug, with Emsvn priced at PKR 321.31 per tablet, whereas Diajard, the least expensive brand, was available at PKR 184.75. Similarly, for Metformin, Glucophage was the highest-priced brand at PKR 33.48, while Metfor was the most cost-effective at PKR 10.8.

TABLE-V

The cost analysis of anti-diabetic medications

Name of Drugs	Number of Times Prescribed	Range of Market Cost (PKR)	Range of Costs Prescribed (PKR)	Remarks
Monotherapy	80	3.88 - 31.50	3.88 - 31.50	Based on brand variations
Metformin	18	3.88 - 5.00	3.88 - 5.00	Cheapest monotherapy
Insulin	30	10.00 - 30.00	10.00 - 30.00	Various types
Empagliflozin	15	25.00 - 31.50	25.00 - 31.50	Costliest monotherapy
Dual Therapy	60	10.00 - 60.00	10.00 - 60.00	Combination therapy varies
Sitagliptin + Metformin	9	15.00 - 35.00	15.00 - 35.00	Common dual therapy
Empagliflozin + Metformin	10	30.00 - 50.00	30.00 - 50.00	Expensive dual therapy
Insulin + Glimepiride	8	20.00 - 45.00	20.00 - 45.00	Used for T2DM
Multiple Therapy	68	15.00 - 90.00	15.00 - 90.00	Complex combinations
Metformin+Pioglitazone+Sitagliptin	7	20.00 - 60.00	20.00 - 60.00	Common triple therapy
Insulin + Metformin + Empagliflozin	6	35.00 - 90.00	35.00 - 90.00	High-cost therapy
Insulin + Glimepiride + Pioglitazone	5	25.00 - 75.00	25.00 - 75.00	Used in insulin resistance

These results emphasize the potential for substantial cost savings by selecting lower-priced yet bioequivalent brands, which could improve the affordability of diabetes management.

Our findings are consistent with previous studies that highlight the high cost of newer anti-diabetic agents, such as sodium-glucose cotransporter-2 (SGLT2) inhibitors, including Empagliflozin.[13] A study by Xie Y et al. reported that SGLT2 inhibitors were significantly more expensive compared to conventional therapies like Metformin and Sulfonylureas, limiting their accessibility in low- and middle-income countries (LMICs).[14] Similarly, a cost-effectiveness study by Pawaskar et al suggested that while SGLT2 inhibitors provide cardiovascular and renal benefits, their high costs pose a financial burden, reinforcing the importance of generic substitution strategies.[15]

Regarding Metformin, the substantial price disparity among brands aligns with previous research. Studies have reported that branded Metformin formulations were priced higher than generics despite demonstrating comparable efficacy and bioavailability.[16,17] This is in line with our spectrophotometric assay literature results, confirming that all tested brands contained 100% of the labeled drug content, supporting the rationale for preferring cost-effective alternatives.

The economic burden of diabetes treatment in resource-limited settings has been widely documented.[18] Studies in Pakistan have highlighted that a significant proportion of diabetic patients struggle with medication affordability, leading to poor adherence and suboptimal glycemic control.[19,20] Our findings further validate these concerns by demonstrating that even within the same drug class, significant price differences exist, reinforcing the need for policies promoting the use of affordable yet clinically equivalent options.

Given the growing prevalence of diabetes and the increasing financial strain on healthcare systems, this study underscores the importance of cost-minimization strategies. Future research should focus on pharmacoeconomic evaluations that integrate long-term clinical outcomes to assess the overall cost-effectiveness of anti-diabetic therapies. Additionally, regulatory authorities should encourage price transparency and promote generic substitution policies to enhance medication accessibility for diabetic patients in low-resource settings.

CONCLUSION

This cost-minimization analysis demonstrates that generic anti-diabetic medications, particularly generic metformin and empagliflozin, offer significant cost savings compared to their branded counterparts, without compromising therapeutic

efficacy. The findings reinforce the critical role of generic prescribing in alleviating the financial burden on patients and healthcare systems, especially in resource-constrained settings like Pakistan. Given the bioequivalence of generics and brands, and the substantial price disparity observed, healthcare providers should be encouraged to prescribe generics as a first-line, cost-effective strategy. Additionally, strengthening regulatory oversight and public awareness about generic drug safety and efficacy can further promote their acceptance. Future pharmacoeconomic studies incorporating real-world data and long-term outcomes are essential to inform national policies and ensure optimal, sustainable diabetes care.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	**Haseeba Mukhtar:** Data collection.
3	**Ahmad Hassan Khan:** Analysis.
4	**Amir Zaman Khan:** Data entry.
5	**Imad Khan:** Study design.
6	**Sarwat Jahan:** Critical revision.

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ORIGINAL ARTICLE

Assessment of medical students' attitude toward the doctor-patient relationship.

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ABSTRACT… Objective: To evaluate the attitudes of medical students in Khyber Pakhtunkhwa (KPK), Pakistan, toward the doctor-patient relationship. **Study Design:** Descriptive Cross Sectional study. **Setting:** Department of Community Medicine, Gomal Medical College Dera Ismail Khan. **Period:** 10th February to 10th May 2025. **Methods:** Using non probability convenient sampling approach. 400 MBBS students from 17 medical colleges in Khyber Pakhtunkhwa (KPK), Pakistan, made up the sample. Data were collected using a validated, structured questionnaire that included the 18-item Patient-Practitioner Orientation Scale (PPOS) measured the "sharing" and "caring" domains. In order to investigate demographic correlations, statistical analysis was conducted with SPSS 27 trial version software, utilizing descriptive statistics, independent t-tests, and ANOVA with Post Hoc test. **Results:** A moderate patient-centered orientation was indicated by the overall mean PPOS score of (3.62 ± 0.45). Higher empathy than collaborative decision-making was suggested by subscale analysis, which showed higher scores in the caring subscale (3.95 ± 0.57) than the sharing subscale (3.30 ± 0.61). Students in the public sector performed better in the sharing domain ($p = 0.044$), while female students performed significantly better in the caring domain ($p = 0.020$). **Conclusion:** This study revealed that medical students in Khyber Pakhtunkhwa (KPK), Pakistan generally have moderately patient-centered attitudes. They are more inclined to provide empathetic care than to share decision-making. These results demonstrate the necessity of enhancing instructional approaches that foster empathy and teamwork in medical education.

Key words: Physician-patient Relationship, Patient-practitioner Orientation Scale, Patient-centered Care, Pakistan, Students Medical.

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INTRODUCTION

The strong rapport that develops between a doctor and a patient during clinical encounters is a vital aspect of the art of medical treatment and clinical practice. The approach where the physician tries to enter the patient's world, to see the illness through the patient eyes so that the doctor can understand the patients ideas, expectations, and feelings about the illness, is gaining increasing popularity.[1] Patient-centered communication provides patients with greater knowledge, influence, and involvement in decision-making processes.[2] Strong doctor-patient relationships are linked to improved disease outcomes, better treatment compliance, and greater trust on the physician.[3] The today medical students will become healthcare professionals in the future.[4] Since medical students represent the future of the medical profession, it is important to understand their perceptions of the doctor-patient relationship in order to assess their beliefs and attitudes.[3] Evaluating their viewpoints on this relationship is essential. While inappropriate attitudes can be addressed during medical education through institutional programs, extracurricular activities, and curricular interventions, positive attitudes can be reinforced and promoted.[5] To assess these attitudes, researchers have employed the Patient-Practitioner Orientation Scale (PPOS), a valid and reliable tool.[6] Brazilian medical students demonstrated highly favorable views toward patient-centered care, with a mean PPOS score of (4.66 ± 0.44).[7] while American students showed nearly identical results, with a mean score of (4.57 ± 0.48).[6] Chinese students, using a revised version of the PPOS, scored (3.63 ± 0.54), indicating a moderate tendency toward patient-centeredness.[8] In contrast, Egyptian students had a lower mean score of (2.71 ± 0.66), reflecting a less patient-centered attitude.[9]

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Given that no study has been carried out to evaluate medical students' attitudes toward the doctor-patient relationship in our province, a significant knowledge gap exists. Therefore, the aim of this study is to assess the attitudes of medical students from both public and private sector medical colleges across Khyber Pakhtunkhwa (KPK) Pakistan towards the doctor-patient relationship.

METHODS

This descriptive, cross-sectional study was conducted at the Department of Community Medicine, Gomal Medical College Dera Ismail Khan, Khyber Pakhtunkhwa (KPK), Pakistan from 10th February 2025 to 10th May 2025. The target population included all MBBS students enrolled in public and private sector medical colleges across Khyber Pakhtunkhwa (KPK), a total population of 9,171 students. A non-probability convenient sampling technique was used to select participants. All MBBS students were included in this study, except those who declined or did not provide informed consent. The sample size was calculated using the Raosoft sample size calculator with a 95% confidence level, 5% margin of error, and an assumed 50% response rate, which yield a required sample of 369. However, data were collected from 400 students to enhance the study validity and reliability.

Data were collected online by mean of Google Form that incorporated a pretested, structured and close-ended scale which had previously been developed and standardized. The tool contained two subscales that assessed central domains in doctor–patient relationships: the Sharing subscale and the Caring subscale. The Sharing domain assessed the belief that patients should equally share power, control, and the flow of information with their doctors. The Caring domain reflected the belief that patients should be treated as complete human beings with an emotional bond, not as cases or diseases.[10] Each subscale had 9 items. The complete questionnaire contained 23 questions. The first five items gathered demographic details including gender, age, year of study, having a family health worker, and being married. These were followed by an 18-questions tool called the Patient Practitioner Orientation Scale (PPOS), which used a 6-point Likert scale ranging from strongly agree (1 point) to strongly disagree (6 points). It gave a mean score of 1 to 6, where higher scores (towards 6) were more patient-centered, while lower scores (towards 1) were more physician-centered.[10] The scale had good internal consistency with an estimated Cronbach's alpha of 0.73.[11]

Statistical analysis was done with the SPSS 27 trial version software. The demographic variables were analyzed by using descriptive statistics technique that yielded frequency and percentages. The same descriptive statistics technique was utilized to determine the mean and standard deviation for all 18 items in the Patient-Practitioner Orientation Scale (PPOS). 18 items of PPOS was equally distributed in sharing subscale (n = 9) and caring subscale (n = 9). Items 1-9 were under the sharing domain, while items 10-18 were in the caring domain. Every item was rated on a six-point Likert scale, namely (1) strongly agree, (2) agree, (3) slightly agree, (4) slightly disagree, (5) disagree, and (6) strongly disagree, for statement 3, 5, 8, 9 and 11 the Likert scale was score reversed (Table-III). An independent samples t-test were conducted to compare mean differences between individual demographic variable and overall PPOS scores, as well as scores of caring and sharing subscale, normality and homogeneity were confirmed via Shapiro Wilk test. Furthermore, one-way analysis of variance (ANOVA), with Post Hoc test was utilized to test mean differences between years of study for both overall PPOS and its subscales. This study employed a p-value ≤ 0.05 as statistically significant.

Ethical approval for this study was obtained from the Ethical Review Committee of Gomal Medical College" (242/GJMS/JC) and permission for data collection with informed consent was granted.

RESULTS

Students from 1st to final years of 17 medical colleges, both Public and Private sector was included in this study. (Table-I & II) show the demographic distribution of study participants. The sample included nearly equal gender distribution (51.4% male, 48.6% female). Most students resided in urban areas (60.3%), had no family health worker background (56.4%), and were unmarried (98%). Students were predominantly from public-sector

institutions (72.0%, n=288).

TABLE-I	
Socio Demographics distribution of all participants (n=400)	
Gender	**N%**
Male	205(51.4)
Female	195 (48.6)
Academic Year	
1st year	36 (9)
2nd year	60 (15)
3rd year	84 (20.9)
4th year	147 (36.7)
Residence	
Rural	159 (39.7)
Urban	242 (60.3)
Family Health Worker	
Yes	175 (43.6)
No	226 (56.4)
Marital Status	
Married	8 (2)
Unmarried	393 (98)
Category	
Public sector	288 (72)
Private sector	112 (28)

Table-III Shows the mean score of each PPOS statement based on the responses of all the Students (n=400). The participant mean scores on the PPOS statements largely indicated patient-Centered attitudes, that is, the average scores are higher than "3" on each sharing and caring subscale.

Table-IV shows the mean scores of the sharing subscale, caring subscale, and overall PPOS for all participants (n=400). The mean score for overall PPOS was 3.62 ± 0.45, whereas the mean scores for the sharing and caring domains were 3.30 ± 0.611 and 3.95 ± 0.57, respectively.

Table-V shows correlations between the demographics (gender, residence, family health worker and marital status and public and private sector categories) of all students (n=400) and their mean scores for the sharing domain, caring domain, and overall PPOS. Statistically significant differences were identified in caring domain for gender (p = 0.020) and in sharing domain for public and private categories (0.040).

The 95% confidence intervals indicate that the population mean PPOS score will fall between 3.58 and 3.66, with significantly lower scores for the sharing sub-scale (3.24–3.36) compared to the caring sub-scale (3.89–4.01), (Table-VI).

TABLE-II	
Distribution of study participants across medical colleges	
Colleges n%	
Gomal Medical College	92 (22.9)
Khyber Medical College	26 (6.5)
Ayub Medical College	17 (4.2)
Women Medical College	25 (6.2)
Nowshehra Medical College	20 (5)
Bacha Khan Medical College	22 (5.5)
Khyber Girls Medical College	26 (6.5)
Bannu Medical College	12 (3)
Saidu Medical College	17 (4.2)
Swat Medical College	13 (3.2)
North west medical School	12 (3)
Abbottabad International Medical College	14 (3.5)
Peshawar Medical College	19 (4.7)
Frontier Medical College	9 (2.2)
Jinnah Medical College	21 (5.2)
Gajju khan Medical College	20 (5)
KMU-Institute of Medical Sciences 36 (9)	

DISSCUSION

This study explores the attitudes of medical students in Khyber Pakhtunkhwa (KPK) province of Pakistan, toward the doctor–patient relationship by using the Patient-Practitioner Orientation Scale (PPOS). The results provide a useful understanding of how the future health professionals conceptualize patient-centered care. The participants mean PPOS score was (3.62 ± 0.45), showing a moderate level of patient-centered attitudes. This finding supports an earlier studies that reported an average score of (3.60 ± 0.47) in 322 students (55.3% male and 44.7% female).[12]

TABLE-III

Mean scores of the Patient-Practitioner Orientation Scale (PPOS) statements of all participants (n=400).

Statements	Mean ± SD
1. The doctor is the one who should decide what gets talked about during a visit.	3.63 ± 1.65
2. It is often best for patients if they do not have a full explanation of their Medical condition.	4.73 ± 1.43
3. Patients should rely on their doctors' knowledge and should not try to find out about Their conditions on their own.	3.00 ± 1.77
4. Many patients continue asking questions even though they are not learning anything new.	3.25 ± 1.33
5. Patients should be treated as if they were partners with the doctor, equal in power and status.	2.59 ± 1.69
6. Patients generally want reassurance rather than information about their health.	4.41 ± 1.28
7. When patients disagree with their doctor, this is a sign that the doctor does not have the patient's respect and trust.	3.68 ± 1.46
8. The patient must always be aware that the doctor is in charge.	2.72 ± 1.32
9. When patients look up medical information on their own, this usually confuses more than it helps.	2.40 ± 1.30
10. Although healthcare is less personal these days, this is a small price to pay for medical advances.	3.33 ± 1.33
11. The most important part of the standard medical visit is the physical exam.	2.48 ± 1.44
12. When doctors ask a lot of questions about a patient's background, they are prying too much into personal matters.	4.40 ± 1.51
13. If doctors are truly good at diagnosis and treatment, then the way they relate to patients is not that important.	4.55 ± 1.45
14. If a doctor's primary tools are being open and warm, the doctor will not have a lot of success.	4.13 ± 1.36
15. A treatment plan cannot succeed if it conflicts with a patient's lifestyle or values.	4.45 ± 1.41
16. Most patients want to get in and out of the doctor's office as quickly as possible.	3.32 ± 1.58
17. It is not that important to know a patient's culture and background in order to treat the person's illness.	4.52 ± 1.61
18. Humor is a major ingredient in the doctor's treatment of the patient.	4.37 ± 1.34

TABLE-IV

Mean scores for the sharing subscale, the caring subscale and overall Patient-Practitioner Orientation Scale (PPOS) of all students (n=400).

Patient-Practitioner Orientation Scale (PPOS) Component Mean ± standard deviation
Sharing subscale 3.30 ± 0.411
Caring subscale 3.95 ± 0.657
Overall Patient-Practitioner Orientation Scale (PPOS) 3.62 ± 0.45

TABLE-V

Correlation between the demographics of all students (n=400) and their mean scores for the sharing subscale, the caring subscale, and overall Patient- Practitioner Orientation Scale (PPOS).

	Sharing Subscale Mean ± Standard Deviation	Caring Subscale Mean ± Standard Deviation	Overall PPOS Mean ± Standard Deviation
Gender			
Male	3.28 ± 0.61	3.88 ± 0.60	3.58 ± 0.47
Female	3.31 ± 0.60	4.01± 0.53	3.67 ± 0.43
p-value	0.511	0.020	0.051
Residence			
Rural	3.33 ± 0.65	3.93 ± 0.59	3.63 ± 0.48
Urban	3.23 ± 0.61	3.96 ± 0.65	3.62 ± 0.43
p- value	0.394	0.603	0.831
Family Health Worker			
Yes	3.29 ± 0.61	3.97 ± 0.57	3.63 ± 0.45
No	3.30 ± 0.61	3.93 ± 0.58	3.62 ± 0.45
p-value	0.774	0.480	0.831
Marital Status			
Married	2.96 ± 0.41	3.87 ± 0.49	3.41± 0.38
Unmarried	3.30 ± 0.61	3.95± 0.58	3.62± 0.45
p-value	0.114	0.712	0.190
Category			
Public sector	3.34 ± 0.59	3.95± 0.55	3.64± 0.44
Private sector	3.20± 0.66	3.94± 0.63	3.57± 0.48
p-value	0.044	0.792	0.125

TABLE-VI

Confidence interval with 95% confidence level

Category	Confidence Interval
Mean PPOS score	3.576 --3.664
Mean sharing sub-scale score	3.240 – 3.360
Mean caring sub-scale score	3.894 – 4.006

In contrast to this study, higher scores were found in a study conducted at the University of Khartoum, Sudan (4.08 ± 0.53)[13], Saudi Arabia (4.0 ± 1.5)[14] and in China (4.68 ± 1.56)[15] which may reflect regional differences affected by cultural and educational background. Analysis of the subscales showed that the caring domain (3.95 ± 0.57) was rated higher than the sharing domain (3.30 ± 0.611); thus, while students have empathy and sympathy with the patient, they are less prepared to cooperate in taking decisions of a mutualistic type and for developing egalitarian and balanced negotiations in consultations. These results are consistent with a study in China, which found the same subscale scores—caring (3.95 ± 0.57) and sharing (3.30 ± 0.61).[15] Likewise, the previous study reported similar subscale results: caring (3.99 ± 0.52) and sharing (3.23 ± 0.66).[12] Gender differences were approached and there was a statistically significant difference in the caring subscale (p = 0.020) for female students who scored higher, implying higher involvement or sensibility towards patient needs. This finding is widely known, since several studies have found that female medical students have more patient-centered orientations than their male colleagues.[13,16,17] Other studies, however, have found no or little gender differences in this area[3], indicating the need for further research. Furthermore, students from public sector medical colleges surpassed those from private medical colleges in the sharing domain (p = 0.044), suggesting that institutional variations might have an impact on how students view shared medical care. The mean PPOS scores of our sample were lower than those reported in Brazil (4.66)[7] and the U.S. (4.57)[6] but higher than those in Egypt (2.71).[9] In comparison to their international peers, Pakistani students exhibit a moderate degree of patient-centeredness.

A relatively low sharing domain score points to a possible weakness in medical students' education regarding active patient involvement in their own treatment. Shared decision-making and patient empowerment have been linked to better clinical outcomes, treatment adherence, and patient satisfaction. This study supports the need for a more patient-centered curriculum.[18] The following perspective is in line with earlier study that demonstrate Pakistani medical students frequently retain a more doctor-centered orientation towards the doctor-patient relationship.[18] These results highlight the value of planned curriculum and extracurricular changes that improve ethical awareness, cultural competency, and doctor-patient communication, all of which are critical components of developing a cooperative, patient-centered clinical practice. This study has a number of shortcomings despite its contributions. Non-probability convenience sampling limits the extent to which the findings can be applied, social desirableness bias in data collection process using online questionnaires.

The cross-sectional study design records attitudes at a single moment in time. Some colleges contributed fewer participants than others, indicating unequal institutional representation. To assess how student attitudes change over the course of medical education, conduct longitudinal studies. Investigate the causes of lower sharing subscale scores using qualitative techniques (such as focus groups and interviews). Carry out a national survey for wider applicability. Examine how particular educational interventions, like workshops on communication skills or patient simulations, affect PPOS results. Incorporate curriculum analysis and faculty viewpoints to determine how institutions affect students' attitudes.

CONCLUSION

This study revealed that medical students in Khyber Pakhtunkhwa (KPK), Pakistan generally have moderately patient-centered attitudes. They are more inclined to provide empathetic care than to share decision-making. These results demonstrate the necessity of enhancing instructional approaches that foster empathy and teamwork in medical education.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Adnan Khan:** Conceptualize, initial draft, methods.
2	**Noor Fatima:** Data analysis, data collection.
3	**Mehran Ullah Bani:** Data entry.
4	**Nosheen Mehsood:** Results.
5	**Iqra Zia:** Data collection.
6	**Saima Bashir:** Final manuscript.

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ORIGINAL ARTICLE

Complete remission rate in advanced-stage diffuse large B-Cell lymphoma following treatment with R-CHOP.

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ABSTRACT… Objective: To evaluate the complete remission (CR) rate in patients with advanced-stage DLBCL following treatment with R-CHOP. **Study Design:** Descriptive Cases-series study. **Setting:** The Institute of Nuclear Medicine and Oncology (INMOL) in Lahore. **Period:** 16th May 2025 to 16th October 2025. **Methods:** Conducted on 60 patients diagnosed with stage III or IV DLBCL and treated with six cycles of R-CHOP chemotherapy at a tertiary care oncology unit were included in this observational study. Demographic baseline data, clinical record, and laboratory data were taken, such as age, gender, performance status, and stage of disease. The clinical evaluation and imaging assessment were used to evaluate response to treatment based on standard response criteria after therapy. **Results:** The average age of the patients was 44.17±12.85 years, and the patients were mostly men (61.7%). Over fifty percent of the patients (55) had stage III disease and forty five percent had stage IV disease. After six cycles of R-CHOP, the complete remission rate was 68.3 and partial remission of 21.7 and disease progression of 10 percent were seen. The CR rate in this study is also in line with other reports found in the literature that range between 65 and 75% of advanced-stage DLBCL. **Conclusion:** R-CHOP chemotherapy is a viable first-line therapy in achieving a high percentage of complete remissions in the advanced stage of DLBCL. However, a subset of patients unable to gain complete remission, which underlines the necessity to detect high-risk cases early and possibly to include new targeted or improved treatment methods.

Key words: Advanced-stage Lymphoma, Complete Remission, Chemotherapy Outcomes, Diffuse Large B-cell Lymphoma, R-CHOP.

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INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is a malignancy of B lymphocytes, which are responsible for antibody production. It represents a subtype of B-cell lymphoma which is aggressive and non-Hodgkin in nature and accounts for nearly 30%[1] among these cases. Clinically, DLBCL typically manifests as a rapidly enlarging mass or localized tissue infiltration and is frequently accompanied by symptoms, including fever, unexplained weight loss, and night sweats.[2]

DLBCL can be classified according to the resemblance of its malignant cells to normal stages of B-cell differentiation. Cases that genetically resemble normal germinal center B cells are categorized as germinal center B-cell–like DLBCL (GCB-DLBCL), while those resembling activated B cells are classified as activated B-cell–like DLBCL (ABC-DLBCL).[3] The Hans algorithm, based on immunohistochemical staining for CD10, MUM1, and BCL6, is commonly used to distinguish between GCB and non-GCB subtypes.[4]

Fluorescence in situ hybridization (FISH) analysis revealing translocations involving both BCL6 with MYC or BCL6 with MYC2 genes identifies "double-hit lymphomas," while the presence of translocations in all three genes defines "triple-hit lymphomas.[5]" These subtypes are classified as high-grade B-cell lymphomas. The standard diagnostic evaluation for DLBCL typically includes a complete blood count (CBC), lactate dehydrogenase (LDH), uric acid, PET/CT or contrast-enhanced CT scan of the pelvis, abdomen and chest, hepatitis B screening, echocardiography, serum electrolytes, liver and renal function tests, and serum calcium measurement.[6]

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Most DLBCL cases arise due to genetic changes, including mutations, altered gene expression, amplifications, and chromosomal translocations, which lead to dysregulation of signaling pathways controlling cell maturation, proliferation, survival, immune evasion, and other malignant behaviors.[7] Commonly affected genes include PAX5, CD79B, CD79A, CREBBO, MYD88, EZH2, MYC, BCL6 and BCL2. As a result, neoplastic cells exhibit overactive NF-κB, Toll-like receptor, B-cell receptor, MAPK/ERK, JAK-STAT, PI3K/AKT/mTOR and NF-κB signaling pathways, promoting uncontrolled malignant behavior.[8,9]

A meta-analysis conducted on combined efficacy of rituximab with chemotherapy showed higher CR rates in the R-CHOP group than in the CHOP group (63.2% versus 50.7%).[10] Other studies comparing R-CHOP with or without additional agents demonstrated CR in 88% of patients and partial remission in 12%, with no significant difference between the arms.[11] Additionally, a study comparing obinutuzumab versus rituximab plus CHOP reported similar CR rates in both treatment arms, whether assessed by Alone CT or combined CT and PET/CT showing values 35.4% vs. 33.9% and 56.5% vs. 59.1% respectively.[12]

METHODS

The study was conducted to determine the efficacy of R-CHOP in B-Cell lymphoma patients. This study was conducted as a descriptive case-series study from 16th May 2025 to 16th October 2025, at the Institute of Nuclear Medicine and Oncology (INMOL) in Lahore over a duration of six months. A total of 60 patients were selected. After ethical approval (IRB#INMOL-53-(200) 18-02-25 was obtained and informed consent was secured, these previously untreated, CD20-positive advanced-stage DLBCL patients aged 20-60 with an Eastern Cooperative Oncology Group performance status of 0 to 2 and no central nervous system involvement were enrolled.

The exclusion criteria ruled out individuals with any other malignancy, prior chemotherapy or radiotherapy, HIV infection, active hepatitis B or C, pregnancy, or other severe diseases. Complete remission was defined as the absence of all detectable disease six weeks after treatment, confirmed by a PET-CT scan showing a Deauville score of 1-3, the complete disappearance of all measurable lesions, and the resolution of all disease-related symptoms. Diffuse Large B-Cell Lymphoma was defined as an aggressive CD20-positive B-cell lymphoma, confirmed by histopathological analysis of a biopsy, with patients having advanced-stage disease at enrollment.

Patients enrolled in this study received complete set of R-CHOP regimen including vincristine, doxorubicine, cyclophosphamide, prednisone and Rituximab administered in six cycles every 21 days. Tumor response was assessed via a PET-CT scan six weeks after treatment completion. For statistical analysis using SPSS version 26.0, qualitative data such as gender and cancer stage were presented as frequency and percentage, while quantitative data like age were presented with mean, median, and standard deviation. The potential effects of modifiers like age and disease stage were controlled through stratification, and a post-stratification Chi-square test was applied to see their impact on outcomes, with significant probability values (0.05).

RESULTS

The study included 60 patients with a mean age of 44.17 ± 12.85 years. Most of the patients were older than 40 years (61.7%), and males comprised 61.7% of the study sample. Regarding cancer stage, 55% of patients were in stage III and 45% in stage IV. According to ECOG performance status, 21.7% of patients were classified as ECOG 0, 41.7% as ECOG 1, and 36.7% as ECOG 2, indicating a predominance of patients with mild to moderate functional limitations [Table-I].

After six months of treatment, 68.3% of patients achieved complete remission, while 31.7% did not. [Figure-1]. The analysis revealed no statistically significant association between remission status and age ($p = 0.646$), gender ($p = 0.682$), cancer stage ($p = 0.759$), or ECOG score ($p = 0.103$). Although patients with lower ECOG scores tended to have higher remission rates, the difference did not reach statistical significance. [Table-II].

TABLE-I

Demographic and baseline characteristics of patients (n=60)

Variable	Categories	Frequency (n)	Percentage (%)
Age (years)	Mean±SD=44.17±12.85		
	≤40 years	23	38.3
	>40 years	37	61.7
Gender	Male	37	61.7
	Female	23	38.3
Cancer stage	III	33	55.0
	IV	27	45.0
ECOG	0	13	21.7
	1	25	41.7
	2	22	36.7

FIGURE-1

Complete remission after 6 months among the patients (n=60)

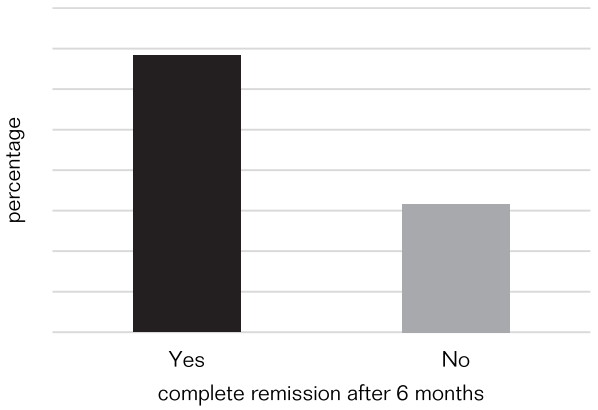

TABLE-II

Association of remission after 6 months with demographic and baseline profile of the patients (n = 60)

Variable	Category	Complete remission after 6 Months: Yes 41 (68.3%)	Complete remission after 6 Months: No 19 (31.7%)	Test of sig.
Age (years)	≤40 years	17 (41.5)	6 (31.6)	χ^2=0.537, d.f=1,p=0.646
	>40 years	24 (58.5)	13 (68.4)	
Gender	Male	26 (63.4)	11 (57.9)	χ^2=0.167, d.f=1,p=0.682
	Female	15 (36.6)	8 (42.1)	
Cancer stage	III	22 (53.7)	11 (57.9)	χ^2=0.094, d.f=1,p=0.759
	IV	19 (46.3)	8 (42.1)	
ECOG	0	12 (29.3)	1 (5.2)	χ^2=4.54, d.f=2,p=0.103
	1	16 (39.0)	9 (47.4)	
	2	13 (31.7)	9 (47.4)	

N (%), chi-square test was applied. Column wise percentage was calculated.

DISCUSSION

Mechanistically, R-CHOP combines cytotoxic agents that target rapidly dividing lymphoma cells with rituximab, an anti-CD20 monoclonal antibody that improves tumor cell clearance through antibody-dependent cytotoxicity and complement activation. The addition of rituximab to CHOP produced one of the most important survival gains in lymphoma therapy history, and the CR rate after R-CHOP reflects both chemosensitivity of the tumor and the immunologic potentiation provided by anti-CD20 therapy.[13,14]

In this cohort of 60 patients with advanced-stage diffuse large B-cell lymphoma (DLBCL) treated with R-CHOP, the observed complete remission (CR) rate of 68.3% is consistent with findings from major clinical trials and population-based studies. Jakobsenet al[15] reported a CR rate of approximately 70% among Danish patients treated with R-CHOP–like regimens, indicating comparable treatment effectiveness in real-world settings. Similarly, Habermannet al[16] demonstrated that adding rituximab to CHOP significantly improved CR rates to around 76%, compared to 63% with CHOP alone, in elderly patients. The MInT trial by Pfreundschuhet al[17] also showed CR rates exceeding 80% in younger, good-prognosis patients treated with R-CHOP. Thus, the CR rate in the present study falls within the expected range for advanced-stage disease, though slightly lower than that of favorable-risk populations.

The mean age in our study (44.17 ± 12.85 years) was lower than that reported in Western cohorts, where the median age is typically around 60–65 years.[18] A younger population may experience fewer comorbidities and better treatment tolerance, potentially explaining the relatively high CR rate despite inclusion of only stage III and IV cases. In contrast, older age has been repeatedly identified as a negative prognostic factor in DLBCL due to

reduced chemotherapy tolerance and biological disease aggressiveness.[18]

Regarding disease stage, all patients in our cohort had advanced disease, with 55% in stage III and 45% in stage IV. This distribution aligns with findings by Musimaret al[19], who also reported a predominance of advanced-stage disease in their real-world series. Despite advanced stage being associated with poorer survival outcomes, our CR rate remained favorable, suggesting effective disease control with standard R-CHOP even in higher stages.

The favorable CR rate observed in our all–advanced-stage cohort is consistent with earlier evidence demonstrating durable remission with R-CHOP, though relapse remains a concern. Frontiers in Oncology reviewed that even after achieving CR, relapse rates in stage III–IV DLBCL remain 25–30%, prompting exploration of consolidative strategies such as radiotherapy or maintenance therapy.[20] Therefore, while short-term remission outcomes in our study are encouraging, long-term follow-up is essential to assess sustained response and survival.

A recent Pakistani cohort conducted by Hassan et al[21] reported an 84.2% CR rate following first-line R-CHOP in newly diagnosed adult DLBCL patients. Major randomized trial data confirm that the addition of rituximab improved CR rates: the long-term update of the GELA study in elderly DLBCL found CR/CRu of 75% in the R-CHOP arm vs 63% in the CHOP arm; and 5-year PFS and OS of 54% and 58% in the R-CHOP arm.[22]

Finally, a large single-centre real-world study (n=1183) of patients who did not complete six cycles of R-CHOP (22% of cohort) observed substantially worse outcomes: 5-year OS significantly higher in those achieving CR/PR and receiving ≥3 cycles (58.5% vs 24.2%).[23]

CONCLUSION

R-CHOP chemotherapy is a viable first-line therapy in achieving a high percentage of complete remissions in the advanced stage of DLBCL. However, a subset of patients unable to gain complete remission, which underlines the necessity to detect high-risk cases early and possibly to include new targeted or improved treatment methods.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Faryal Azhar:** Article writing, Literature search.
2	**Fatima Mehak Zia:** Statistical analysis.
3	**Amber Amin:** Drafting.
4	**Zeeshan Badar:** Data collection.
5	**Faraz Saif:** Revision.
6	**Muneeb Nasir:** Data collection.

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CASE REPORT

A diagnostic dilemma: Severe hypokalemia presenting with GBS-like clinical feature.

Imtiaz Alam Afridi[1], Bella Virk[2]

ABSTRACT… Acute flaccid paralysis is a potentially life- threatening presentation necessitating prompt and precise diagnosis. Guillain-Barre' Syndrome (GBS) is often the first consideration due to its prevalence and severity. However, non-neurological conditions, particularly metabolic disturbances such as hypokalemia, can clinically and electrophysiologically mimic GBS. Hypokalemic paralysis, albeit rare, represents a reversible etiology of acute limb weakness. It may present with symptoms indistinguishable from GBS, including areflexia and ascending limb paralysis, resulting in a diagnostic dilemma. A misdiagnosis can delay appropriate treatment and subject the patient to unnecessary interventions. This case report elucidates a patient who exhibited classic features of GBS but was ultimately diagnosed with severe hypokalaemia. It underscores the imperative of good clinical assessments including correctly identifying serum electrolytes abnormalities in all patients presenting with acute neuromuscular weakness.

Key words: Acute Flaccid Paralysis, Diagnostic Challenge, Electrolyte Imbalance, Guillain-Barre Syndrome Mimic, Hypokalemic Paralysis, Quadriplegia, Reversible Paralysis.

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CASE PRESENTATION

A 23-year-old previously healthy male presented to the emergency department of Farooq Hospital (Bahria Enclave Branch) Islamabad, Pakistan with a one-day history of progressive quadriplegia. The weakness commenced abruptly first in the lower limbs and quickly progressed to involve the upper limbs. He reported difficulty in walking, standing from a seated position, and lifting objects but there was no swallowing or breathing difficulty. There were no other symptoms such as sensory symptoms, fever or bladder or bowel dysfunction and there was no history of trauma, vaccination or toxin exposure prior to these symptoms. The only relevant history we could find was that the patient had 4 days of watery diarrhea episode approximately 6-7 days prior to hospital admission.

He had been referred from a tertiary care hospital in Islamabad, where he had already been diagnosed with Guillain-Barre Syndrome (GBS), based on clinical presentation. Baseline investigations conducted revealed a serum potassium level (K+) of 2.7mmol/L. He came to us specifically for the management and treatment of GBS, including lumbar puncture, electromyography (EMG), nerve conduction studies and comprehensive GBS treatment.

On Examination Revealed:	GCS 15. Neurological Examination
1.Motor	Flaccid Paralysis (Grade 1/5 Strength) in all LIMBS.
2.Reflexes	Absent Deep Tendon Reflexes
3.Sensory	Intact
4.Cranial Nerves	Normal
5.Gait	Not Testable Due to Weakness

It is noteworthy that Farooq hospital's Bahria Enclave branch had been operational for only one month at that time, and certain diagnostic facilities were not yet available on-site. Given the acute, symmetrical, ascending flaccid paralysis with areflexia, a clinical diagnosis of Guillain-Barre Syndrome was initially entertained. The patient was admitted for further evaluation. We repeated his baseline investigations, which revealed a critically low serum potassium level 1.1mmol/L.

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Routine Laboratory Investigations Revealed	
Laboratory Investigations	**Results**
White Cell Count	7.2 (cell/μL)
Hemoglobin	15g/dL
Platelets	278 x 10^9/L
Serum Potassium	1.1 mmol/L
Serum Sodium	136mmol/L
Serum Magnesium	1.7mg/Dl
Renal Function	Normal
Arterial Blood GAS	Mild Metabolic Alkalosis

ECG revealed U-waves and flattened T-waves consistent with hypokalemia. Meanwhile, potassium chloride replacement therapy was immediately initiated. The patient was diagnosed with hypokalemic paralysis. Intravenous potassium chloride was administered with close monitoring in Intensive Care Unit. Remarkably, within 12 hours of starting treatment, the patient began to exhibit the signs of recovery with the return of reflexes. In the next few hours, we noted progressive improvement the patient's muscle power and reflexes and finally within 48 hours, the patient had regained full muscle strength of power 5/5 with normal tendon reflexes. By day third, he was discharged with oral potassium supplementation and dietary counselling. No further investigations such as Nerve Conduction Studies, MRI or Cerebrospinal Fluid (CSF) analysis were done.

DISCUSSION

Hypokalemia paralysis is a rare yet reversible cause of acute flaccid paralysis. It may be primary (often familial) or secondary to conditions such as renal losses, gastrointestinal losses, thyrotoxicosis, or certain medications. Hall mark features include acute-onset muscle weakness, hyporeflexia or areflexia, and significantly low serum potassium levels.

Clinically, hypokalemic paralysis can close resemble Gillian Barre Syndrome (GBS), particularly in cases presenting with symmetrical ascending paralysis, absent reflexes and a history of diarrhoea preceding the onset muscle weakness. However, distinguishing feature include a rapid and dramatic improvement with potassium correction, normal nerve conduction studies, and absence of sensory or cranial nerves involvement.

In contrast, GBS is an immune-mediated demyelinating polyneuropathy that usually follows an infection and requires treatment with intravenous immunoglobulin (IVIG) or plasmapheresis.

Misdiagnosis of hypokalaemia paralysis as GBS can lead to unnecessary interventions, prolonged hospital stays, and increased healthcare costs.

CONCLUSION

This case study underscores the need to consider severe hypokalemia as a differential diagnosis in patients presenting with symptoms suggestive of Guillain-Barré Syndrome (GBS). More importantly, it emphasizes the value of a thorough clinical and biochemical assessment in distinguishing between these conditions, particularly if resources are limited, as was in our case. A simple and relatively inexpensive step of repeating the serum electrolyte test as we did to eliminate the chances of lab errors, may save the day. This helped us in reaching a diagnosis quickly which led us to the early initiation of correct treatment without unnecessary investigations and potentially harmful treatments like immunoglobulin therapy, resulting in improved patient outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Imtiaz Alam Afridi:** Study concept, data analysis.
2	**Bella Virk:** Design, protocol writing, data collection, data analysis, manuscript writing.

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IMAGE

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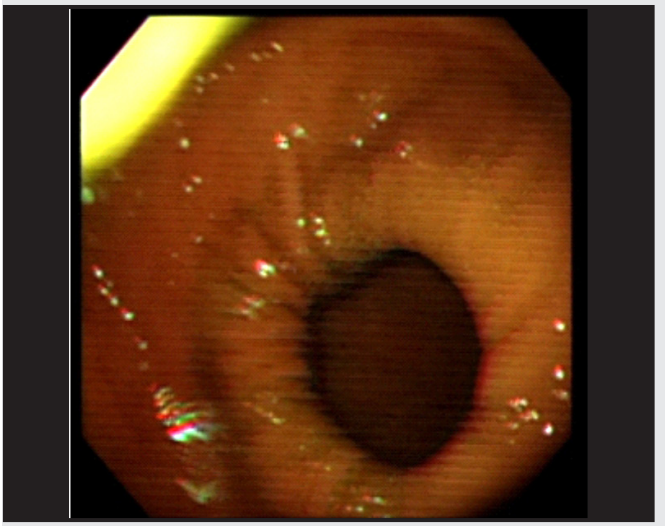
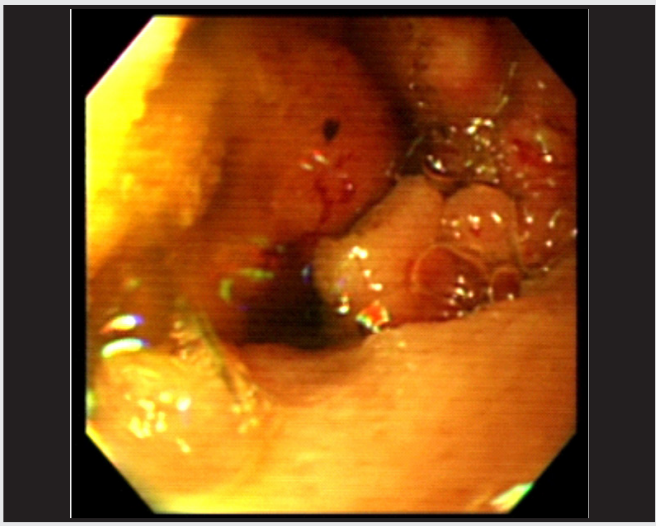
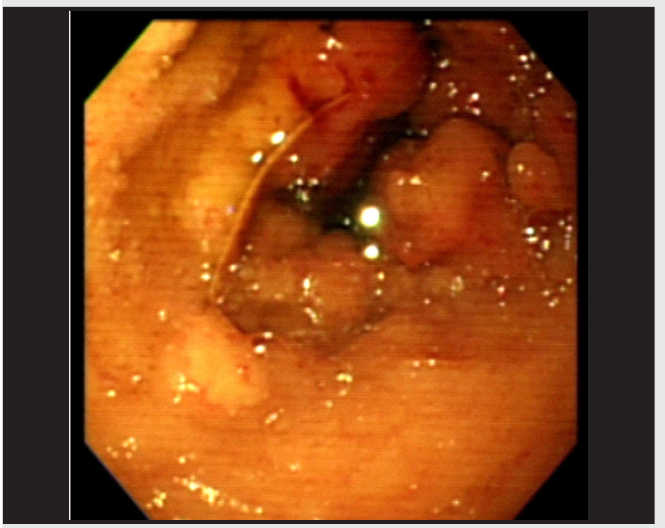
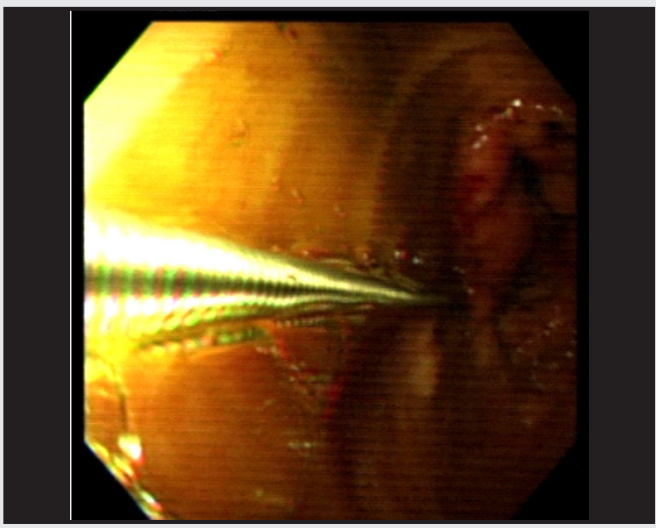
TUMOUR AT SECOND PART OF DUODENUM









A 63 year old male presented with gastric outlet obstruction. He underwent CT-Scan and contrast studies. On endoscopy and biopsy it was a adeno-carcinoma of duodeum.

Patient underwent palliative gastro jejunostomy.

Courtesy:
Prof. Awais Shuja FRCS, FCPS, MCPS-HPE
Department of Surgery
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This guide is written to help you peer review manuscripts submitted to THE PROFESSIONAL MEDICAL JOURNAL. Reading this should answer most of the queries you have and guide you in completing a peer review report in the most thorough and prompt way to ensure the paper is properly reviewed and published quickly. If you have any further queries please submit them to our Editorial Offices.

Our philosophy on peer review
Authors have historically complained of the time it takes to get a paper published. THE PROFESSIONAL MEDICAL JOURNAL tries hard to process papers as thoroughly, fairly and rapidly as possible. As a result, peer reviewers are asked to submit their comments within 28 days.

All manuscripts submitted to THE PROFESSIONAL MEDICAL JOURNAL are subject to double blind peer review. We believe that using anonymous peer reviewers is the best way to get honest opinions on papers. THE PROFESSIONAL MEDICAL JOURNAL requires that peer reviewers not contact authors directly. You should consider the COPE Ethical Guidelines for Peer Reviewers before accepting to review a manuscript and throughout the peer review process.

What is peer review?
Peer review is the process in which manuscripts are sent to impartial experts in the field who evaluate their quality and scientific soundness before publication. The exact process used for peer review varies between publishers and from journal to journal, but generally the method will fall into one of three categories:

Single blind:
Authors' identities are known to reviewers, but reviewers are anonymous

Double blind:
Both authors' and reviewers' identities are kept from each other

Open peer review: authors' and reviewers' identities are disclosed, and reviewer comments and author responses are publicly available

There is a fourth model, referred to as post publication peer review, in which peer review occurs after publication. This is often performed in addition to traditional pre-publication peer review, and attempts to provide a platform for the wider research community to discuss published papers and authors to respond to comments on their work.

Why is peer review important?
Peer reviewers' comments and recommendations are an essential guide to inform the editor's decision on a manuscript. Peer review ensures that manuscripts receive unbiased critique and expert feedback, allowing authors to improve their manuscript and therefore high quality scientific research and reviews to be published. It also helps the readers to trust the scientific integrity of the article and to make informed decisions where peer reviewer comments are available.

The Peer Reviewer
After receiving a request to peer review it is essential that peer reviewers respond in a timely fashion, particularly if they cannot do the review, to avoid unnecessarily delaying the process.

Peer reviewers should declare any conflicts of interest (seeking advice from the publisher if they are unsure), and possess sufficient knowledge in the field to perform a thorough assessment of the manuscript. You can find further information on competing interests here.

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THE PROFESSIONAL MEDICAL JOURNAL requires that all authors, peer reviewers and editors disclose all potential conflicts of interests. All authors must also complete the International Committee of Medical Journal Editors (ICMJE) form for Disclosure of Potential Conflicts of Interest.

Editors and reviewers are also required to declare any competing interests and will be excluded from the peer review process if a competing interest exists.

Editors-in-Chief must declare any financial and/or personal conflict of interest for each submitted manuscript, and decisions on manuscripts in which they have a conflict of interest will be made by another editor. The Editor-in-Chief is sent conflict of interest forms for every author on the paper he/she is reviewing. To preserve editorial integrity and eliminate bias, the Editor-in-Chief is not aware of the fee structure for any of the papers he/she reviews. Editorial decisions for manuscripts commissioned or solicited by the Editor-in-Chief will not be made by that Editor-in-Chief. Where the Editor-in-Chief, Associate Editor, or Editorial Board member submits a paper to their own Dove Medical Press journal, the policy is that another Editor on that journal is responsible for making the editorial decision (in accordance with section 9 of the COPE Ethical Editing guide, see also COPE case number 05-22 "Editor as author in own journal"). In this case we would also require a minimum of three sets of independent peer-review comments.

The author(s) of a manuscript submitted to any THE PROFESSIONAL MEDICAL JOURNAL are required to complete a declaration of competing interest for any commercial associations or financial interests held by the author or immediate members of the author's family, which might be construed as posing a conflict of interest, including but not limited to consultancies, employment, expert testimony, honoraria, retainers, stock holdings or options, and membership on boards of for-profit organizations with a financial interest in the article. All competing interests will be listed in the declarations at the end of the article.

The authors should consider the following questions when completing their competing interest declaration:

Financial competing interests
In the past three years have they received any funding from an organization that may have a financial interest in the manuscript?

Do they hold any stock holdings or options in an organization that may have financial interest in the publication of this manuscript?

Does the content of the manuscript relate to any patents they hold or are they currently applying for?

Have they received any funding or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

Do they have any other financial competing interests?

Non-financial competing interests

Are there any non-financial competing interests to declare in relation to the manuscript? Examples of non-financial competing interests include family associations, political, religious, academic or any other.

If the authors are unsure as to whether they, or one their co-authors, has a competing interest, they should discuss this with the editor.

THE PROFESSIONAL MEDICAL JOURNAL subscribes to the general intent of the principles adopted by the International Committee of Medical Journal Editors (ICMJE) on the control of data in publications arising from sponsored research. The author submitting a manuscript for any study funded by an organization with a proprietary or financial interest in the outcome shall have access to all the data in that study, and to have complete responsibility for the integrity and accuracy of the data, and the decision to publish.

Peer reviewers must keep any information regarding the identity of the authors and the content of the manuscript confidential.

Peer review comments should be objective and constructive without being of a hostile or derogatory nature.

Further information on ethical peer review issues and conflicts of interest can be found in the COPE guidelines.

Writing the Report

Peer reviewers should assess the major strengths and weaknesses of the manuscript as well as look at the statistical power of the study if relevant.

In the first part of their report, peer reviewers should write a short summary describing their assessment of the manuscript. They should then provide general comments to be addressed, followed by any specific comments they may have. Comments should be numbered so that authors can easily refer to them in their point-by-point response to referee comments. All requested major revisions should be clearly outlined. Minor revisions should also be mentioned where peer reviewers feel these will improve the manuscript's clarity and purpose.

If any form of misconduct is suspected such as plagiarism, undeclared conflicts of interest, falsification of results etc., these should be expressed directly in confidence to the Editor-in-Chief of the journal.

Peer reviewers must ensure that they answer the following questions in their report:

In general, is the paper easy to follow and does it have a logical flow?

Does the English grammar, punctuation or spelling need to be corrected?

Does the paper fit the aims and scope of the journal? (Each journal has an "Aims and Scope" link on the upper right of its home page).

Do the title and abstract cover the main aspects of the work?

Are the results novel? Does the study provide an advance in the field?

Did the study gain ethical approval appropriate to the country in which the research was performed if human or animal subjects were involved and is it stated in the manuscript?

Are the methods clear and replicable?

Is the statistical analysis appropriate to the study design?

Are the controls appropriate for the study design?

Do all the results presented match the methods described?

Is the data clearly and appropriately presented using clear language?

Did the authors make the underlying data available to the readers?

Do the conclusions correlate to the results found?

Does the paper raise any ethical concerns?

Are images appropriate for the article? If there are any concerns about duplication or manipulation in images, please raise potential issues by email or in your report.

Peer reviewers should provide the Editor-in-Chief with a recommendation regarding the suitability of the manuscript for publication. They can recommend that the manuscript should be accepted for publication with revisions ("revise and resubmit"), accepted without revisions, or rejected.

Peer reviewers should clearly fill the structured review performa.

Discretionary Revision: An optional revision that may improve the overall quality of the manuscript but does not affect the scientific validity of the study.

Minor Revisions: Issues that must be addressed by the author(s) before publication in order to adhere to scientific reporting standards, or issues affecting clarity.

Major Revisions: Major revisions needed which may consist of a lack of ethical consent statement, a conclusion contradicted by results, further experiments needed to support the conclusions (e.g. controls), unclear figures and tables etc.

Re-review request

Peer reviewers may be requested to re-review the authors' revised manuscript and point-by-point responses to their comments. Upon re-review, peer reviewers must ensure that all issues raised in the initial peer review report have been addressed and, if necessary, amended by the authors appropriately. Peer reviewers should once more assess the manuscript using the guidelines above and provide a revised recommendation.