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ORIGINAL ARTICLE

Salt at the table: A blessing or a curse for cardiovascular disease among people 60-75-year-old aged Karachi, Pakistan. Case- control study.

Fareeha Shahid[1], Muzaiyyena Qureshi[2], Sarwa Hameed[3], Uzair Qureshi[4], Hira Shaikh[5], Ahmad Khan[6]

ABSTRACT… Objective: To examine the association between discretionary salt use—specifically adding salt at the table—and the risk of cardiovascular disease (CVD) among adults aged 60–75 years in Karachi, Pakistan. **Study Design:** Case-control study. **Setting:** Department of Community Health Sciences, Bahria University Health Sciences, Karachi, Pakistan. **Period:** June 2024 to November 2024. **Methods:** A total of 592 participants were enrolled, including 296 diagnosed CVD patients with chronic hypertension (cases) and 296 age- and gender-matched controls without CVD (controls). Data were collected using a structured, closed-ended questionnaire in English and Urdu via Google Forms. Participants' salt consumption behaviors, blood pressure readings, sociodemographic data, and beliefs about salt use were recorded. Data were analyzed using SPSS version 26. The chi-square test ($p \leq 0.05$) was applied to determine associations between salt use and CVD, and odds ratios (ORs) were calculated to assess risk levels. **Results:** Participants who frequently added salt at the table had significantly higher odds of developing CVD. A total of 72% of CVD cases reported added salt intake compared to 28% of controls ($p = 0.0001$). The odds ratio for CVD among high salt users was 4.894 (95% CI: 3.395–6.926). Additional risk factors included higher blood pressure, lower education, smoking, and a family history of heart disease. **Conclusion:** The study reveals a strong link between discretionary salt use and increased cardiovascular disease risk in older adults. Targeted public health strategies, including dietary counseling and awareness campaigns, are recommended to reduce salt intake and prevent CVD in this age group.

Key words: Cardiovascular Disease (CVD), Case-control Study, Discretionary Salt, Hypertension, Karachi, Older Adults, Salt Intake.

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INTRODUCTION

The development of atherosclerosis in the epicardial coronary arteries is one of the characteristics of coronary artery disease (CAD).Thirty-two million deaths from diabetes, cancer, heart disease, and chronic respiratory illnesses (80%) and eighty-three million deaths from non-communicable diseases (20%) were ascribed to these ailments, respectively. Every year, 17.9 million deaths globally are ascribed to CVDs.[1] Dietary factors cause the bulk of CVD deaths in Europe's population. In 2015, dietary factors were responsible for 48% of deaths in women from CVD and 56% of fatalities in men.[2,3]

Over 1.28 billion adults worldwide, or roughly two thirds of the world's population, have hypertension. Only 42% of adults with hypertension are recognized and receiving appropriate treatment, with an estimated 46% of hypertensive adults being ignorant of their illness. High salt consumption and less than 3.5 grams of potassium per day can both lead to hypertension and increase the risk of stroke.[4]

Low sodium intake is advised by several blood pressure guidelines for the general public. The rationale behind this recommendation is that lowering sodium intake, regardless of level, will lower blood pressure and, consequently, reduce the incidence of cardiovascular disease. According to the findings of earlier research, a diet heavy in salt increases blood pressure as well as the risk of death and cardiovascular disease (CVD). It has been demonstrated that promoting behavioral modifications to limit salt intake lowers blood pressure.[5,6] There was a correlation found between masculine gender and alcohol intake and a higher liking for salt.

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The elderly and those with Afro-descendant hypertension (HTN) are most sensitive to salt.[7,8]

Many people have the practice of adding salt to their meal either before or after tasting it, despite the fact that a high sodium intake is strongly linked to the occurrence and progression of CVD. Two studies that used sizable, nationally representative samples of UK households estimated that between 31.7% and 40.2% of families' regularly added salt to their meals. According to evidence from national data, over 40% of different racial/ethnic groups in the USA said they regularly added salt to their food.[9,10,11]

The findings of this study could have significant implications for public health strategies aimed at reducing the burden of cardiovascular diseases in Karachi. If the study confirms a strong association between high salt intake and CVD risk, it would underscore the importance of promoting dietary modifications and salt reduction initiatives targeted at older adults. Moreover, the study could serve as a foundation for future research, exploring other lifestyle factors, genetic predispositions, and potential interventions to mitigate the risks associated with high salt consumption among the elderly population in Karachi.

METHODS

It was carried out through structured closed ended questionnaire, developed through Google form. The study was conducted over a period of six month from June'2024 to November'2024 approved by the Institutional Review Board of the Bahria University Health Sciences Campus, Karachi (Ref No: BUHS-IRB # 080-24, Dated: 07/06/2024). Consent was also taken from all the participants.

A total of 592 participants were enrolled in the case-control study after their written consent developed English and Urdu. Out of the 592, 296 cases and 296 controls sample size was calculated by the calculator tool with 95% confidence level, 5% margin of error ,80% statistical power and 1:1 ratio between case and control groups. All 296 cases of CVD diagnosed patients with chronic hypertension (more than 6 months) and use of added salt consumption more than the WHO recommendations were included in the study and they compared to 296 individuals age (plus or minus 2 years) and gender-matched community participants, visitors or relatives of patients from non-cardiac wards those who have not been diagnosed with CVD. History of depression and those lacking informed consent were excluded.

Data was received in the form of excel spreadsheet, was entered and analyzed by using Statistical Package for Social Sciences (SPSS), version 26. Analysis was carried through descriptive statistics to calculate the frequency and percentages of main variables like age, education level, frequency and dietary habits, blood pressure values and family history of heart disease are associated with cardiovascular disease risk Multi-variable analysis was done using the Chi-Square test to compare the added salt intake with and without CVD with all socio-demographic, disease related and medical variables. The results were considered as significant when p value was ≤ 0.05. Matching and restriction techniques help isolate the specific impact of salt consumption on cardiovascular disease outcomes.

RESULTS

The findings of this study highlight that reducing added salt intake at the population level is a viable and impactful strategy for lowering cardiovascular stress. By identifying a strong association between additional salt use and cardiovascular disease (CVD), this research underscores the importance of dietary interventions in public health planning. Furthermore, the study supports the concept of individualized treatment for salt-sensitive individuals. Tailoring dietary advice for these patients can lead to better blood pressure control, particularly in hypertensive individuals, thereby reducing the overall incidence and burden of cardiovascular disease. These outcomes reinforce the need for awareness campaigns, behavior modification strategies, and policy measures aimed at promoting salt reduction, especially in older adults who are at higher risk.

A total of 592 participants were included, with 296 cases (Group A) and 296 age- and gender-matched controls (Group B). Salt consumption patterns varied significantly between the groups (p=0.0001), with a higher proportion of cases using larger salt

quantities. The odds ratio showed that individuals with high salt intake had approximately 4.9 times greater risk of developing cardiovascular disease (CVD). Table 1 presents associations between demographic, behavioral, and clinical variables with CVD status. Significant factors included blood pressure levels, educational status, beliefs about salt, smoking, and family history of heart disease. Notably, 100% of cases had moderate to severe BP elevation, while most controls had normal or mildly elevated BP. There was no significant difference in residence (urban vs. rural).

Analysis showed that 72% of cases reported added salt intake compared to only 28% of controls. A strong association with an OR of 4.894 (95% CI: 3.395–6.926), reinforcing that excess salt consumption substantially increases CVD risk.

TABLE-I

Association between salt intake and cardiovascular disease risk

Variable	Group A (CVD Cases)	Group B (Controls)	P-Value
Age (years)			0.0001
60–65	111 (37.5%)	138 (46.6%)	
66–70	114 (38.5%)	101 (34.1%)	
71–75	65 (22.0%)	35 (11.8%)	
>75	6 (2.0%)	22 (7.4%)	
BP on Check			0.0001
Normal/Mild	—	296 (100%)	
Moderate/Severe	296 (100%)	—	
Education			0.0003
Illiterate/Primary	189 (64%)	160 (54%)	
Secondary+	107 (36%)	136 (46%)	
Residence			0.7
Rural	124 (42%)	128 (43%)	
Urban	172 (58%)	168 (57%)	
Salt Use in Food	203 (69%)	125 (42%)	0.0001
Extra Salt While Eating			0.0001
None	27 (9%)	69 (23%)	
Pinch (300 mg)	109 (37%)	133 (45%)	
Spoon (1700–2300 mg)	160 (54%)	94 (32%)	
Salt Use Frequency			0.0001
Never/Once	60 (20%)	93 (31%)	
≥Twice	236 (80%)	203 (69%)	
Belief: Reduce Salt Helps CVD	Yes: 138 (47%)	200 (68%)	0.0001
Belief: Extra Salt = Heart Risk	Yes: 175 (59%)	68 (23%)	0.0001
Smoking	Yes: 179 (60%)	206 (70%)	0.025
Family History of CVD	Yes: 191 (65%)	107 (36%)	0.0001
Signs of HTN	Yes: 296 (100%)	0 (0%)	0.0001

DISCUSSION

While it is widely believed that a high-salt diet raises blood pressure, not everyone who consumes excess salt develops hypertension (HTN). This variation is due to individual differences in salt sensitivity—those who are salt-sensitive are more likely to experience elevated blood pressure and an increased risk of cardiovascular disease (CVD). Although numerous international studies have linked added salt intake to hypertension and CVD[12], there is a lack of local evidence from Pakistan.

In a Cochrane review of trials on salt reduction, it was discovered that a daily intake of salt caused a drop in blood pressure of 5.4/≥4 wk, or 4.4 g in 2.8 mm Hg for hypertensive people and 2.4/1.0 mm Hg for normotensive people. In hypertensive people, blood pressure decreased by 5.02/2.78 mm Hg, while in normotensive people, it decreased by 1.08/0.24 mm Hg, according to a more current Cochrane study.[13]

Reducing salt intake could lessen the burden of non-communicable diseases (NCDs) in the population. This will contribute to the low-cost global reduction of the burden of NCDs.[14] Strict dietary salt restriction may negatively alter neurohormonal activity, serum lipid levels, and insulin resistance—factors that increase the risk of heart failure and cardiovascular disease.[15]

A lower risk of cardiovascular events or fatalities from cardiovascular disease was linked to sodium excretion of less than 2.3 g/day (as opposed to 3.6–

4.8 g/day), according to the Trials of Hypertension Prevention (TOHP) study.[16]

More than 75% of deaths from CVD occur in low- and middle-income nations.[17] Reducing the sodium content of processed foods may raise the intake of carbohydrates and starches, which in turn may raise blood pressure and the risk of cardiac-metabolic disease in general.[18]

Numerous research' findings have linked inadequate salt intake to an increased risk of death. Elevated salt consumption has also been linked to a higher death rate. The rise in CVD risk factors has also been linked to a lack of knowledge. There is evidence that the risk of CVD is higher in urbanized populations than in rural ones, for both men and women. Nonetheless, there is currently a dearth of research on Pakistani CVD risk factors.[19] Elevated sodium consumption has been linked to increased cardiovascular disease mortality in the whole population. Nevertheless, a previous study indicated that decreased sodium excretion was linked to increased cardiovascular disease mortality. It is recommended to do a primary prevention study that focuses on the entire community. This is because there is limited evidence of a major threshold effect, as the risks of cardiovascular disease increase continuously across the range of blood pressure levels.[20]

Several scientists maintain the belief that higher salt intake is associated with an increased likelihood of developing cardiovascular diseases and experiencing death due to these conditions. Further study may involve the development of optimal strategies for reducing salt intake and establishing objectives for population-wide consumption. There is a lack of research on the correlation between the amount of salt consumed in one's diet and the outcomes of cardiovascular disease in older age groups.[5]

The impact of salt intake on global incidence of cardiovascular disease (CVD) is still uncertain. Recent research and the absence of a definitive randomized controlled trial indicate that reducing salt consumption to low levels can decrease the risk of cardiovascular disease (CVD), which has sparked a renewed discussion about the optimal target for sodium intake. Despite numerous research studies analyzing the correlation between salt intake, blood pressure, and cardiovascular disease (CVD).[21] Recent studies have found that individuals who add salt at the table had a 15% increased risk of heart failure compared to those who do not add extra salt.[22]

The evidence on the relationship between sodium intake and cardiovascular outcomes in older adults is mixed. Some studies found that higher sodium intake was associated with increased blood pressure and CVD risk, while others found a J-shaped association, with both low and high sodium intake associated with higher CVD risk.[23]

Some studies reporting J- or U-shaped associations between sodium intake and cardiovascular risk relied on a single 24-hour urine sodium measurement, which may not reflect usual intake. In contrast, more recent studies using average 24-hour urine sodium values have shown a clear, positive linear relationship between sodium intake and blood pressure, cardiovascular outcomes, and mortality. These findings suggest that earlier inconsistencies were due to methodological differences.[24]

Factors like salt sensitivity, frailty, and underlying health conditions may modify the association between sodium and CVD risk in this age group. A 10-year study examining dietary sodium intake through a food frequency questionnaire in older adults (mean age 73.6 years) found no significant association between sodium intake and mortality, cardiovascular disease (CVD), or heart failure (HF). Despite most participants consuming over 2300 mg/day of sodium, higher intake did not significantly impact outcomes, even after adjusting for demographic, caloric, and BMI factors. Subgroup analyses showed no consistent effects across sex, race, or hypertension status. These findings suggest that, within the observed intake range, sodium consumption may not strongly influence long-term cardiovascular outcomes in older adults.[25]

CONCLUSION

Frequent addition of salt at the table is linked to a higher risk of cardiovascular disease (CVD) in adults aged 60–75. However, the broader relationship

between overall sodium intake and cardiovascular outcomes in this age group remains complex and requires further study. Given the rising CVD burden in low- and middle-income countries, standardized research methods and population-specific interventions are essential to effectively reduce sodium intake and manage CVD risk in older adults.

RECOMMENDATIONS

This study has important public health implications for reducing the CVD burden in Karachi. The strong link between high salt intake and CVD underscores the need for dietary changes and salt reduction efforts, especially in older adults. The findings support targeted awareness campaigns and policy measures to limit discretionary salt use. They also lay the groundwork for future research into other lifestyle, genetic, and preventive factors influencing CVD risk in the elderly.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Fareeha Shahid:** Data collection.
2	**Muzaiyyena Qureshi:** Writing.
3	**Sarwa Hameed:** Data analysis.
4	**Uzair Qureshi:** Discussion writing.
5	**Hira Shaikh:** Review of manuscript.
6	**Ahmad Khan:** Data analysis.

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ORIGINAL ARTICLE

Comparison of metformin plus modified release gliciazide with metformin plus sitagliptin for treatment of diabetes mellitus.

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ABSTRACT… Objective: To compare the efficacy of metformin plus modified-release gliclazide versus metformin plus sitagliptin in reducing HbA1c levels in patients with type II diabetes mellitus. **Study Design:** Randomized Controlled Trial. **Period:** August'2021 to January'2022. **Setting:** Medical Outdoor, Allied Hospital Faisalabad. **Methods:** Total 200 patients with type II diabetes mellitus of either gender of age 30-60 years were selected. Group A patients took combination of metformin (1000 mg/day) and modified release gliclazide (60 mg/day) for 12 weeks. Group B patients took combination of metformin (1000 mg/day) and sitagliption (100 mg/day) for 12 weeks. **Results:** The mean age of patients in group A was 43.43 ± 9.76 years and in group B was 45.83 ± 7.86 years. Out of 200 patients, 86 (43.0%) were males and 114 (57.0%) were females with male to female ratio of 1:1.3. In my study, mean HbA1c after 12 weeks of treatment with combination of metformin and Gliclazide was 6.53% ± 0.18 and with combination of metformin and sitagliptin it was 6.40% ± 0.10 (p-value = 0.0001). **Conclusion:** This study concluded that thecombination of Metformin and Sitagliptan is better than combination of Metformin and for modified release Gliclazid treatment of type II diabetes mellitus in terms of mean HbA1c.

Key words: HbA1c, Sitagliptin, Type 2 Diabetes.

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INTRODUCTION

A group of metabolic illnesses that are collectively referred to as diabetes can be characterized by hyperglycemia that is brought on by abnormalities in either the function or synthesis of insulin, or both.[1,2] Globally, the prevalence of diabetes mellitus ranges from 10% to 14%.[3] One of the defining characteristics of diabetes mellitus type 2, sometimes referred to as noninsulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes, is the presence of high blood glucose levels in the context of insulin resistance and relative insulin deficiency. It is possible for there to be no insulin at all if the pancreatic islet cells are taken out of the equation.[2]

Sulfonylureas, including modified-release (MR) gliclazide, and DPP-4 inhibitors, such as sitagliptin, are commonly employed as second-line treatments. Both improve glycaemic control, although they do so in different ways, have different risks of hypoglycemia, affect weight differently, and cost different amounts. In ordinary clinical practice, comparing the effectiveness and safety of metformin + gliclazide MR with metformin + sitagliptin can help find the best treatment for people with T2DM. When it comes to the treatment of type 2 diabetes mellitus, a comparison of metformin with modified-release gliclazide and metformin plus sitagliptin reveals significant differences in terms of both efficacy and safety profiles: Metformin decreases hepatic glucose production and improves insulin sensitivity; gliclazide stimulates insulin secretion as a sulfonylurea; and sitagliptin is a DPP-4 inhibitor that increases glucose-dependent insulin secretion. Both combinations are aimed at glycaemic control; however, they differ in the mechanisms by which they accomplish this. It has been demonstrated through clinical research that the combination of gliclazide MR and metformin is more effective in lowering HbA1c levels than the combination of sitagliptin and metformin.[4] Furthermore, the combination of these two medications has a similar impact that lasts longer and patients continue to take it.

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Sitagliptin, a DPP-4 inhibitor, lowers blood glucose by preserving incretin hormones and enhancing insulin secretion. It offers advantages such as no weight gain, low risk of hypoglycemia, and may improve islet cell function by promoting proliferation, reducing apoptosis, and suppressing glucagon secretion. Furthermore, sitagliptin increases islet cell proliferation, decreases cell apoptosis, and reduces glucagon secretion in vitro.[5] In a study, mean HbA1c after 12 weeks of treatment with combination of metformin and Gliclazide was 6.5% ± 0.15 (6.4-7) and with combination of metformin and sitagliptin it was 6.4% ± 0.175 (6.3 -7).[6]

When compared to DPP-4 inhibitors like as sitagliptin, sulfonylureas have the potential to pose a higher risk of hypoglycemia. However, gliclazide MR has been around for a longer period of time and has proven to be successful in lowering blood glucose levels. The choice between these combinations is frequently determined by patient-specific factors such as glycaemic objectives, the risk of hypoglycemia, considerations regarding weight, and ability to tolerate the medication.[7] The progressive metabolic disease known as type 2 diabetes mellitus (T2DM) is steadily receiving international attention as a possible pandemic.

The International Diabetes Federation (IDF) has projected that by the year 2040, the number of people who have diabetes will have increased to 642 million, which is equivalent to one in ten adults. As of 2015, the number of people who have diabetes is 415 million, which is equivalent to one in eleven adults.[8] There is still a lack of direct comparative data between these two regimens, particularly in conditions that are representative of the actual world. In patients with type 2 diabetes who are not effectively managed by metformin monotherapy, the purpose of this study is to evaluate the effectiveness, safety, and tolerability of metformin plus modified-release gliclazide in comparison to metformin plus sitagliptin. This study aims to compare the efficacy of two metformin-based dual-combination therapies for managing type II diabetes mellitus in a local setting, where limited local data currently exists.

METHODS

The primary objective is to assess the mean HbA1c levels after 12 weeks of treatment with either metformin plus modified-release gliclazide or metformin plus sitagliptin. The hypothesis posits that the metformin-sitagliptin combination will yield better glycemic control (lower HbA1c) than the metformin-gliclazide combination. Type II diabetes mellitus is operationally defined as fasting blood sugar ≥126 mg/dL or random blood sugar ≥200 mg/dL, while HbA1c is measured via hospital pathology laboratory tests after the 12-week intervention.

The study is designed as a randomized controlled trial conducted at the Medical Outdoor Department of Allied Hospital, Faisalabad after the approval of CPSP and Institutional Ethical Review Board (Reference.No.869, Date: 13-07-2021). Using the WHO sample size calculator for two means, a total of 200 participants (100 per group) were determined, with an anticipated mean HbA1c of 6.5%, a test value of 6.4%, a pooled standard deviation of 0.16, a 5% significance level, and 80% power. Non-probability consecutive sampling was employed for recruitment.

Inclusion criteria consist of patients aged 30 to 60 years with HbA1c values between 6.5% and 11%, currently administered metformin at a dosage of 1000 mg/day, and with a BMI of less than 40 kg/m^2. important cardiovascular events, increased liver enzymes (AST/ALT >2.5× upper limit), elevated serum creatinine (men: >1.5 mg/dL; women: >1.4 mg/dL), systemic corticosteroid use in the prior 12 weeks, insulin therapy, or pregnancy are all important reasons why someone might not be included. After getting permission from the ethics board, eligible OPD patients gave their informed consent and were randomly put into either Group A (metformin + gliclazide MR 60 mg/day) or Group B (metformin + sitagliptin 100 mg/day). At 12 weeks, HbA1c was tested, and follow-ups were done by phone.

SPSS Version 23 was used to analyse the data. The mean ± SD was used to report age, disease duration, and HbA1c, while frequencies and percentages were used to describe the gender distribution. An independent samples t-test was conducted to evaluate post-treatment HbA1c levels between groups, incorporating stratification for effect modifiers such as age, disease duration, and

gender, followed by post-stratification t-tests. A p-value of less than or equal to 0.05 was considered statistically significant. This study aims to inform local treatment decisions by assessing the optimal dual-therapy approach for glycaemic management in type II diabetes.

RESULTS

There were 200 patients with type II diabetes mellitus in the study, and they were randomly put into two therapy groups. Group A got metformin and modified-release gliclazide, whereas Group B got metformin and sitagliptin. The average age of all the people who took part was 44.66 ± 8.65 years. Group A's average age was 43.43 ± 9.76 years, while Group B's average age was 45.83 ± 7.86 years. Of the 200 people who took part, 86 were men (43%) and 114 were women (57%). This means that there were about 1.3 men for every woman. The average weight was 75.63 ± 8.35 kg, the average height was 165.86 ± 14.76 cm, and the average body mass index (BMI) was 29.12 ± 3.31 kg/m^2. The average length of time that people had diabetes was 9.87 ± 3.84 years. 45% of people had it for less than 10 years, while 55% had it for more than 10 years.

After 12 weeks of treatment, Group B (metformin + sitagliptin) showed much improved glycaemic control, with a mean HbA1c of 6.40 ± 0.10%, compared to 6.53 ± 0.18% in Group A (metformin + gliclazide). The p-value of 0.0001 was very significant.

Stratified analysis showed that all subgroups had the same patterns. When divided by age, patients aged 30–45 years had HbA1c levels of 6.55 ± 0.17% in Group A and 6.40 ± 0.11% in Group B. Those aged 46–60 years had values of 6.51 ± 0.20% and 6.39 ± 0.11%, respectively. Both groups showed statistically significant differences (p = 0.0001). When looking at the data by gender, it was found that men in Group A had a mean HbA1c of 6.53 ± 0.17% while women in Group B had a mean HbA1c of 6.54 ± 0.19%. Again, both comparisons were statistically significant (p = 0.0001). Similarly, patients with a duration of diabetes ≤10 years had mean HbA1c values of 6.54 ± 0.16% in Group A and 6.39 ± 0.08% in Group B. Among those with >10 years duration, the values were 6.53 ± 0.20% and 6.41 ± 0.12%, respectively (p = 0.0001 for both).

These results collectively demonstrate that the combination of metformin and sitagliptin consistently leads to greater reductions in HbA1c levels compared to metformin and gliclazide MR, regardless of patient age, gender, or duration of diabetes.

TABLE-I

Baseline characteristics of study participants (N = 200)

Variable	Group A (n = 100)	Group B (n = 100)	Total (n = 200)
Age (years)	43.43 ± 9.76	45.83 ± 7.86	44.66 ± 8.65
Gender (Male/Female)	41 / 59	45 / 55	86 / 114 (M:F = 1:1.3)
BMI (kg/m^2)	-	-	29.12 ± 3.31
Height (cm)	-	-	165.86 ± 14.76
Weight (kg)	-	-	75.63 ± 8.35
Duration of Diabetes (years)	9.81 ± 3.87	9.95 ± 3.97	9.87 ± 3.84

TABLE-II

HBA1C after 12 weeks of treatment

Group	Mean HbA1c (%) ± SD	P-Value
Group A (Metformin + Gliclazide MR)	6.53 ± 0.18	
Group B (Metformin + Sitagliptin)	6.40 ± 0.10	0.0001

TABLE-III

Stratification of HBA1C by age, gender, and duration of diabetes

Stratification Variable	Category	Group A HbA1c (Mean ± SD)	Group B HbA1c (Mean ± SD)	P-Value
Age (years)	30–45	6.55 ± 0.17	6.40 ± 0.11	0.0001
	46–60	6.51 ± 0.20	6.39 ± 0.11	0.0001
Gender	Male	6.53 ± 0.17	6.42 ± 0.11	0.0001
	Female	6.54 ± 0.19	6.38 ± 0.10	0.0001
Duration of Diabetes	≤10 years	6.54 ± 0.16	6.39 ± 0.08	0.0001
	>10 years	6.53 ± 0.20	6.41 ± 0.12	0.0001

DISCUSSION

The chronic metabolic condition known as type 2 diabetes mellitus (T2DM) is characterized by insulin resistance, increasing β-cell dysfunction, and impaired glucose metabolism, which ultimately results in prolonged hyperglycemia. There is a continuing increase in the global burden of diabetes, with estimates showing that more than 530 million adults are currently affected by the condition. It is anticipated that this figure will approach 780 million by the year 2045. It is still essential to maintain optimal glycemic control as the foundation of diabetes therapy in order to lessen the likelihood of developing microvascular and macrovascular problems.[9]

Due to its efficacy, safety profile, cardiovascular advantages, and weight-neutral effect, metformin is regarded to be the pharmacologic agent of first-line treatment.

In 2014, it was projected that 9% of individuals worldwide had diabetes, with 90% of these instances being type 2 diabetes (T2D). With fasting plasma glucose (FPG) alone, the probable incidence of diabetes in individuals aged ≥30 years in Korea is 10.5%, and with both FPG and HbA1c, it is 12.4%, according to the Korea National Health and Nutrition Examination Survey 2011.[10]

In 30% to 50% of patients, diabetes is closely linked to both microvascular and macrovascular problems that cause damage to organs and tissues, and the risk of these complications is substantially correlated with prior hyperglycemia.[11] Even if subsequent therapy is less rigorous, diabetes has a positive momentum that might last for 10 years or more.[12] The new paradigm of therapy for T2D that aims to reach glycemic objectives early is supported by these recent findings individuals.[13]

When the initial HbA1c levels are greater than 7.5% (58 mmol/mol), the American Association of Clinical Endocrinologists (AACE) treatment algorithm recommends the early use of mixed therapy with metformin. This is because it has been demonstrated that reaching HbA1c levels below 7.0% (53 mmol/mol) is essential for achieving a prolonged reduction in microvascular complications, and possibly macrovascular complications as well. The American Diabetes Association (ADA) 2015 Standards of Medical Care in Diabetes recommend that patients with a high baseline HbA1c (≥9.0% [75 mmol/mol]) begin treatment with a combination of two non-insulin oral antihyperglycemic agents (AHAs). This is due to the fact that metformin monotherapy is not likely to assist these patients in reaching their target HbA1c.[14] As a result, individuals with type 2 diabetes may benefit greatly from the early commencement of combination treatment using AHAs that function via distinctively diverse pathways.

Prior research evaluating the safety and effectiveness of sitagliptin and metformin combination treatment in the Korean population has indicated that this dual medication is both effective and well-tolerated. According to a recent study, drug-naïve Korean patients who received metformin-based combination therapies with either sitagliptin, pioglitazone, or a sulfonylurea (glimepiride or gliclazide modified release) showed comparable glycemic effectiveness across a broad range of baseline HbA1c levels.[15] In another trial, glycemic control significantly improved when sitagliptin 100

mg/day was administered to Korean patients who had previously received combination therapy (dual or triple combination therapies with metformin). The incidence of hypoglycemic episodes actually dropped in the group that went from glimepiride to sitagliptin, indicating that patients with recurrent fasting hypoglycemia may want to think about doing so.[16]

The benefits of combination therapy were evaluated using a meta-analysis of 15 randomised clinical studies, which included the participation of about 7,000 persons who were diagnosed with type 2 diabetes respectively. The average age range in this study was 48.4–62.7 years, the average baseline HbA1c was 7.2–9.9%, and the average duration of diabetes was 1.6–4.1 years. All of these values were representative of the population. In these research, metformin was administered in conjunction with a number of other drugs, including thiazolidinediones (TZDs), insulin secretagogues, dipeptidyl peptidase-4 (DPP-4) inhibitors, and sodium glucose transporterase (SGLT-2) inhibitors. In contrast to metformin monotherapy, combined therapy was found to result in significant reductions in HbA1c levels. As a result of the combination treatment, the FPG was reduced, and the HbA1c goal level accomplishment was increased (HbA1c <7%).[17]

According to the findings of this study, the combination of Metformin and Sitagliptan is superior to the combination of Metformin and for modified release Gliclazid treatment of type II diabetes mellitus in terms of the mean HbA1c. Therefore, in order to lessen the morbidity associated with type II diabetes mellitus, we suggest that metformin and sitagliptan be utilised as the primary medication for regulating blood sugar levels in patients with this condition.

CONCLUSION

This study concluded that the combination of Metformin and Sitagliptan is better than combination of Metformin and for modified release Gliclazid treatment of type II diabetes mellitus in terms of mean HbA1c. So, we recommend that Metformin and Sitagliptan should be used as a primary treatment for controlling blood sugar in type II diabetes mellitus in order to reduce their morbidity.

LIMITATIONS

It was conducted at a single tertiary care hospital. Secondly, the follow-up period was limited, which does not allow for evaluation of long-term glycemic control, medication adherence, or sustainability of therapeutic effects. The use of non-probability consecutive sampling could have introduced selection bias. Additionally, the study did not mention any blinding of participants or investigators, increasing the risk of performance and detection bias. The focus was solely on HbA1c levels as the primary outcome, without consideration of other clinically significant parameters such as incidence of hypoglycemia, changes in body weight, or patient-reported outcomes. Furthermore, the safety and tolerability of the drug combinations were not assessed, which is essential for making informed treatment decisions in routine clinical practice.

RECOMMENDATIONS

Incorporating blinding in study design would reduce potential bias and improve the reliability of results. It is also recommended that future studies include additional outcome measures such as the frequency of hypoglycemic episodes, changes in body weight, patient satisfaction, and adherence to therapy. Monitoring adverse drug reactions and overall tolerability should be an integral part of study protocols. Lastly, a cost-effectiveness analysis comparing the two treatment combinations would provide valuable insights for healthcare providers and policy-makers, especially in resource-constrained settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Numra Shabbir:** Data collection, analysis.
2	**Saba Gulnaz:** Data collection, paper writing.
3	**Madeeha Qamar:** Data analysis.
4	**Salman Azhar:** Discussion writing.
5	**Wasif Baig:** Review of manuscript.
6	**Muhammad Afham Shahid:** Data analysis.

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ORIGINAL ARTICLE

Clinical significance of low HDL-C levels in managing acute coronary syndrome.

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ABSTACT… Objective: To investigate the clinical relevance of low HDL-C levels in the management of ACS, focusing on their association with adverse outcomes. **Study Design:** Prospective Observational study. **Setting:** Faisalabad Institute of Cardiology, Faisalabad. **Period:** December 2021 to May 2022. **Methods:** 384 patients diagnosed with ACS, admitted to a tertiary care hospital in Pakistan. HDL-C levels were measured within 24 hours of admission, and participants were stratified into low HDL-C (<40 mg/dL) and normal HDL-C (≥40 mg/dL) groups. Adverse outcomes, including 30-day mortality, recurrent myocardial infarction, heart failure, and hospital stay duration, were analyzed using multivariate logistic regression and Kaplan-Meier survival analysis. Statistical significance was set at $p < 0.05$. **Results:** Low HDL-C levels were observed in 210 patients (54.7%). These patients experienced significantly higher rates of 30-day mortality (21.4% vs. 6.9%), recurrent myocardial infarction (24.8% vs. 8.6%), and heart failure (31.9% vs. 13.2%) compared to those with normal HDL-C levels ($p < 0.001$ for all). Kaplan-Meier survival analysis showed reduced survival rates at 30 days (78.6% vs. 93.1%) and 90 days (65.2% vs. 88.7%) in the low HDL-C group ($p < 0.001$). Multivariate analysis identified low HDL-C as the strongest independent predictor of adverse outcomes (OR 2.85, 95% CI: 1.85–4.39, $p < 0.001$). **Conclusion:** Low HDL-C levels are a significant independent predictor of adverse outcomes in ACS patients, highlighting their importance in risk stratification and management. These findings emphasize the need for targeted therapeutic strategies to address low HDL-C levels, particularly in resource-limited settings.

Key words: Acute Coronary Syndrome, Cardiovascular Outcomes, HDL-C, Low HDL-C, Lipid Management, Pakistan, South Asian Population.

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INTRODUCTION

Cardiovascular diseases (CVDs) have continued to be the primary cause of death and disability globally; ACS is one of the most severe presentations of CVDs. ACS ranges from STEMI in which the blood flow distal to the occlusion is completely blocked to NSTEMI in which the blood flow is partially occluded and unstable angina.[1] These conditions are usually caused by atherosclerotic plaque formation within coronary arteries which subsequently becomes ulcerated, with accompanied thrombosis that results to partial or complete blockage in blood delivery to the myocardial mass. In Pakistan CVD are on the increase and account for 30-40% of all deaths every year.[2] Of these, ACS contributes considerable health care cost and burden because it presents abruptly, consumes a large amount of resource, and gives long-term complications.[3] Such abnormalities especially with lipid profile are among the main features associated with the development of ACS which is rooted in atherosclerosis. Although high levels of LDL-C is well understood to cause plaque build-up and eventual plaque rupture, the adequate levels of HDL-C have emerged to be equally important but under-recognized determinant of cardiovascular health. HDL-C, often referred to as "good cholesterol," plays a central role in reverse cholesterol transport, whereby it removes cholesterol from peripheral tissues and transports it to the liver for metabolism and excretion.[4] Beyond this, HDL-C exhibits numerous vasoprotective properties, including anti-inflammatory, antioxidative, and antithrombotic effects. These attributes make HDL-C a crucial biomarker and potential therapeutic target in managing cardiovascular risk.[5]

Emerging evidence has identified low HDL-C levels as a strong independent predictor of cardiovascular

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events, including ACS. International studies have shown that patients with low HDL-C levels are at higher risk of recurrent ischemic events, heart failure, and mortality after an ACS episode.[6] However, the majority of these studies are conducted in Western populations, with limited exploration of these associations in South Asian populations, including Pakistan.[7] Specifically, the South Asians are metabolically abnormal with a high prevalence of central obesity, insulin resistance and the resulting type 2 diabetes, dyslipidemia, characterized by reduced levels of HDL-C. These facts call therefore for an examination of the details of the actual effects of low levels of HDL-C on ACS results within the population of Pakistan.[8] In our country as well as in other countries, studies have also confirmed high rates of dyslipidemia as cardiovascular risk indicator.[9] For example, the cross-sectional reports from the tertiary care hospitals, Karachi and Lahore revealed that a large number of patients presenting with ACS have low levels of HDL-C. These studies also show a considerable unexpected shortage in assessment and management of the role of HDL-C in the clinical practice where most approaches are aimed at achieving a low LDL-C value.[10] Despite the benefit of statins and other lipid reducing therapies in reducing cardiovascular risk in ACS, there still exists a significant risk that remains even with normalisation of lipid parameters.[11] This raises an important question: Should low levels of or 'dysfunctional' HDL-C be used as a predictor or treatment intervention in the context of acute management of ACS?

The relative neglect of HDL-C in cardiovascular practice in Pakistan can also be explained by deficiencies in availability and expenditure on medical services as well as dearth of enthusiastic public health campaigns aimed at encompassing all lipid profiles.[12] In contrast to LDL- C which has formed a rationale of most lipid management approaches, HDL-C is generally deemed ancillary despite its proven benefits for cardiovascular health.[11] This lack of clinical emphasis along with additional burden of ACS in Pakistan calls for research to investigate the clinical relevance as to whether HDL-C is significantly different in acute setting of coronary events.[13] Moreover, the use of HDL-C for adding value in risk models may assist the clinician in defining the subjects at high risk and allow for more accurate therapeutic approach. As in any population, there is a need for focus on low levels of HDL-C as a common but neglected risk factor for ACS in Pakistan. To the best of our knowledge and on the backdrop of global progress in lipid management, there is sparse focus given to HDL-C with regard to research and out-patient care in Pakistan.[14] Filling this gap appears to be crucial to enhancing cardiovascular status of populations characterized by certain genetic and environmental biomarkers. It is the objective of this study to look at the relationship between low levels of HDL –C and unfavourable outcomes in A tendency to such information may help in catering for better risk assessment of patients as well as coordinating effective treatments for such cases.

METHODS

The goal of this prospective observational research was to assess the clinical usefulness of reduced HDL-C in treating acute coronary syndrome (ACS). The first aim was to determine the rationale for low HDL-C in patients with ACS, primarily concerning the prognosis of the disease in patients with ACS. The study comprised of both genders, participant selected according to the inclusion criteria of age, rigorously diagnosed with ACS, admitted in the Cardiology department of Faisalabad Institute of Cardiology, Faisalabad for a period of six months from December 2021 to May 2022 after approval from ethical review committee (Ref No. 13/DME/FCI/FSD, dated: 23-12-2020.ACS was operationally defined using the American Heart Association typology, which includes, unstable angina, NSTEMI, and STEMI. The criteria for selection of patients involved admitting a diagnosis of ACS and having either a fasting or non-fasting baseline HDL cholesterol result before 24 h from admission. Patient with CKD stage 4 or above, having familial dyslipidemia or those patients on lipid-lowering therapy before admission were excluded.

Data Collection

These data were collected from participating patients' medical records and laboratories during routine patient care and therapeutic interactions for a prospective period before the interview. A structure data collection form was formulated to make sure

that documentation was professional and inclusive. The following detailed procedures were followed:

Initial Assessment

At enrollment, patient data were collected from patients themselves by trained clinical staff through interview and included demographic data, symptoms presented and clinical past history. Physical examination results were recorded initially and they comprised of pulse rate, blood pressure, weight and overall height for calculation of BMI.

Clinical History and Risk Factors

Patients were directly asked about their hypertension, DM, smoking habits, dyslipidemia, and family history of CVD, and such expressed data were later confirmed with the patient's documents.

Laboratory Investigations

Venous blood specimens were taken in the first 24 hours of the patients' stay for lipids measurement including; HDL-C, total cholesterol, triglycerides and LDL-C. The colorimetric assays were enzyme based and the experiments were done in a laboratory that complies with institutional and quality control requirements. Other analyses included cardiac biomarkers levels of Troponin and Creatine kinase MB, Full blood count, Renal profile and blood glucose.

Cardiac Assessments

Initial ECG was done on admission and subsequent ECGs were done according to the type of ACS-unstable angina, NSTEMI or STEMI. Further evaluation of left ventricle function and possible complications including regional wall motion abnormality or cardiac effusion was done by echocardiography.

Treatment and Interventions

Data on in-hospital treatment, such as antiplatelet, statin, beta-blocker, and anticoagulant therapies, PCI, or CABG, were documented.

Follow-Up During Hospital Stay

Case–based daily clinical progress notes were evaluated to define the adverse event of recurrent myocardial infarction, cardiac arrhythmia, heart failure, or in-hospital mortality. It was noted whether there were alterations in medication or other different management measures were taken.

HDL-C Measurement

Fasting blood samples were collected within 24 hours of admission to measure lipid profile, including HDL-C levels. HDL-C was analyzed using enzymatic colorimetric methods standardized in the institutional laboratory.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range), depending on the distribution. Categorical variables were expressed as frequencies and percentages. The relationship between low HDL-C levels (<40 mg/dL in men and <50 mg/dL in women) and adverse outcomes was analyzed using multivariable logistic regression models. Adjustments were made for potential confounders, including age, sex, BMI, diabetes, and hypertension. Statistical significance was set at $p < 0.05$.

Ethical Considerations

The study was approved by the Institutional Review Board of Faisalabad Institute of Cardiology Faisalabad Pakistan, and written informed consent was obtained from all participants.

RESULTS

The study population consisted of 384 individuals with acute coronary syndrome. The mean age of the participants was 58.3 years (±12.5). A majority of the participants were male, with 276 individuals (71.9%), while females accounted for 108 individuals (28.1%). Among the population, 145 individuals (37.8%) were smokers. Hypertension was present in 195 participants (50.8%), and diabetes mellitus was noted in 168 individuals (43.8%). Dyslipidemia was prevalent in 243 participants (63.3%). Low HDL-C levels (<40 mg/dL) were observed in 210 participants (54.7%), whereas 174 participants (45.3%) had normal HDL-C levels (≥40 mg/dL). Table-I

The data presented in Table-II demonstrated the significant clinical impact of low HDL-C levels on outcomes in patients with acute coronary syndrome (ACS). Patients with low HDL-C showed a markedly

higher 30-day mortality rate, with 45 cases (21.4%) compared to 12 cases (6.9%) in the normal HDL-C group ($p < 0.001$). Similarly, recurrent myocardial infarction (MI) was significantly more frequent in the low HDL-C group, affecting 52 patients (24.8%) compared to 15 patients (8.6%) in the normal HDL-C group ($p < 0.001$). Heart failure was also more prevalent among those with low HDL-C, occurring in 67 patients (31.9%) versus 23 patients (13.2%) with normal HDL-C levels ($p < 0.001$). Additionally, the average length of hospital stay was significantly longer in patients with low HDL-C, at 8.7 ± 2.4 days compared to 5.2 ± 1.9 days for those with normal HDL-C levels ($p < 0.001$).

The multivariate analysis highlighted that low HDL-C levels (<40 mg/dL) are the most significant predictor of adverse outcomes in acute coronary syndrome, with an odds ratio (OR) of 2.85 (95% CI: 1.85–4.39, p<0.001), indicating a nearly threefold increased risk. Age ≥50 years is also a significant factor, showing an OR of 1.72 (95% CI: 1.20–2.46, p=0.003). Diabetes mellitus further contributes to adverse outcomes with an OR of 1.56 (95% CI: 1.04–2.34, p=0.031). Male gender (OR 1.32, 95% CI: 0.91–1.91, p=0.135) and hypertension (OR 1.25, 95% CI: 0.86–1.80, p=0.240) did not reach statistical significance in this analysis. These findings underscore the critical role of low HDL-C levels in risk stratification and management of acute coronary syndrome. Table-III

The Kaplan-Meier survival analysis presented in Table 4 highlights significant differences in survival rates between patients with low HDL-C levels and those with normal HDL-C levels over time. At 7 days, survival rates were 89.0% for the low HDL-C group compared to 96.5% for the normal HDL-C group (p<0.001). This disparity widened at 30 days, with survival rates of 78.6% and 93.1%, respectively (p<0.001). By 90 days, the low HDL-C group showed a markedly lower survival rate of 65.2%, while the normal HDL-C group maintained a survival rate of 88.7% (p<0.001). These findings underscore the clinical importance of low HDL-C levels as a predictor of poorer survival outcomes in patients with acute coronary syndrome. Table-IV

TABLE-I

Baseline characteristics of study population (n = 384)

Variable	Mean ± SD	n (%)
Age (years)	58.3 ± 12.5	
Male Gender		276 (71.9)
Female Gender		108 (28.1)
Smoking Status		145 (37.8)
Hypertension		195 (50.8)
Diabetes Mellitus		168 (43.8)
Dyslipidemia		243 (63.3)
Low HDL-C Levels (<40 mg/dL)		210 (54.7)
Normal HDL-C Levels (≥40 mg/dL)		174 (45.3)

TABLE-II

Clinical outcomes by HDL-C levels (n = 384)

Outcome	Low HDL-C (n = 210)	Normal HDL-C (n = 174)	P-Value
Mortality (30-day)	45 (21.4)	12 (6.9)	<0.001
Recurrent MI	52 (24.8)	15 (8.6)	<0.001
Heart Failure	67 (31.9)	23 (13.2)	<0.001
Length of Hospital Stay (days)	8.7 ± 2.4	5.2 ± 1.9	<0.001

TABLE-III

Multivariate analysis of predictors of adverse outcomes (n = 384)

Variable	Odds Ratio (OR)	95% CI	P-Value
Low HDL-C Levels (<40 mg/dL)	2.85	1.85 – 4.39	<0.001
Age (≥50 years)	1.72	1.20 – 2.46	0.003
Male Gender	1.32	0.91 – 1.91	0.135
Diabetes Mellitus	1.56	1.04 – 2.34	0.031
Hypertension	1.25	0.86 – 1.80	0.240

TABLE-IV			
Kaplan-meier survival analysis (n = 384)			
Time Period (Days)	Low HDL-C Survival (%)	Normal HDL-C Survival (%)	Log-Rank P-Value
7	89.0	96.5	<0.001
30	78.6	93.1	<0.001
90	65.2	88.7	<0.001

DISCUSSION

According to the present investigation, low HDL-C levels are important element in caring and evaluation of patients with acute coronary syndrome (ACS). Significantly, the real-life data show that levels of <40 mg/dL imply not only significantly worse short-term and long-term outcomes but also are independent predictors of mortality and adverse cardiovascular events. These findings are in line with, and enhance on, previous research within this line of research.

Low HDL-C Levels and Adverse Outcomes

Low HDL-C level was found significantly associated with higher 30 days mortality (21.4% vs 6.9%, p< 0.001), recurrent Myocardial infarction (24.8% vs 8. 6% , P < 0.001) and heart failure (31.9% vs 13.2 %, p < 0.001) in this study. These observations are also in accord with Mateos et al., (2005)[15] Their study suggested that patients with low levels of 'HDL-C' are at markedly higher risk of CVD events post ACS regardless the 'LDL-C' levels.[8] In the course of different investigations, it has been described that low levels of HDL-C are directly associated with the cardiovascular risk, even when LDL-C levels are under control.[12,16] This emphasizes the individual and the additive predisposing role of low HDL-C in cardiopathology.

Comparison with Existing Studies

Two of the pioneering epidemiological studies that established a link between low levels of HDL-C and CHD are the Framingham Heart Study by Bartlett and his colleagues.[17] Extending from this knowledge, we establish that low levels of HDL-C associate not only with CHD risk but also with the prognosis of ACS, including survival. Therefore, using similar rationale, the Atherosclerosis Risk in Communities (ARIC) study[18,] and Lipid Research Clinics (LRC) Program[19], pointed towards the association of HDL-C with reduced cardiovascular events. In this study, the Kaplan-Meier survival analysis performed here is consistent with these findings with significantly lower survival probabilities in the patients group with low HDL-C levels at 7, 30 and 90 days. Our own findings are also in line with the observations made by Cheng et al. (2024) who showed that measured LDL-C and low levels of HDL-C are critical in these patients because they predict cardiovascular events in cases when LDL-C is within the normal range.[20] In addition, there is the JUPITER trial by Negi and Ballantyne et al., (2010) and a meta-analysis by Peng et al. (2022) which highlighted the unaddressed CV risk linked to low levels of HDL-C, meaning that HDL-C interventions could enhance LDL-C manipulations[21,22]

Risk Stratification and Other Predictors

In addition to low HDL-C, our study identified age of 50 years and above and diabetes mellitus as variables that contributed most to an adverse outcome. Absolute age and diabetes are also confirmed risk factors, according to the authors of the UK Prospective Diabetes Study (UKPDS) Group (1998). Notably from the present study male gender and hypertension which were common in the cohort under study were not statistically significant to the outcomes. This is in contrast with INTERHEART study which found physical inactivity and raised BMI as important causes of myocardial infarction worldwide.[23] The failure to achieve significance in our analysis could be due to the fact that some of these conditions are perhaps very common in our study population, and their presence exert masking or confounding influences on our findings.

Functional Role of HDL-C

The patient can have high quantitative levels of HDL-C, but to have good outcomes, the function of the high density lipoprotein cholesterol is very important. Research by (Vallejo-Vaz and Ray et al. in 2015 and Cheng et al. in 2022 showed that the capacity to measure cholesterol efflux, a property of HDL-C, is a better marker for CAD events than HDL-C itself.[24,25] It is important to note that our study did not evaluate the functionality of HDL, and accordingly, the present results imply that simple quantitative assessment of HDL-C can yield further prognostic information in ACS patients.

Implications for Clinical Practice

Collectively, the results of the present work underscore the necessity of taking into account HDL-C levels while assessing risk and treating ACS. Current guidelines, both the ACCF and ESC guidelines as well as other recent scientific statements and guidelines, focus mainly on LDL-C in the management of dyslipidaemia. But here, contrary to our finding and the literature, there is a call for a holistic perspective on lipid management that involves targeting HDL-C. Novel method aiming at improving the functionality of HDL-C has potential to render improved outcome in cardiovascular disease; apoA-I mimetics, CETP inhibitors and HDL infusion therapies. Some interventions have been tested in clinical trials like the dal-OUTCOMES and the ASSURE[23,26] trials, outcomes of which show that there is still much more that needs to be done to make HDL-targeting drugs the panaceas they are touted to be.

CONCLUSION

Hence this study provides an important clinical correlation of low levels of HDL-C (<40 mg/d), especially in patients presenting with an acute coronary syndrome. As expected low levels of HDL-C were again associated with adverse outcomes, 30-day mortality, reinfarction, heart failure, and length of stay in hospital. Kaplan-Meier survival analysis done also further strengthened figures in supporting that the survival rate in this group is significantly low over time. Multivariate analysis also showed that low HDL-C level was the strongest predictor of poor outcome with odds ratio estimated at almost three folds. Importantly, both high-sensitivity C-reactive protein and low HDL-C levels were independent predictors of MACE in men and women with ACS, underpinning the importance of using low HDL-C as a risk score to suggest efficient individual management in this group of patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Maria Andleeb:** Manuscript writing.
2	**Muhammad Yasir:** Drafting.
3	**Munir Ahmad:** Data collection.
4	**Naeem Asghar:** Critical revision.
5	**Hafiz Muhammad Faiq Ilyas:** Critical revision.
6	**Ahmed Salman:** Data analysis.

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ORIGINAL ARTICLE

Occurrence of anxiety and its scores in chronic obstructive pulmonary disease patients.

Khalid Khan[1], Bella Virk[2], Alvina Khan[3], Binish Gull Arshad[4], Muhammad Asad Khan[5], Arsalan Mufti[6]

ABSTRACT… Objective: To find out the frequency and severity of anxiety in patients presented with chronic obstructive pulmonary disease. **Study Design:** Cross-sectional study. **Setting:** Accident and Emergency Medicine Department, Farooq Hospital, Islamabad. **Period:** March 2024 to September 2025. **Methods:** On chronic obstructive pulmonary disease patients was diagnosed with COPD using GOLD standard criteria with an age of 40 years and above were screened for anxiety by using Generalised Anxiety Disorder (GAD)-7 criteria. GAD-7 scores were distributed to classify anxiety severity into minimal (0-4), mild (5-9), moderate (10-14), and severe (15-21). **Results:** Of the 129 COPD patients, male patients were in the majority (82.2%, n=106), and female patients were in minority (17.8%, n=23). The mean age was 67.98±7.01 years. The overall mean GAD-7 score was 8.12±2.88. Anxiety severity was minimal in 3.1% (n=4), mild in 72.9% (n=94), moderate in 20.1% (n=26) and severe in 3.9% (n=5) COPD patients. Anxiety severity was significantly associated with gender (p-value<0.001) and age (p-value=0.006). **Conclusion:** The frequency of anxiety was high in patients presented with chronic obstructive pulmonary disease, with most of the patients suffering from mild anxiety, followed by moderate and severe anxiety.

Key words: Anxiety, Chronic Obstructive Pulmonary Disease, Disease Progression, Quality of Life.

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INTRODUCTION

One of the most prevalent medical conditions affecting people worldwide is chronic obstructive pulmonary disease (COPD). It is characterized by persistent respiratory symptoms with restricted airflow.[1,2] Despite being a preventable and treatable condition, COPD is linked to poor outcomes since there aren't many disease-modifying medications that work for most patients.[2,3]

COPD is a severe public health issue that has a significant financial and medical impact. Additionally, it is becoming a more significant cause of disease, disability, and fatalities worldwide.[4] Globally, the prevalence of COPD is steadily rising. In 2020, the prevalence of COPD was 10.6%, accounting for 480 million cases throughout the world. The number of COPD cases is expected to increase to 592 million by 2050, which is a 23.3% increase over 2020.[5] The World Health Organization reports that COPD ranks as the fourth most common cause of death worldwide.[6] In Pakistan, 6.9 million people suffer from COPD. The prevalence of undiagnosed COPD is roughly 31.1% in Pakistan's rural areas.[7]

It is becoming more widely acknowledged that COPD is strongly associated with severe psychological disorders, particularly anxiety. Despite being one of the most prevalent comorbidities in COPD, anxiety is frequently misdiagnosed. Anxiety is more common in COPD patients than in the general population. Among COPD inpatients, the prevalence of anxiety varies from 10% to 55%, whereas among outpatients, it ranges from 13% to 46%.[8,9] Anxiety has been remarkably associated with increased probability of COPD exacerbations, more frequent admissions to hospital, prolonged stays in hospital, higher utilisation of healthcare resources, decreased adherence to medications, decreased quality of life and higher rates of mortality. Early screening and collaborative care, including psychosocial, behavioural, and non-pharmacological interventions, have been suggested to enhance COPD outcomes and quality of life. Therefore, it is

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highly recommended that people with COPD should undergo early screening for anxiety disorders.[8-10]

Anxiety is highly prevalent in patients with COPD and associated with poorer health-related outcomes. The purpose of the study is the early recognition and management of anxiety in COPD, which may improve outcomes and potentially decrease health service utilisation.

METHODS

A cross-sectional study on chronic obstructive pulmonary disease patients was conducted in accident and emergency department of Farooq Hospital, Islamabad from March 2024 to September 2025. Patients were consecutively enrolled in the study from the accident and emergency medicine department. Open Epi software was used to determine the research sample size. A sample size of 129 was determined using the variables listed below: the expected frequency was 20.6%, with a 95% confidence interval and a 7% margin of error, based on a prior study by Sharma et al. that found 20.6% prevalence of anxiety in COPD patients.[11]

The study consist of patients fulfilling the following criteria: (1) patients diagnosed with COPD using GOLD standard criteria, (2) age of 40 years and above, (3) either gender, and (4) patients who are interested to participate in the study. The study excludes the patients fulfilling the following criteria: (1) COPD patients with a history of acute exacerbation within the last four weeks, (2) patients with other diseases such as cancer, chronic heart, liver or kidney failure etc., (3) patients with previous history of chest trauma, pulmonary tuberculosis, or lung infections, (4) patients with anaphylactic reactions, and (5) patients not interested to participate in the study.

The study permission was obtained from the Institutional Review Board of Farooq Hospital, Islamabad (Akhtar Saeed Medical College Rawalpindi) via letter no: 0601 dated 21st March 2024. Patients were given information about the study prior to their enrolment in the study, and then their signed informed consent was acquired. Patients who fulfilled the study's criteria for inclusion were recruited and demographic (gender and age) and medical details were obtained. Patients diagnosed with COPD using GOLD standard criteria were evaluated about the presence of anxiety by using Generalised Anxiety Disorder (GAD)-7 criteria. GAD-7 scores were distributed to classify anxiety severity into minimal (0-4), mild (5-9), moderate (10-14), and severe (15-21). The Statistical Package for Social Sciences (SPSS version 25) was a tool used for statistical analysis. Chi-square test and One way ANOVA were used for comparing anxiety severity with gender and age with p-value of ≤ 0.05. Before analysis, data was cleaned for removing duplicate entries and missing values, making sure that the final analysed data was complete for statistical analysis.

RESULTS

Of the 129 COPD patients, male patients were in the majority (82.2%, n=106), and female patients were in minority (17.8%, n=23) [Figure-1]. The mean age was 67.98±7.01 years, ranging from 53 to 85 years.

Among the 129 COPD patients, "Not being able to stop or control worrying" was the most commonly reported question with 65.1% (n=84) reporting it on several days and 13.2% (n=17) on nearly everyday. Similarly, "Being so restless that it is hard to sit still" was the second most commonly reported question with 63.6% (n=82) reporting it on several days and 14.7% (n=19) on more than half the days. In contrast, "Feeling nervous, anxious, or on edge" was the least commonly reported question with 40.3% (n=52) reporting it not at all [Table-I].

The overall mean GAD-7 score was 8.12±2.88. Anxiety severity was minimal in 3.1% (n=4), mild in 72.9% (n=94), moderate in 20.1% (n=26) and severe in 3.9% (n=5) COPD patients [Figure-2].

Anxiety severity was significantly associated with gender (p-value<0.001) [Table-II] and age (p-value=0.006) [Figure-3]. Male COPD patients were mostly suffering from anxiety as compared to female patients [Table-II]. Anxiety severity was also significantly increasing with increasing age. Mean age was 60.0 years in COPD patients diagnosed with minimal anxiety, which increased to 67.2 years in mild anxiety, 70.9 years in moderate anxiety and 73.0 years in severe anxiety [Figure-3].

FIGURE-1

Gender of COPD Patients

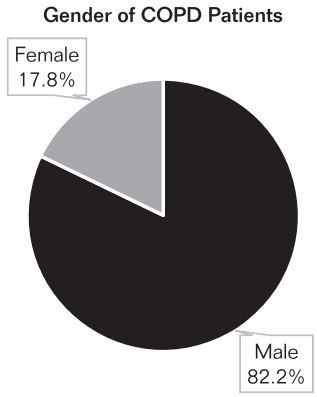


FIGURE-2

Anxiety in COPD patients

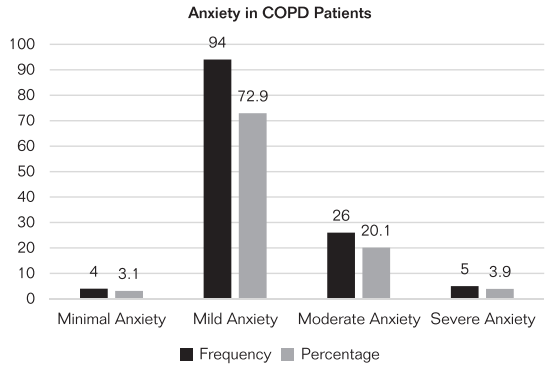
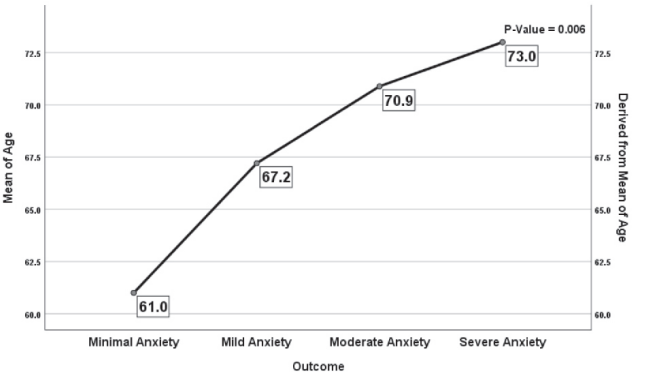


FIGURE-3

Anxiety in COPD patients



DISCUSSION

This study was conducted to find out the frequency and severity of anxiety in patients presented with chronic obstructive pulmonary disease at tertiary care hospital of Islamabad. In this study, 129 COPD patients were selected; most of them were male (82.2%, n=106), whereas females were few (17.8%, n=23). The mean age was 67.98±7.01 years, ranging from 53 to 85 years. These findings are similar with previous studies where Liu et al. reports the male prevalence of 88.5% and female prevalence of 11.5% with a mean age of 67.5 ± 7.3 years[9],

TABLE-I

GAD-7 Questions & Answers

Over the last 2 weeks, how often have you been bothered by the following problems?	Not al All	Several Days	More than Half the Days	Nearly Every Day
Q. 1 Feeling nervous, anxious, or on edge	52 (40.3%)	60 (46.5%)	13 (10.1%)	4 (3.1%)
Q. 2 Not being able to stop or control worrying	13 (10.1%)	84 (65.1%)	15 (11.6%)	17 (13.2%)
Q. 3 Worrying too much about different things	14 (10.9%)	63 (48.8%)	31 (24.0%)	21 (16.3%)
Q. 4 Trouble relaxing	30 (23.3%)	75 (58.1%)	21 (16.3%)	3 (2.3%)
Q. 5 Being so restless that it is hard to sit still	23 (17.8%)	82 (63.6%)	19 (14.7%)	5 (3.9%)
Q. 6 Becoming easily annoyed or irritable	51 (39.5%)	32 (24.8%)	36 (27.9%)	10 (7.8%)
Q. 7 Feeling afraid as if something awful might happen	14 (10.9%)	52 (40.3%)	41 (31.8%)	22 (17.1%)

TABLE-II

Anxiety and gender

Gender	Outcome				P-Value
	Minimal Anxiety	Mild Anxiety	Moderate Anxiety	Severe Anxiety	
Male	3 (75.0%)	85 (90.4%)	16 (61.5%)	2 (40.0%)	<0.001
Female	1 (25.0%)	9 (9.6%)	10 (38.5%)	3 (60.0%)	
Total	4 (100.0%)	94 (100.0%)	26 (100.0%)	5 (100.0%)	

Ayub et al. reports the male prevalence of 76.8% and female prevalence of 23.2% with a mean age of 64.1±7.01 years[12], and Siddiqui et al. reports the male prevalence of 80% and female prevalence of 20% with a mean age of 64.1±7.01 years.[13] The majority of studies show a higher prevalence of COPD in male patients and people over the age of 60, due to increased smoking rates and occupational exposures. The prevalence of COPD in older patients can be explained by the fact that it is a progressive disease with symptoms that usually appears decades after exposure. Additionally, biological differences, healthcare-seeking behaviour, and diagnostic variations all explain male predominance in many ethnicities.

In this study, overall mean GAD-7 score was 8.12±2.88. Most of the COPD patients were presented with mild anxiety (72.9%, n=94), followed by moderate anxiety (20.1%, n=26), severe anxiety (3.9%,(n=5) and minimal anxiety (3.1%, n=4). In this study male COPD patients were mostly suffering from mild anxiety as compared to female patients who were suffering from severe anxiety. Anxiety severity was also significantly increasing with increasing age. Mean age was 60.0 years in COPD patients diagnosed with minimal anxiety, which increased to 67.2 years in mild anxiety, 70.9 years in moderate anxiety and 73.0 years in severe anxiety. Our study findings shows that patients with minimal anxiety experienced fewer symptoms, indicating that anxiety was unlikely to interrupt daily activities. Patients with mild anxiety were those who worried sometimes or moderately, while those with moderate and severe anxiety showed more regular and clinically significant symptoms that might affect day-to-day functioning and the treatment of COPD. Our study findings also shows that mild anxiety predominates in COPD patients.

These findings are similar with previous studies conducted in Pakistan, where Ayub et al. reports the anxiety in 70.4% of COPD patients[12], Siddiqui et al. reports the anxiety in 32.2% of COPD patients[13], and Khanum et al. reports the anxiety in 38% of COPD patients.[14] International studies also reports the higher burden of anxiety in COPD patients such as, Semeer et al. reports the anxiety in 68.4% of COPD patients and 35.7% of COPD having anxiety and depression[15], and Gupta et al. reports that the most of the COPD patients were presented with mild anxiety (41%), followed by moderate anxiety (20.5%), minimal anxiety (19.5%), and severe anxiety (3.9%,(n=5) and minimal anxiety (18.7%).[16] Overall, these findings indicate that mild anxiety is common among COPD patients, while moderate to severe anxiety affects a lower proportion, suggesting the importance of early detection of anxiety and targeted therapies.

The study has several limitations. First, it focused exclusively on anxiety and did not assess comorbid depression or other mental disorders, which are also common in COPD patients and may influence outcomes. Second, the sample size of 129 patients may limit the generalizability of the findings and reduce statistical power for subgroup analyses. Third, as a single-center study, the results may not fully represent the broader COPD population across different regions. Finally, self-report bias, lack of COPD staging, and the cross-sectional design prevents evaluation of causal relationships or changes in anxiety symptoms over time.

CONCLUSION

The frequency of anxiety was high in patients presented with chronic obstructive pulmonary disease, with most of the patients suffering from mild anxiety, followed by moderate and severe anxiety. Early screening by using GAD-7 criteria and early intervention (cognitive-behavioral therapy) for anxiety should be added into the management of COPD patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

PIVKA-II value in the diagnosis of hepatocellular carcinoma in patients with inconclusive imaging findings or AFP levels.

Muhammad Abdullah[1], Aman Nawaz Khan[2], Ummara Siddique Umer[3], Muhammad Kamran Khan[4], Abdullah Safi[5], Hadia Abid[6]

ABSTRACT… Objective: To evaluate the diagnostic accuracy of Protein Induced by Vitamin K Absence-II (PIVKA-II; des-γ-carboxy prothrombin) in patients with suspected HCC who had nondiagnostic AFP or atypical imaging findings. **Study Design:** Retrospective Cross-sectional study. **Setting:** Rehman Medical Research Institute, Peshawar. **Period:** May 2018 and September 2024. **Methods:** Among 128 patients with suspected HCC the patients were 106 men and twenty two women, average age 60.3 years. Data from electronic medical records including demographics, hepatitis status, imaging results, laboratory markers and biopsy results were collected. PIVKA-II levels were analyzed and diagnostic accuracy has been calculated (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy). The performance of PIVKA-II was evaluated by receiver operating characteristic curve analysis. **Results:** Of 128 patients, 86 (67.2%) had HCC confirmed on biopsy. PIVKA-II was abnormal in 81/128 patients (71 HCC, 10 non-HCC). Using these counts, PIVKA-II showed sensitivity 82.6%, specificity 76.2%, PPV 87.7%, NPV 68.1%, and accuracy 80.5%. AUROC was 0.776 (p = 0.002). **Conclusion:** PIVKA-II is a useful biomarker for diagnosis of HCC when AFP is non-diagnostic or imaging results are inconclusive. It demonstrates high sensitivity and reasonable specificity to justify its use for early detection and differentiation of HCC from other liver lesions. Future studies should address the limitations of this single-institution, retrospective study to confirm the clinical utility of PIVKA-II.

Key words: Biomarkers, Diagnostic Accuracy, Hepatocellular Carcinoma, PIVKA-II, AFP.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver cancer worldwide[1] and is particularly prevalent in regions with high burdens of chronic liver disease, including hepatitis C, hepatitis B, alcoholic cirrhosis, and non-alcoholic fatty liver disease.[2] Early diagnosis is critical for initiating timely management, improving outcomes, and increasing survival.

The diagnosis of HCC can be challenging because of varied early clinical presentations.[4] Current diagnostic tools include imaging and laboratory markers, with biopsy reserved for cases that remain inconclusive. Imaging modalities such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are widely used[5], but not all lesions display the classical features needed for a confident diagnosis.

Among blood-based markers, alpha-fetoprotein (AFP) has historically been the most utilized, though it lacks adequate sensitivity and specificity. Protein induced by vitamin K absence or antagonist-II (PIVKA-II), also known as des-γ-carboxy prothrombin (DCP), has emerged as a complementary biomarker.[6-7] PIVKA-II is an abnormal form of prothrombin resulting from impaired vitamin K-dependent carboxylation.[8] In HCC, malignant hepatocytes dysregulate this process, leading to significantly elevated serum levels, which have been linked to tumor size, vascular invasion, and poor prognosis.[9]

Several studies have demonstrated that PIVKA-II may improve early detection of HCC, including in cases where AFP is normal or only mildly elevated.[10] Reported diagnostic cutoff values vary widely (40–150 mAU/mL) depending on the assay and population studied.[11] Elevated PIVKA-II has also been associated with more aggressive tumor biology and unfavorable outcomes.

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Despite its usefulness, PIVKA-II is not specific to HCC; elevations may also occur in other malignancies such as gastric, pancreatic, and cholangiocarcinoma.[12] Therefore, PIVKA-II is best interpreted in combination with AFP and imaging findings.[13] Based on this rationale, our study aimed to assess the diagnostic role of PIVKA-II in patients with suspected HCC who presented with nondiagnostic AFP or inconclusive imaging features.

METHODS

Our study population consisted of 128 suspected HCC patients using convenience sampling. These patients were 106 men and 22 women. The average age of patients had been 60.3 yrs. This study was conducted in interventional radiology department Rehman Medical Research Institute, Peshawar. Data collection period: May 2018 to September 2024. This retrospective study was approved by the Institutional Review Board (RMI/RMI-REC/ArticleApproval/120), with the requirement for individual informed consent waived. Data collected retrospectively from electronic medical record including demographics, hepatitis status, imaging results, laboratory markers and biopsy results. The gathered data have been analyzed by SPSS 26. Demographic descriptive statistics including mean and standard deviation were calculated. Diagnostic accuracy of PVKA in diagnosing HCC was calculated as sensitivity, specificity, positive predictive value, negative predictive value and accuracy. The overall performance of PVKA in the diagnosis of HCC was evaluated by receiver operating characteristic (ROC) curve analysis and AUC calculation were made. The significance of results was based on chi-square and t tests and a p-value below 0.05 is significant.

Inclusion Criteria

Adult patients (≥18 years)

Patients with focal liver lesions on imaging (ultrasound, CT, or MRI) that were suggestive but not diagnostic of HCC (i.e., inconclusive or not fulfilling LI-RADS 5 criteria).

Patients with nondiagnostic or normal AFP levels at the time of evaluation.

Patients who underwent PIVKA-II testing as part of their diagnostic workup.

Patients with histopathological confirmation available (biopsy).

Exclusion Criteria

Patients with a known prior history of HCC who had already received treatment (e.g., TACE, resection, ablation, systemic therapy).

Patients in whom histopathological confirmation was not available.

Patients with insufficient clinical or laboratory data in the medical records.

Patients with non-hepatic primary malignancies involving the liver at presentation, unless specifically included as non-HCC comparator cases.

Patients under 18 years of age.

All patients were selected on abnormal imaging or nondiagnostic alpha-fetoprotein (AFP) levels.

Definition of Inconclusive Imaging/AFP

Inconclusive imaging: Cases where contrast-enhanced CT or MRI demonstrated focal liver lesions with atypical enhancement patterns that did not fulfill LI-RADS 5 criteria for hepatocellular carcinoma (e.g., absence of classical arterial phase hyperenhancement with washout, indeterminate LI-RADS 3–4 lesions, or discordant findings between modalities).

Inconclusive AFP: Serum alpha-fetoprotein values that were within the normal reference range or elevated but below the institutional diagnostic threshold (typically <200 ng/mL), and therefore not diagnostic for HCC when considered alone.

RESULTS

We examined 128 individuals for hepatocellular carcinoma (HCC). Participants were assigned to age groups, detailed in Table-I. We collected patients' hepatitis serology data, which is a risk factor for HCC. Of these 128 patients, predominant were hepatitis C (n 87). Histopathology confirmed HCC in 86 patients (67.2%); 42 patients had non-HCC diagnoses (metastatic malignancy or benign disease).

TABLE: I

PIVKA-II diagnostic 2×2 table (using the laboratory's abnormal designation):

	HCC (Histology)	Non-HCC (Histology)
PIVKA-II abnormal (positive)	71	10
PIVKA-II normal (negative)	15	32
Total	86	42

- True positives (TP) = 71
- False positives (FP) = 10
- False negatives (FN) = 15
- True negatives (TN) = 32

Diagnostic Performance

Sensitivity = 82.6% (71/86), Specificity = 76.2% (32/42), PPV = 87.7% (71/81), NPV = 68.1% (32/47), Accuracy = 80.5% (103/128).

AUROC = 0.776 (p = 0.002).

PIVKA-II levels: 81/128 patients had abnormal PIVKA-II values (71 HCC and 10 non-HCC). Among these, 46 patients had PIVKA-II > 1600 IU. AFP was abnormal in 50 patients (all 50 had HCC); AFP was reported as 'undetermined' in 78 patients (36 HCC, 42 non-HCC).

Tables and Graphs Study Participants Demographics

TABLE-II

Summarizes the demographic characteristics of the 128 patients.

Category	Sub-category	Number of Patients
Gender	Male	106
	Female	22
Age Group	25-50 years	24
	50-75 years	96
	75-100 years	8
Hepatitis Serology	Hepatitis C positive	87
	Hepatitis B positive	26
	Negative for both	15

Correlation of PIVKA-II and AFP Levels with Diagnosis

TABLE-III

Summarizes the distribution of PIVKA-II and AFP levels in the study population and their correlation with the final diagnosis of HCC.

Bio-marker	Condition	Number of Patients	Diagnosis (HCC)	Diagnosis (Non-HCC)
PIVKA-II	Abnormal Levels	81	71	10
	> 1600 IU	46	46	0
AFP	Abnormal Levels	50	50	0
	Undetermined	78	36	42

PIVKA-II Diagnostic Performance Metrics

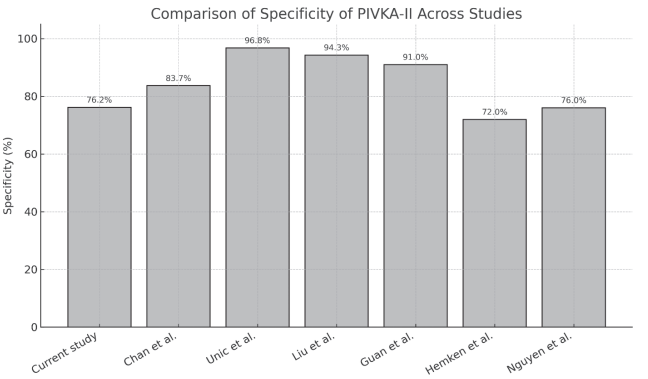
TABLE-IV

Displays the key diagnostic performance metrics for PIVKA-II in detecting hepatocellular carcinoma (HCC).

Metric	Value	
Sensitivity	82.6%	71/86
Specificity	76.2%	32/42
Positive Predictive Value (PPV)	87.7%	71/81
Negative Predictive Value (NPV)	68.1%	32/47
Accuracy	80.5%	103/128

FIGURE-1

Showing the comparative specificities of different studies.



DISCUSSION

In this retrospective cohort, PIVKA-II demonstrated a high positive predictive value (nearly 88%) and acceptable sensitivity (about 83%) and specificity (about 76%) for the diagnosis of hepatocellular

carcinoma in patients who had inconclusive imaging or nondiagnostic AFP levels. The area under the ROC curve (0.776) further supports its utility as a discriminative biomarker. Taken together, these results suggest that PIVKA-II provides clinically meaningful diagnostic information in settings where conventional diagnostic tools are insufficient.

Our findings are consistent with all those noted in prior reports assessing the diagnostic functionality of PIVKA-II for hepatocellular carcinoma (HCC) in indeterminate alpha-fetoprotein (AFP) quantities. A meta-analysis of 37 studies encompassing over 2,000 patients reported that PIVKA-II possessed a sensitivity of 89% and a specificity of 83%, much like our findings.[14]

Compared with the sensitivity rates of other studies, our sensitivity of 82.6% falls within the reported range but is slightly lower than several published values. Nguyen et al. documented a sensitivity of 91.0%, while Chan et al. and Hemken et al. reported sensitivities of 86.9% and 86.0%, respectively.
In terms of specificity, our study demonstrated a rate of 76.2%. This value is somewhat lower than those reported in several published series. For example, Chan et al. reported a specificity of 83.7%, Unic et al. observed 96.8%, and Liu et al. 94.3%. Similarly, Guan et al. documented a specificity of 91.0%. On the other hand, our findings are more comparable to the lower ranges reported by Hemken et al. (72.0%) and Nguyen et al. (76.0%), highlighting the variability across studies depending on assay method, cutoff, and patient population (FIGURE-1)

The diagnostic value of PIVKA-II can be explained by its unique pathophysiological basis. PIVKA-II is an abnormal prothrombin molecule produced when malignant hepatocytes fail to carboxylate the prothrombin precursor due to defective vitamin K metabolism. Unlike AFP, which is also elevated in non-malignant conditions such as hepatitis and cirrhosis, PIVKA-II production is more directly linked to malignant transformation and tumor biology. Elevated PIVKA-II levels correlate with tumor angiogenesis, vascular invasion, and more aggressive disease behavior. This biologically plausible link explains why PIVKA-II tends to perform better than AFP in distinguishing malignant from benign liver disease, particularly when imaging features are equivocal.

From a clinical standpoint, our results suggest that PIVKA-II is a valuable adjunct in the diagnostic algorithm for HCC. In patients with liver nodules that do not meet LI-RADS 5 imaging criteria and with AFP levels in the normal or borderline range, PIVKA-II can help guide the decision toward biopsy or closer surveillance. Furthermore, combining PIVKA-II with AFP has been shown in multiple studies to increase overall diagnostic accuracy, and future algorithms should incorporate this dual biomarker approach alongside imaging. Beyond diagnosis, PIVKA-II may also hold prognostic value, as high levels have been associated with larger tumor burden, microvascular invasion, and poorer treatment response, suggesting potential utility in risk stratification. There is also growing interest in exploring PIVKA-II in surveillance of high-risk populations, though more prospective evidence is needed before it can be adopted in that role.

Our study has several important limitations. First, it is a single-center retrospective analysis, which introduces potential selection bias, as only patients referred for biopsy after inconclusive imaging or nondiagnostic AFP were included. Second, while diagnostic metrics were carefully recalculated, the exact assay manufacturer, units, and cutoff values for PIVKA-II were not consistently documented, limiting external comparability. Third, detailed information on tumor size, BCLC stage, and vascular invasion was not uniformly available, preventing correlation of biomarker levels with disease severity. Finally, the study cohort was drawn from our region with high prevalence of hepatitis B and C, and the findings may not be generalizable to populations with different etiological backgrounds such as non-alcoholic steatohepatitis. Prospective multicenter studies using standardized assays and including comprehensive tumor staging are required to validate our findings and clarify the optimal role of PIVKA-II in clinical practice.

CONCLUSION

This study supports the potential role of PIVKA-II as a complementary biomarker in the diagnosis of hepatocellular carcinoma, particularly in patients

with inconclusive imaging or nondiagnostic AFP levels. PIVKA-II demonstrated good positive predictive value and acceptable sensitivity and specificity, reinforcing its clinical utility as an adjunct rather than a standalone test. While our findings are encouraging, prospective multicenter studies using standardized assays and clearly defined cutoffs are required to validate and refine its place within diagnostic algorithms for HCC.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Relation of hypoalbuminemia with tumor parameters in hepatocellular carcinoma patients.

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ABSTRACT… Objective: To determine the frequency of hypoalbuminemia in patients with hepatocellular carcinoma (HCC) and its relation with tumor parameters. **Study Design:** Descriptive, Cross-sectional Study. **Setting:** Department of Medicine, Nishtar Hospital, Multan. **Period:** March 11th, 2025, to September 10th, 2025. **Methods:** A total of 118 cases of HCC of either gender were enrolled in the study. After informed consent and patient characteristics, all the patients underwent laboratory testing for serum albumin and tumor markers, and an ultrasound for the number of liver nodules and the size of the largest nodule. After descriptive statistics and prevalence of hypoalbuminemia, the relation of hypoalbuminemia with multifocality, tumor size groups, and serum alpha-fetoprotein groups was assessed through the chi-square test, and a p-value ≤0.05 was taken as significant. **Results:** The mean age was 56.58 ± 10.68 years. The mean duration of liver cirrhosis was 8.25±4.3 years. The average number of liver nodules was 2.94±1.44. Regarding the size of liver nodules, the mean size was 7.18±2.96 (cm). The mean serum AFP was 422.36±443.34 (ng/ml). The serum mean albumin was 3.26±0.72 (g/dl). The prevalence of hypoalbuminemia was present in 58.5% (n=69) of patients presenting with HCC. No statistically significant association was found between hypoalbuminemia and multifocality (p = 0.426), tumor size group (p = 0.716), or serum alpha-fetoprotein levels (p = 0.405), indicating that hypoalbuminemia was not significantly related to these tumor parameters in the study population. **Conclusion:** Hypoalbuminemia was frequent among patients with HCC in our setting. However, it showed no significant association with tumor multifocality, size, or AFP levels.

Key words: Alpha Fetoproteins, Hepatocellular Carcinoma, Hypoalbuminemia, Liver Neoplasms, Serum Albumin, Tumor Burden, Ultrasonography.

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INTRODUCTION

Hepatocellular Carcinoma (HCC) is the most common liver malignancy, and globally, it's the third most common cause of mortality due to cancer.[1] Common risk factors include hepatitis B&C, aflatoxins, and contaminated water, especially in rural regions.[2] HCC ranks among the primary causes of mortality in individuals with liver cirrhosis, with cirrhosis occurring in 80-90% of HCC patients.[3] Latest statistics indicate that Hepatitis C infection has risen in incidence and mortality of HCC, predominantly in industrialized countries. The estimated incidence in Pakistan is 8 per 100,000 annually.[4]

Patients with cirrhosis require regular imaging evaluations, such as ultrasound and computed tomography, alongside serum alpha-fetoprotein (AFP) measurement.[5,6] The fetal yolk sac, intestine, and liver mainly produce AFP. Increased levels indicate HCC in the relevant clinical context[7], which is observed in 60-70% of HCC patients. AFP is not just a marker of HCC presence but also a marker of the severity of tumor size.[8] In a study by Abbasi et al. there was a significant correlation was observed between serum AFP levels and tumor size in HCC ($r = 0.472$, $p < 0.0001$).[9] Apart from novel tumor markers in HCC, like Glypican-3, DCP (Des-gamma-carboxy prothrombin, etc.), albumin level is a traditional marker of cirrhosis, and has been correlated with HCC in a few studies. In a study by Carr et al. Hypoalbuminemia was observed in 45.7% (n=1889) of the HCC patients. HCC patients exhibiting lower serum albumin levels demonstrated significantly increased tumor diameters, multifocality, and elevated α-fetoprotein levels compared to those with higher albumin levels.[10]

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Keeping in view the disease burden of HCC that is commonly diagnosed at an advanced stage in South Punjab due to low levels of surveillance and the late presentation, serum albumin is a low-cost and readily available marker that depicts liver function in this population with a high burden of cirrhosis. Moreover, there is little local data related to this study available, especially in the South Punjab population. So, this is a study of the frequency of hypoalbuminemia and how it's associated with tumor parameters to produce the evidence that's local and relevant.

METHODS

After the approval of the institutional ethical review committee (3602/NMU; dated 10-03-2025), a descriptive, cross-sectional Study was done at the Department of Medicine, Nishtar Hospital, Multan, over a period of 6 months (March 11th, 2025, to September 10th, 2025) after approval of the synopsis. After the informed consent, a total of 118 patients were enrolled in the study, using the non-probability consecutive sampling technique. The Sample size was calculated through the WHO sample size calculator using the formula for a single proportion, where: frequency of hypoalbuminemia=45.7%[10], absolute precision=9%, confidence level = 95%. The minimum sample size was 118. The inclusion criteria of my study were: Patients 40 – 75 years of age, either male or female gender, cases of hepatocellular carcinoma ≤ 3 months. Patients with recent blood transfusion (≤ 4 weeks), on treatment with radiotherapy or chemotherapy, were excluded from the study. Patients with known cases of liver cirrhosis having liver nodules> 1cm and serum alpha protein levels > 20 ng/ml and triphasic CT showing a hypervascular lesion on hepatic arterial phase images that becomes iso- to hypoattenuating relative to the liver on portal venous images were deemed positive.

After informed consent, the patient characteristics, including age, gender, duration of liver cirrhosis, and Child-Pugh class, were recorded. All the patients underwent venipuncture aseptically, and 2 mL of blood was sent to a single laboratory for serum albumin and tumor markers assessment as per hospital protocol. Hypoalbuminemia was labelled as serum albumin levels <2.5 g/dL on presentation. Tumor parameters included were serum alpha fetoprotein ng/mL, categorized as < 40, 40 – 400, and > 400. All patients underwent an ultrasound by a consultant radiologist with ≥3 years of post-fellowship experience to document the number of liver nodules and the size of the largest nodule. Tumor was labelled as multifocal if >1 nodule on ultrasound and tumor size (cm) on USG abdomen, and categorized as <5-cm and ≥5-cm. All the data was recorded on a proforma.

SPSS version 23 was used for data analysis. Normality of numerical data was checked through the Shapiro-Wilk test. Age, duration of liver cirrhosis, number of liver nodules, size of the largest nodule, serum alpha protein, and serum albumin were presented as mean and standard deviation. Gender, Child-Pugh, hypoalbuminemia, multifocality, tumor size groups, and serum alpha fetoprotein groups were presented as frequencies and percentages. The correlation of hypoalbuminemia with multifocality, tumor size groups, and serum alpha-fetoprotein groups was assessed through the chi-square test. Data were stratified on age, gender, duration of cirrhosis, and Child-Pugh class to determine the effect on the relationship between hypoalbuminemia and tumor parameters. Post-stratification chi-square test was applied, and a p-value ≤0.05 was taken as significant.

RESULTS

A total of 118 patients were included in the study. The mean age was 56.58 ± 10.68 years. The mean duration of liver cirrhosis was 8.25±4.3 years. The average number of liver nodules was 2.94±1.44. Regarding the size of liver nodules, the mean size was 7.18±2.96 (cm). The mean serum AFP was 422.36±443.34 (ng/ml). Descriptive statistics are shown in Table-I. The serum mean albumin was 3.26±0.72 (g/dl). The prevalence of hypoalbuminemia was present in 58.5% (n=69) of patients presenting with HCC, as shown in Figure-1. No statistically significant association was found between hypoalbuminemia and multifocality (p = 0.426), tumor size group (p = 0.716), or serum alpha-fetoprotein levels (p = 0.405), indicating that hypoalbuminemia was not significantly related to these tumor parameters in the study population (Table-II).

TABLE-I

Baseline characteristics of patients with HCC (n = 118)

Variable	Category	n (%)	Variable	Category	n (%)
Age Groups	40-60 (years)	74 (62.7)	Multifocality	Yes	91 (77.1)
	61-75 (years)	44 (37.3)		No	27 (22.9)
Gender	Male	65 (55.1)	Tumor size group (cm)	<5-cm	34 (28.8)
	Female	53 (44.9)		≥5-cm	84 (71.2)
Child-Pugh class	1	42 (35.6)	Serum AFP (ng/ml)	<40	40 (33.9)
	2	37 (31.4)		40-400	33 (28.0)
	3	39 (33.1)		>400	45 (38.1)

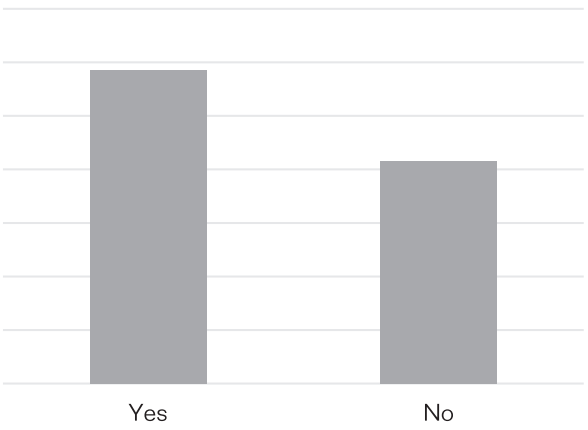
TABLE-III

Association of hypoalbuminemia with tumor multifocality, tumor size, and serum alpha-fetoprotein levels (n=118)

Variable	Category	Hypoalbuminemia		Test of sig.
		Yes	No	
Multifocality	Yes	55 (79.7%)	14 (20.3%)	χ^2=0.63, p=0.426
	No	36 (73.5%)	13 (26.5%)	
Tumor size (cm)	<5-cm	19 (27.5%)	50 (72.5%)	χ^2=0.132, p=0.716
	≥5-cm	15 (30.6%)	34 (69.4%)	
Serum AFP (ng/ml)	<40 (ng/ml)	20 (29%)	20 (40.8%)	χ^2=1.8, p=0.405
	40-400 (ng/ml)	21 (30.4%)	12 (24.5%)	
	>400 (ng/ml)	28 (40.6%)	17 (34.7%)	

FIGURE-1

Prevalence of hypoalbuminemia among patients with HCC (n=118)



DISCUSSION

This study evaluated the prevalence of hypoalbuminemia in HCC patients and its association with tumor characteristics. A descriptive cross-sectional design was employed; this is the design used in many prognostic biomarker studies. Similar designs have been employed in recent studies on a regional and international level to test nutritional and inflammatory markers in HCC patients.[11-13] The strength in the present methodology is the standardized laboratory testing and the ultrasound-based tumor evaluation by experienced radiologists. This helps in minimizing measurement bias and improving internal validity. However, unlike some cohort-based studies that evaluated survival outcomes, this study evaluated tumor burden parameters only.[14,15] This difference in methodology may in part explain differences in associations. Many of the recent studies have used longitudinal designs to assess albumin as a prognostic marker and not a variable of correlation.[16,17] Despite this, cross-sectional analysis is still valuable for estimating the burden of disease and producing evidence of local importance, especially in resource-limited tertiary care settings such as South Punjab.

The average age in this study was 56.6±10.7 years. This is similar to the data from Pakistan showing a mean age at diagnosis of 54-58 years.[18,19] Similar age distributions have been reported from China and Egypt, where HCC presents essentially in the sixth

decade of life.[20,21] The male predominance (55.1%) in our cohort is similar to data from other parts of the world where male-to-female ratios range from 1.5:1 to 3:1.[22] The mean duration of cirrhosis was more than eight years, which is similar to findings from cohorts in the region showing longstanding liver disease before diagnosis This pattern is similar to other tertiary care studies in Pakistan where delayed diagnosis is still common.[18,24]

Hypoalbuminemia was present in 58.5% of patients in our study. This frequency is higher than in Carr et al, who found hypoalbuminemia in 45.7% of the HCC patients.[25] Recently, Asian studies have shown a prevalence of 48%-62%, depending upon the cut-off value used.[16,20] This study from Karachi, Pakistan, seems to have a prevalence of hypoalbuminemia in 55% of the HCC patients, which is close to the results in our study.[19] The slightly higher frequency in our population may be due to advanced disease stage, poor nutritional status, and low access to early screening programs in rural South Punjab. These regional differences have also been underscored in recent national reports on cancer.[14,16]

In our study, there was no significant association of hypoalbuminemia with multifocality, tumor size, or alpha-fetoprotein. However, several international studies have reported a strong association between low albumin levels and multifocal disease.[10,15] One possible explanation is that serum albumin is a reflection of hepatic synthetic function and not solely a function of tumor biology. In patients with advanced chronic liver disease, albumin levels may be uniformly low in all cases, making discrimination difficult.[16,17] In a recent study from Pakistan, where ultrasound-based measurements have been used, results have also failed to show a consistent relationship between albumin levels and tumor size, supporting our results.[18,19] Studies with CT-based volumetric assessment have shown larger tumors in hypoalbuminemic patients.[20,25] The lack of association between hypoalbuminemia and AFP levels (p=0.405) is interesting. Several studies have reported an increased AFP level in patients with low albumin.[20,25] However, recent evidence suggests an elevation of AFP is not dependent on the liver synthetic function but depends on the differentiation of the tumor and molecular subtype.[13,16] A 2022 multicenter Asian study showed that serum albumin was not independently associated with serum AFP after adjusting for Child-Pugh class.[16] Similar results were observed in a study based in Lahore, where AFP levels varied considerably among the albumin strata.[24] These results support the present study observations.

CONCLUSION

Hypoalbuminemia was frequent among patients with hepatocellular carcinoma in our setting. However, it showed no significant association with tumor multifocality, size, or AFP levels. These findings differ from some international reports but align with recent regional data using similar methodologies. The results highlight the influence of underlying liver dysfunction and late disease presentation on biochemical markers. Further prospective studies using advanced imaging and survival outcomes are recommended.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Javeria Shamim:** Conception of idea, data collection.
2	**Shahzad Alam Khan:** Data analysis.
3	**Fatima Zuhra:** Interpretation, report writing.

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ORIGINAL ARTICLE

Clinical profile and predictors of outcomes of guillain-barré syndrome variants among patients admitted in tertiary care hospital.

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ABSTRACT… Objective: To evaluate the clinical profile, outcomes, and independent predictors of poor prognosis in patients diagnosed with Guillain-Barré Syndrome. **Study Design:** Cross-sectional Observational study. **Setting:** Department of Neurology, Nishtar Hospital, Multan. **Period:** November 2024 to April 2025. **Methods:** A total of 134 adult patients diagnosed with GBS were enrolled using non-probability consecutive sampling. Data were collected prospectively through structured clinical assessment, nerve conduction studies, and cerebrospinal fluid analysis. Outcome was measured using the Hughes Disability Score. Statistical analysis was performed in SPSS v26.0, applying chi-square test and binary logistic regression with $p < 0.05$ considered significant. **Results:** Among 134 Guillain-Barré Syndrome patients, 72.4% were aged 18–45 years and 63.4% were male. Gastrointestinal infection (40.3%) was the most common antecedent. Acute Inflammatory Demyelinating Polyradiculoneuropathy (43.3%) was the predominant variant; albuminocytologic dissociation was present in 79.1%. Symmetric ascending weakness (91.0%), quadriparesis (67.9%), and facial palsy (29.9%) were frequent. Mechanical ventilation (21.6%) and ICU admission (30.6%) were required. Good outcome occurred in 72.4% of cases. Poor outcome (27.6%) was significantly associated with older age ($p < 0.001$), subacute progression ($p = 0.039$), absent ACD ($p < 0.001$), neck weakness, ventilation, and ICU admission ($p < 0.05$). **Conclusion:** Favorable outcomes in GBS were associated with early presentation and AIDP subtype, while poor prognosis correlated with old age, delayed admission, absence of albuminocytologic dissociation, and ICU care.

Key words: Albuminocytologic Dissociation, Clinical Profile, Guillain-Barré Syndrome, Intravenous Immunoglobulin, Outcome Predictors.

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INTRODUCTION

Guillain-Barré Syndrome (GBS) represents a complex, immune-mediated acute poly radiculoneuropathy characterized by its remarkable clinical heterogeneity and potentially devastating neurological consequences.[1] Globally, the syndrome manifests with an annual incidence ranging from 0.4 to 3 per 100,000 population, with notable geographic variations and increasing prevalence in certain regions.[2] The disease demonstrates a distinct epidemiological profile, with risk incrementally rising by approximately 20% per decade of life and a notable male preponderance, presenting a male to female ratio of 1.5–2.3:1.[3] Risk factors encompass a broad spectrum of demographic and physiological variables, with age, prior infections, and individual immunological susceptibility playing crucial roles in syndrome manifestation.[4]

The clinical spectrum of GBS is varied and influenced by geographic, environmental, and genetic factors.[5] In developed countries, Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP) is the predominant subtype, whereas Acute Motor Axonal Neuropathy (AMAN) and Acute Motor and Sensory Axonal Neuropathy (AMSAN) are more common in Asian regions including India, Pakistan, Bangladesh, and China, with reported axonal variant incidences ranging from 28% to 67%.[6,7] The axonal variants, particularly AMAN and AMSAN, are frequently linked with more rapid progression, severe disease, and poorer prognosis compared to demyelinating forms.[8]

Typically, GBS is prefaced by an antecedent illness, most commonly gastrointestinal or respiratory infections, notably Campylobacter jejuni.

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These infections are hypothesized to trigger immune-mediated injury through molecular mimicry, resulting in demyelination or axonal degeneration.[9,10] Clinically, patients may present with ascending weakness, paresthesia, cranial nerve palsies, bulbar dysfunction, respiratory distress, and autonomic instability.[11] The disease course is variable, ranging from full recovery to prolonged disability or death. Early cranial nerve involvement, rapid disease progression (within 7 days), respiratory failure, and axonal electrophysiological patterns are poor predictors of outcomes.[12,13]

Early diagnosis and classification using nerve conduction studies (NCS) and cerebrospinal fluid (CSF) analysis are pivotal. NCS not only confirms the diagnosis but also classifies the disease into electrophysiological subtypes and aids in prognostication. AIDP typically shows demyelinating features, while axonal variants exhibit low or absent CMAP amplitudes. The presence of albuminocytologic dissociation in CSF is seen in over 80% of cases by the second week of illness.[13] Despite the availability of specific immunotherapies such as IVIg and plasmapheresis, which are most effective when initiated early, outcomes in GBS remain variable. Approximately 20–30% of patients need mechanical ventilation, and 3–14% die during the acute phase, especially in cases with rapid disease progression, bulbar involvement, or autonomic dysfunction.[14]

In South Asia, particularly in Pakistan, data on the clinical spectrum, electrophysiological variants, and outcome predictors of GBS are limited. Existing regional studies report a high prevalence of axonal variants and young male predominance, but prognostic indicators remain inconsistently described. Given these gaps, this study aims to describe the clinical and demographic profile of adult GBS patients, determine the frequency of electrophysiological variants using NCS, evaluate outcomes including recovery, ICU admission, need for mechanical ventilation, and in-hospital mortality, and identify predictors of poor outcomes.

METHODS

A cross-sectional observational study was executed at Nishtar Hospital, Multan, in the Neurology Department from November 2024 to April 2025. Ethical approval for the study was obtained from the Institutional Ethical Review Board of Nishtar Medical University, Multan (Approval Reference No. 18937/NMU), and informed consent was taken from all patients before enrollment. A non-probability consecutive sampling technique was utilized for participant enrollment. A sample size of 134 patients was calculated using WHO sample size calculator with a confidence interval of 95%, expected proportion of AMAN as 14.6% and absolute precision of 6%.[15]

Inclusion and Exclusion Criteria

Patients aged 18 to 75 years, diagnosed with Guillain-Barré Syndrome as per Brighton Collaboration criteria and confirmed by NCS and CSF analysis (CSF protein >45 mg/dL with leukocyte count <50/mm^3), were included after informed consent. Only those admitted within 2 weeks of symptom onset were enrolled. Patients with alternative causes of acute flaccid paralysis (e.g., poliomyelitis, botulism, myasthenia gravis, vasculitic or toxic neuropathies), central nervous system disorders, or incomplete diagnostic evaluation were excluded. Additionally, patients who were pregnant or lactating, HIV reactive, known to have selective IgA deficiency, or receiving immunosuppressive therapy including recent corticosteroid use were not included.

Data Collection Procedure

A proforma was used to gather the baseline demographic and clinical data, including age, sex, residence and antecedent illnesses. Duration from symptom onset to admission and disease progression classified as acute (≤7 days) or subacute (8–14 days) were noted. A comprehensive neurological exam was performed. Motor strength was graded using the MRC scale (0–5). Symmetric ascending weakness was defined by bilateral limb involvement with ≤1 grade inter-limb difference. Paraparesis involved lower limbs only, while quadriparesis included all four limbs. Neck flexor weakness was identified as inability to lift the head against gravity (MRC ≤3). Muscle pain in proximal regions was considered significant if VAS score was ≥4. Sensory findings including paresthesia were confirmed through light touch, pinprick, and vibration testing with a 128 Hz tuning fork.

Cranial nerve involvement was assessed clinically. Facial palsy was graded ≥II on the House-Brackmann scale. Ophthalmoplegia was based on restricted eye movements. Dysphagia was scored ≥3 using the DOSS, and dysarthria was noted with a Frenchay score ≥2. Bulbar weakness was recorded based on clinical signs and bedside swallow assessment. Autonomic features included bladder dysfunction—defined as urinary retention (post-void residual ≥100 mL) or incontinence—and blood pressure fluctuations, defined as systolic changes ≥30 mmHg or diastolic ≥15 mmHg over 24 hours, monitored every 4 hours. NCS was performed and interpreted by neurophysiologists to classify patients into specific GBS variants, including AIDP, AMAN, AMSAN and MFS variant. Outcomes were assessed using the Hughes Disability Score (0–6) at admission and discharge. Good outcome was defined as HDS ≤2, confirmed at discharge. ICU admission was based on clinical need—breath count ≤20, autonomic instability, bulbar dysfunction, or respiratory compromise. In-hospital death was also. Data were collected prospectively by trained investigators under supervision, ensuring accuracy and adherence to predefined clinical and diagnostic criteria.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Quantitative variables (age, duration from onset to admission, and Hughes Disability Scores) were presented as mean ± standard deviation and compared using the independent samples t-test. Categorical variables (gender, residence, clinical features, treatment, and outcomes) were expressed as frequencies and percentages and compared using the Chi-square test. Variables with $p < 0.05$ in Chi-square analysis were included in a binary logistic regression model using backward stepwise likelihood ratio method to identify independent predictors of poor outcome. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A p-value < 0.05 was considered statistically significant.

RESULTS

The mean age of patients diagnosed with GBS was 39.87 ± 13.04 years. The average duration from symptom onset to hospital admission was 6.61 ± 2.95 days. Among 134 patients with GBS, the majority were aged 18–45 years (72.4%), male (63.4%), and residing in urban areas (61.2%). The most frequent antecedent illness was gastrointestinal infection (40.3%). Acute disease progression (≤7 days) was observed in 72.4% of patients, and albuminocytologic dissociation was present in 79.1%. AIDP was the predominant variant (43.3%), followed by AMAN (29.9%) and AMSAN (13.4%). IVIG was the most administered therapy (50.0%), and 21.6% required mechanical ventilation. Good outcome was achieved in 72.4% of patients, whereas 7.5% succumbed to illness. Detailed distribution of baseline and clinical characteristics is provided in Table-I.

TABLE-I

Baseline demographic and clinical characteristics of patients diagnosed with guillain-barré syndrome (n = 134)

Variable	n (%)
Age Group	
18 to 45 years	97 (72.4)
46 to 75 years	37 (27.6)
Gender	
Male	85 (63.4)
Female	49 (36.6)
Residence	
Urban	82 (61.2)
Rural	52 (38.8)
Antecedent Illness	
Gastrointestinal Infection	54 (40.3)
Respiratory Infection	31 (23.1)
Fever	25 (18.7)
Surgery	9 (6.7)
None	15 (11.2)
Disease Progression	
Acute (≤ 7 days)	97 (72.4)
Subacute (> 7 days)	37 (27.6)
Albuminocytologic Dissociation	106 (79.1)
GBS Variants	
AIDP	58 (43.3)
AMAN	40 (29.9)
AMSAN	18 (13.4)
MFS	3 (2.2)
Not Classified	15 (11.2)
Motor Features	

Symmetric Ascending Weakness	122 (91.0)
Paraparesis	16 (11.9)
Quadriparesis	91 (67.9)
Neck Flexor Weakness	60 (44.8)
Muscle Pain	45 (33.6)
Sensory Feature	
Paresthesia	45 (33.6)
Cranial Nerve Involvement	
Facial Palsy	40 (29.9)
Ophthalmoplegia	6 (4.5)
Dysarthria	21 (15.7)
Dysphagia	16 (11.9)
Bulbar Weakness	18 (13.4)
Autonomic Features	
Bladder Involvement	12 (9.0)
BP Fluctuations	15 (11.2)
Treatment Received	
IVIG Only	67 (50.0)
Plasmapheresis Only	19 (14.2)
Both (IVIG + Plasmapheresis)	9 (6.7)
Supportive Care Only	39 (29.1)
Need for Mechanical Ventilation	29 (21.6)
ICU Admission	41 (30.6)
Outcome	
Good Outcome	97 (72.4)
Poor Outcome	37 (27.6)
Mortality	10 (7.5)

AIDP – Acute Inflammatory Demyelinating Polyneuropathy; AMAN – Acute Motor Axonal Neuropathy; AMSAN – Acute Motor-Sensory Axonal Neuropathy; MFS – Miller Fisher Syndrome; IVIG – Intravenous Immunoglobulin; BP – Blood Pressure.

The mean age was lower in patients with good outcomes (37.16 ± 10.70 years) compared to those with poor outcomes (46.97 ± 15.85 years). Similarly, the average duration from symptom onset to admission was shorter in good outcome group (5.62 ± 2.15 days) than in the poor outcome group (9.22 ± 3.20 days). The mean Hughes Disability Score at admission was 3.63 ± 0.49 in the good outcome group versus 4.76 ± 0.44 in the poor outcome group, while at discharge it was 1.00 ± 0.61 and 3.76 ± 0.44, respectively ($p < 0.001$).

Patients aged 46–75 years had significantly higher poor outcomes compared to younger patients ($p < 0.001$). Subacute disease progression (>7 days) was more frequent among those with poor outcomes (40.5% vs. 22.7%, $p = 0.039$). Absence of albuminocytologic dissociation was significantly associated with poor outcomes (43.2% vs. 12.4%, $p < 0.001$). Among GBS variants, AMAN and AMSAN were more common in poor outcome groups, whereas AIDP was predominant in those with good recovery ($p = 0.009$). Neck flexor weakness ($p = 0.012$), paresthesia ($p = 0.023$), facial palsy ($p = 0.001$), bulbar weakness ($p = 0.022$), and autonomic features including bladder involvement ($p < 0.001$) and blood pressure fluctuations ($p = 0.003$) were significantly linked with poor outcomes. Supportive care alone was linked to a higher proportion of poor outcomes, while patients receiving both IVIG and plasmapheresis showed only good outcomes ($p = 0.006$). Need for mechanical ventilation ($p = 0.001$), ICU admission ($p < 0.001$), and in-hospital mortality ($p < 0.001$) were also significantly linked with adverse outcomes (Table-II).

TABLE-II

Association of baseline demographic and clinical characteristics with patient outcomes in guillain-barré syndrome (GBS) (n = 134)

Characteristics	Good Outcome n = 97	Poor Outcome n = 37	P-Value
Age Group			< 0.001
18 to 45 years	79 (81.4%)	18 (48.6%)	
46 to 75 years	18 (18.6%)	19 (51.4%)	
Gender			0.322
Male	64 (66.0%)	21 (56.8%)	
Female	33 (34.0%)	16 (43.2%)	
Residence			0.799
Urban	60 (61.9%)	22 (59.5%)	
Rural	37 (38.1%)	15 (40.5%)	
Antecedent Illness			0.019
Gastrointestinal Infection	45 (46.4%)	9 (24.3%)	
Respiratory Infection	21 (21.6%)	10 (27.0%)	
Fever	19 (19.6%)	6 (16.2%)	
Surgery	3 (3.1%)	6 (16.2%)	
None	9 (9.3%)	6 (16.2%)	
Disease Progression			0.039

Acute (≤ 7 days)	75 (77.3%)	22 (59.5%)	
Subacute (> 7 days)	22 (22.7%)	15 (40.5%)	
Albuminocytologic Dissociation	85 (87.6%)	21 (56.8%)	< 0.001
GBS Variants			0.009
AIDP	49 (50.5%)	9 (24.3%)	
AMAN	24 (24.7%)	16 (43.2%)	
AMSAN	9 (9.3%)	9 (24.3%)	
MFS	3 (3.1%)	0 (0.0%)	
Not Classified	12 (12.4%)	3 (8.1%)	
Motor Features			
Symmetric Ascending Weakness	88 (90.7%)	34 (91.9%)	0.832
Paraparesis	12 (12.4%)	4 (10.8%)	0.803
Quadriparesis	69 (71.1%)	22 (59.5%)	0.196
Neck Flexor Weakness	37 (38.1%)	23 (62.2%)	0.012
Muscle Pain	37 (38.1%)	8 (21.6%)	0.070
Sensory Feature			
Paresthesia	27 (27.8%)	18 (48.6%)	0.023
Cranial Nerve Involvement			
Facial Palsy	21 (21.6%)	19 (51.4%)	0.001
Ophthalmoplegia	6 (6.2%)	0 (0.0%)	0.122
Dysarthria	12 (12.4%)	9 (24.3%)	0.089
Dysphagia	9 (9.3%)	7 (18.9%)	0.124
Bulbar Weakness	9 (9.3%)	9 (24.3%)	0.022
Autonomic Features			
Bladder Involvement	3 (3.1%)	9 (24.3%)	< 0.001
BP Fluctuations	6 (6.2%)	9 (24.3%)	0.003
Treatment Received			0.006
IVIG Only	54 (55.7%)	13 (35.1%)	
Plasmapheresis Only	13 (13.4%)	6 (16.2%)	
Both (IVIG + Plasmapheresis)	9 (9.3%)	0 (0.0%)	
Supportive Care Only	21 (21.6%)	18 (48.6%)	
Need for Mechanical Ventilation	14 (14.4%)	15 (40.5%)	0.001
ICU Admission	19 (19.6%)	22 (59.5%)	< 0.001
Mortality	0 (0.0%)	10 (27.0%)	< 0.001

Pearson Chi-Square test was applied to assess the association between clinical and demographic characteristics and outcomes in patients with GBS. A p-value < 0.05 was considered statistically significant.

Binary logistic regression analysis identified several independent predictors of poor outcome in patients with GBS. Age between 46 and 75 years was significantly linked with higher odds of poor recovery (AOR = 5.053; 95% CI: 1.621–15.750; p = 0.005). Subacute disease progression exceeding seven days also increased the likelihood of poor outcome (AOR = 6.201; 95% CI: 1.925–19.979; p = 0.002). Absence of albuminocytologic dissociation was a strong negative prognostic indicator (AOR = 8.527; 95% CI: 2.502–29.061; p = 0.001). Conversely, the presence of neck flexor weakness (AOR = 0.175; 95% CI: 0.053–0.574; p = 0.004), the need for mechanical ventilation (AOR = 0.208; 95% CI: 0.062–0.701; p = 0.011), and ICU admission (AOR = 0.099; 95% CI: 0.031–0.321; p < 0.001) were significantly correlated with unfavorable outcomes (Table-III).

TABLE-III

Binary Logistic Regression Analysis for Predictors of Poor Outcome in Patients with Guillain-Barré Syndrome (n = 134)

Predictors	P-Value	Adjusted Odds Ratio	95% CI
Age Group (46–75 years)	0.005	5.053	1.621 – 15.750
Disease Progression (>7 days)	0.002	6.201	1.925 – 19.979
Albuminocytologic Dissociation (No)	0.001	8.527	2.502 – 29.061
Neck Flexor Weakness (Yes)	0.004	0.175	0.053 – 0.574
Mechanical Ventilation (Yes)	0.011	0.208	0.062 – 0.701
ICU Admission (Yes)	<0.001	0.099	0.031 – 0.321

Binary logistic regression using the Enter method was applied to identify independent predictors of poor outcome among patients with GBS. The variables retained in the final model were age group, disease progression duration, absence of albuminocytologic dissociation, presence of neck flexor weakness, need for mechanical ventilation, and ICU admission. A p-value < 0.05 was considered statistically significant.

DISCUSSION

This study analyzed the clinical profile, management strategies, and outcomes of 134 patients diagnosed with GBS at a tertiary care hospital in Pakistan. The average age of patients was 39.87 ± 13.04 years, with the majority (72.4%) aged between 18 and 45 years. These findings are aligned with those of Tewedaj et al., who reported 76.7% of their patients in the 14 to 34 year range, and Siddiqui et al., where 61% were under 40 years.[13,16] In contrast, Rajabally and Uncini reported a wider age distribution (18–84 years), with increased mortality in older adults. Importantly, advancing age was observed as an independent predictor of poor outcome in the present study (AOR = 5.053; 95% CI: 1.621–15.750; p = 0.005), consistent with Kalita et al. and their finding of age ≥50 years as a significant prognostic factor (OR = 1.96; p = 0.03).[7,17]

A history of gastrointestinal illness was the most common antecedent factor in the present study (40.3%), followed by respiratory infections (23.1%) and fever (18.7%). These findings are aligned with Siddiqui et al., who reported gastrointestinal symptoms in 21% and respiratory illness in 14.5%. Kalita et al. similarly noted diarrhea in 19.4% and sore throat or URTI in 20.7% of their cases.[7,13] Acute progression (≤7 days) was observed in 72.4% of the study population. Siddiqui et al. reported similar findings, with 71% presenting within 7 days. Kalita et al. recorded a median symptom onset of 8 days, while Tewedaj et al. documented a mean of 8.77 ± 7.25 days.[7,13,16] In the present study, subacute progression (>7 days) was significantly correlated with poor outcome (p = 0.039), and regression analysis confirmed this association (AOR = 6.201; p = 0.002). A similar association was highlighted by Rafique et al. (2023) (OR = 3.2; p = 0.01).[18]

AIDP was the predominant GBS variant in this study (43.3%), followed by AMAN (29.9%) and AMSAN (13.4%). These results are comparable to those reported by Siddiqui et al. (AIDP: 53%, AMAN: 29%, AMSAN: 11%) and Rafique et al. (AIDP: 41.3%, AMAN: 26.1%, AMSAN: 30.4%).[13,18] In the current study, AMAN and AMSAN were significantly more prevalent in poor outcome groups (p = 0.009). Albuminocytologic dissociation (ACD) was detected in 79.1% of patients. This rate closely matches findings by Ruiz-Sandoval et al. (81%) and Tewedaj et al. (82.9%). Siddiqui et al. reported ACD in 64% of patients who underwent lumbar puncture.[13,16,19] In this study, absence of ACD was an independent predictor of poor outcome (AOR = 8.527; p = 0.001), highlighting its prognostic relevance.

Symmetric ascending weakness was observed in 91.0% of patients, comparable to findings by Siddiqui et al. (93%) and Sharma et al. (90%).[13,20] Quadriparesis and paraparesis were observed in 67.9% and 11.9% of cases, respectively. Notably, neck flexor weakness was significantly associated with poor outcome (p = 0.012), and also emerged as a negative prognostic marker in regression analysis (AOR = 0.175; p = 0.004), in line with Verma et al. and Khedr et al.[20,21] Sensory involvement (paresthesia) was documented in 33.6% of patients, higher than the 3% reported by Siddiqui et al. but similar to Sharma et al. (31.7%) and Kalita et al. (52.7%). Among cranial nerve findings, facial palsy (29.9%) and bulbar weakness (13.4%) were significantly correlated with poor outcome (p = 0.001 and p = 0.022, respectively), consistent with Kalita et al. and Rafique et al., who all observed strong associations with disease severity and ventilation requirements.[7,20]

Treatment modalities showed 50% of patients receiving IVIG, 14.2% plasmapheresis, 6.7% both, and 29.1% managed with supportive care alone. Patients treated with IVIG or plasmapheresis had better outcomes, while supportive care alone was associated with poor prognosis (p = 0.006). Bhatia et al. similarly reported the protective role of both treatments in outcome improvement. However, studies by Kalita et al. and Tewedaj et al. reported no significant outcome differences by treatment type, possibly due to delayed therapy.[7,16] Mechanical ventilation was needed in 21.6% of patients and was independently associated with poor outcome (AOR = 0.208; p = 0.011), consistent with findings from Verma et al., Sharma et al. and Tewedaj et al. ICU admission was also significantly associated with poor prognosis (AOR = 0.099; p < 0.001), aligning with Ahmed et al. and Singh et al.[14,19]

This study offers comprehensive analysis of clinical predictors and outcomes in Guillain-Barré

Syndrome, integrating both bivariate and multivariate statistical models with a relatively robust sample size. However, limitations include its single-center design and short-term outcome assessment. Moreover, potential confounding variables such as comorbidities were not explored. Future multicenter studies with extended follow-up, inclusion of neurophysiological and biomarker profiling, and assessment of long-term disability and quality of life are recommended to validate and expand upon the current findings for improved risk stratification and patient care.

CONCLUSION

This study identified key clinical and demographic predictors influencing outcomes in patients with Guillain-Barré Syndrome. Younger age, early presentation, presence of albuminocytologic dissociation, and absence of neck flexor weakness were significantly associated with favorable outcomes. In contrast, age above 45 years, subacute progression, absence of albuminocytologic dissociation, need for mechanical ventilation, and ICU admission independently predicted poor outcomes. These findings underscore the importance of early diagnosis, timely intervention, and prognostic stratification to improve clinical outcomes in GBS patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Anahita Khan:** Conception and design of study, methodology, data collection, and final approval of the manuscript.
2	**Sohaib Hassan:** Study design methodology, data collection, and final approval of the manuscript.
3	**Muhammad Ali Qureshi:** Data analysis, methodology, interpretation and final approval of the manuscript.
4	**Muhammad Irfan Jamil:** Data analysis, results formulation, discussion writing and final approval.
5	**Adeel Ahmed:** Study design methodology, data collection, and final approval of the manuscript.
6	**Maria Jabeen:** Data analysis, methodology, interpretation and final approval of the manuscript.

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ORIGINAL ARTICLE

To study the impact of poor glycemic control (Elevated HbA1c) on post-operative frequency of acute kidney injury after coronary artery bypass graft (CABG) surgery.

Riaz ul Haq[1], Muhammad Mujahid[2], Muhammad Farooq Ahmad[3], Muhammad Hussnain Raza[4], Muneeza Dilpazeer[5], Muhammad Azam[6]

ABSTRACT… Objective: To compare the frequency of acute kidney injury in diabetic patients with HbAlc ≥7% and HbA1c <7% undergoing CABG surgery and to determine the severity of AKI and adverse outcome in diabetic patients undergoing CABG surgery. **Study Design:** Comparative Cross-sectional study. **Setting:** The study was conducted in Cardiac Surgery Department, Faisalabad Institute of Cardiology, Faisalabad. **Period:** The duration of study was from 05/05/2023 to 04/05/2024. **Methods:** The present study involved 100 diabetic patients undergoing CABG surgery assimilated into two equal groups; Group-A (HbA1c ≥7.0%) and Group-B (HbA1c <7.0%). These patients were followed in the post-operative period and occurrence of AKI was noted along with its severity according to RIFLE criteria. These patients were managed as per department protocols and adverse outcome in the form of mortality was noted. Frequency of AKI, its severity and adverse outcome was compared between the groups. **Results:** The calculated mean age of the participants was 51.5 years, with a standard deviation of ±7.4 years. There was male predominance (M:F; 7.3:1). Following cardiac surgery, the mean of peak serum creatinine was significantly higher (1.25±0.36 vs. 1.03±0.24 mg/dl; p-value<0.001) while the mean glomerular filtration rate was significantly lower (66.14±21.17 vs. 75.96±17.52 mL/min/1.73m^2; p-value=0.013) in patients with elevated HbA1c (≥7.0%). The frequency of post-operative AKI was significantly higher in patients with poor glycemic control (44.0% vs. 12.0%; p-value<0.001). Among the 28 patients having AKI, 15 (53.6%) patients were categorized as risk while 13 (46.4%) patients were categorized as injury under RIFLE criteria. Adverse outcome was noted in 4 (4.0%) patients. When compared the frequency of adverse outcome comparably higher in individuals with increased HbA1c ≥7.0% (8.0% vs. 0.0%; p-value=0.041) and AKI (14.3% vs. 0.0%; p-value=0.005). **Conclusion:** In diabetic patients undergoing CABG, poor preoperative glycemic control was identified as a key predictor of postoperative AKI and mortality. This emphasizes the importance of HbA1c in risk stratification and optimizing glycemic management for better patient outcomes.

Key words: Acute Kidney Injury, Coronary Artery Bypass Graft, Diabetes, Glycemic Control, Mortality.

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INTRODUCTION

Glycated hemoglobin or HbA1c shows blood glucose control of the patients during last 3 to 4 months. When stable glycated hemoglobin is formed by irreversible binding of blood glucose to hemoglobin, is called HbA1c. Due to normal life span of 90-120 days of red blood cells, elimination of HbA1c is only possible upon replacement of red cells. That is why, short-term glycemic changes do not affect HbA1c due to continuous turnover of red cells. So, glucose control can be better assessed for a period of 3-4 months with the help of HbA1c.[1]

HbA1c increases reactive free radicals within blood cells, altering membrane properties. This leads to higher blood viscosity, cell aggregation, and impaired circulation. Additionally, HbA1c induces inflammation, contributing to atheroma formation.[2]

Postoperative AKI is a prevalent complication among cardiac surgery patients, with incidence rates reported between 20% and 49%.[3,4,5,6] Even a minor elevation in creatinine (0.3 mg/dL) can result in long-term renal impairment, increasing the risk of CKD progression and mortality.[7,8,9]

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Identified AKI risk factors include diabetes mellitus, gender, age, metabolic syndrome, and preoperative creatinine levels, while prolonged surgery and emergency procedures further contribute.[3,10,11] Both acute and chronic hyperglycemia have been associated with endothelial dysfunction, heightened infection risk, and cardiac complications post-CABG.[2,12,13,14] Furthermore, hyperglycemia is a well-recognized risk factor for perioperative morbidity and mortality, particularly in patients with renal dysfunction.[3,10,15]

For evaluation of chronic hyperglycemia and diabetes control in diabetic patients, HbA1c is an established parameter[16] and it is widely used to diagnose diabetes mellitus. Besides this, HbA1c has been reported as a vital marker for atherosclerosis, acute hyperglycemia, insulin resistance and endothelial dysfunction.[2,12]

The purpose of this study is to investigate the occurrence of acute kidney injury in patients with suboptimal glycemic control (HbA1c>7%) undergoing CABG surgery and to compare the frequency of AKI in patients with HbAlc > 7% and HbA1c < 7% undergoing CABG surgery. Additionally, the study will analyze the severity of acute kidney injury (AKI) in diabetic patients undergoing CABG surgery and its influence on postoperative outcomes, aiding in better risk assessment and management strategies.

METHODS

This research employed a comparative cross-sectional design, enrolling 100 diabetic patients scheduled for coronary artery bypass grafting (CABG) surgery during the period May 5, 2023, to May 4, 2024. Prior to study initiation, ethical approval was secured from the hospital's Ethical Review Committee (24-2019/DME/FIC/FSD), ensuring compliance with institutional guidelines and ethical research standards. The authors confirm no conflicts of interest in relation to this study. We included both genders with known history of diabetes within the age range of 40 to 70 years, with a serum creatinine level below 1.2 mg/dL, who were scheduled for elective CABG surgery.Patients requiring redo surgeries, those with an estimated glomerular filtration rate (eGFR) below 60 ml/min, and individuals with a left ventricular ejection fraction (LVEF) of less than 30% were excluded. Prior to participation, eligible patients received detailed counseling and structured interviews explaining the study's objectives and procedures. After taking routine consent (informed), patients were subsequently admitted to the cardiac surgery ward for further management.

CABG was performed following standard surgical protocols, including median sternotomy, arterial and venous graft harvesting, pericardiotomy, heparinization, cannulation, and cardiopulmonary bypass (CPB) under moderate hypothermia. Aortic cross-clamping (20–140 min) and antegrade cold blood cardioplegia were utilized. The required number of grafts were anastomosed, followed by rewarming, cross-clamp removal, CPB weaning, protamine administration, pacing wire and drain placement, hemostasis, and chest closure. For strict monitoring all operated cases were moved to ICU. Serum creatinine levels were recorded on the 1st, 2nd, and 4th postoperative days and compared with baseline values. Baseline serum creatinine was measured from a blood sample taken at hospital admission, and GFR was calculated using the CKD-EPI equation. The primary objective was to determine the incidence of AKI at any stage postoperatively, based on KDIGO criteria, which align with AKIN and STS guidelines. AKI was classified as:

- Stage 1: Serum creatinine increase of 0.3 mg/dL within 48 hours post-surgery or 1.5–1.9 times the baseline.
- Stage 2: Creatinine rise of 2.0–2.9 times the baseline.
- Stage 3: Creatinine increase of ≥3.0 times the baseline or necessity for renal replacement therapy.

Standard laboratory tests, including HbA1c and serum creatinine levels, were performed upon admission. HbA1c ≥7.0% at admission was classified as preoperative hyperglycemia, while postoperative hyperglycemia was defined as fasting serum glucose ≥126 mg/dL at any point during the postoperative period. Patients were stratified into two groups:

- Group A: HbA1c ≥7.0%
- Group B: HbA1c<7.0%

All patients remained under intensive care following surgery, and creatinine levels were recorded on the 1st, 2nd, and 4th postoperative days. Data entry and statistical analysis were conducted using SPSS version 23.0.Numerical variables (e.g., age, duration of surgery, HbA1c levels, preoperative and postoperative GFR, preoperative creatinine, and peak postoperative creatinine) were expressed as mean ± standard deviation (SD).However, variables (e.g., gender, AKI occurrence, severity of AKI, and adverse outcomes) were reported as frequency and percentage. The incidence, severity, and association of AKI with adverse outcomes were compared between Group A and Group B to determine statistical significance. To adjust for potential confounders, data were stratified based on gender, age, and surgical duration before further analysis.

RESULTS

The patients had age between 40-70 years with a mean of 51.5±7.4 years. 67 (67%) patients were aged ≤55 years and 33 (33%) patients were aged above 55 years. There were 88 (88%) males and 12 (12%) females. Ratio between male to female patients was of 7.3:1. Duration of surgery ranged from 3.5-8.0 hours with a mean of 5.29±1.07 hours. It was ≤5 hours in 59 (59%) patients and >5 hours in 41 (41%) patients as given in Table-I. Both study groups exhibited similar demographic profiles, as detailed in Table-II.

Plasma HbA1c level ranged from 6.1-13.8% with a mean of 7.27±1.03%. Group A exhibited a significantly higher value compared to Group B: (7.96±1.05 vs. 6.57±0.28%; p-value<0.001). The average serum creatinine levels in both groups were statistically comparable, 0.96±0.22 vs. 0.94±0.17 mg/dl; p-value=0.615) and mean glomerular filtration rate (92.78±12.25 vs. 93.88±14.47 mL/min/1.73m^2; p-value=0.683) at baseline. However, following cardiac surgery, the mean of peak serum creatinine was significantly higher (1.25±0.35 v/s. 1.03±0.22 mg/dl; p-value<0.001) while the mean glomerular filtration rate was significantly lower (66.14±21.17 vs. 75.96±17.52mL/min/1.73m^2; p-value=0.013) in patients with elevated HbA1c (≥7.0%) as shown in Table-III.

Following, cardiac surgery, acute kidney injury was noted in 28 (28.0%) patients (Table-IV). As indicated in Table-V, AKI occurred significantly more frequently in patients with HbA1c ≥7.0% than in those with lower HbA1c levels (44% v/s. 12%; p<0.001). This difference persisted across subgroups stratified by age, gender, and surgical duration. However, there was an increased rate of AKI with increasing duration of surgery irrespective of study group as shown in Table-VI.

Among the 28 patients having AKI, 15 (53.6%) patients were categorized as risk while 13 (46.4%) patients were categorized as injury under RIFLE criteria. Both groups exhibited comparable distributions of AKI severity grades. Furthermore, stratified analyses based on age, gender, and surgical duration was computed as of no difference statistically between the groups.

On comparison the occurrence of adverse outcome was found significantly more in those with increased HbA1c ≥7.0% (8.0% vs. 0.0%; p-value=0.041) as evident from Table-VII. On comparison same difference was observed between groups in different subgroups on age, gender and duration of surgery as evident from Table-VIII. The rate of adverse outcome was also much higher in patients who developed AKI after surgery (14.3% vs. 0.0%; p-value=0.005) as indicated by Table-IX.

TABLE-I

Baseline demographic and clinical arameters of the study group

Characteristics	Participants n=100
Age (years)	51.5±7.4
≤55 years	67 (67.0%)
>55 years	33 (33.0%)
Gender	
Female	12 (12.0%)
Male	88 (88.0%)
Duration of Surgery (hours)	5.29±1.07
≤5 hours	59 (59.0%)
>5 hours	41 (41.0%)

TABLE-II

Baseline characteristics of the study groups n=100

Characteristics	HbA1c ≥7 n=50	HbA1c <7 n=50	P-Value
Age (years)	51.6±7.5	51.4±7.4	0.894
≤55 years	33 (66.0%)	34 (68.0%)	0.832
>55 years	17 (34.0%)	16 (32.0%)	
Gender			
Male	45 (90.0%)	43 (86.0%)	0.538
Female	5 (10.0%)	7 (14.0%)	
Duration of Surgery (hours)	5.22±1.12	5.36±1.03	0.516
≤5 hours	29 (58.0%)	30 (60.0%)	0.839
>5 hours	21 (42.0%)	20 (40.0%)	

TABLE-III

Comparison of renal profile before and after cardiac surgery n=100

Parameter	HbA1c ≥7 n=50	HbA1c <7 n=50	P-Value
Creatinine at Baseline(mg/dl)	0.96±0.22	0.94±0.17	0.615
GFR at Baseline (mL/min/1.73m^2)	92.78±12.25	93.88±14.47	0.683
Creatinine after Surgery (mg/dl)	1.25±0.36	1.03±0.24	<0.001
GFR after Surgery (mL/min/1.73m^2)	66.14±21.17	75.96±17.52	0.013

TABLE-IV

Frequency of post-operative AKI in the study cohort n=100

AKI	Frequency (n)	Percent (%)
Yes	28	28.0 %
No	72	72.0 %
Total	100	100.0%

AKI; Acute Kidney Injury

TABLE-V

Comparison of frequency of post-operative AKI n=100

AKI	HbA1c ≥7 n=50	HbA1c <7 n=50	P-Value
Yes	22 (44.0%)	6 (12.0%)	<0.001
No	28 (56.0%)	44 (88.0%)	
Total	50 (100.0%)	50 (100.0%)	

TABLE-VI

Comparison of frequency of post-operative AKI n=100

Subgroups	Acute Kidney Injury n/n (%)		P-Value
	HbA1c ≥7 n=50	HbA1c <7 n=50	
Age			
≤55 years	14/33 (42.4%)	4/34 (11.8%)	0.005
>55 years	8/17 (47.1%)	2/16 (12.5%)	0.031
Gender			
Male	20/45 (44.4%)	5/43 (11.6%)	0.001
Female	2/5 (40.0%)	1/7 (14.3%)	0.310
Duration of Surgery			
≤5 hours	11/29 (37.9%)	3/30 (10.0%)	0.012
>5 hours	11/21 (52.4%)	3/20 (15.0%)	0.012

TABLE-VII

Comparison of frequency of post-operative adverse outcome n=100

Adverse Outcome	HbA1c ≥7 n=50	HbA1c <7 n=50	P-Value
Yes	4 (8.0%)	0 (0.0%)	0.041
No	46 (92.0%)	50 (100.0%)	
Total	50 (100.0%)	50 (100.0%)	

TABLE-VIII

Comparison of frequency of post-operative adverse outcome across various subgroups n=100

Subgroups	Adverse Outcome n/n (%)		P-Value
	HbA1c ≥7 n=50	HbA1c <7 n=50	
Age			
≤55 years	2/33 (6.1%)	0/34 (0.0%)	0.239
>55 years	2/17 (11.8%)	0/16 (0.0%)	0.485
Gender			
Male	4/45 (8.9%)	0/43 (0.0%)	0.117
Female	0/5 (0.0%)	0/7 (0.0%)	-
Duration of Surgery			
≤5 hours	2/29 (6.9%)	0/30 (0.0%)	0.237
>5 hours	2/21 (9.5%)	0/20 (0.0%)	0.488

TABLE-IX

Comparison of frequency of post-operative adverse outcome between patients with versus without post-operative AKI n=100

Adverse Outcome	AKI n=28	No AKI n=72	P-Value
Yes	4 (14.3%)	0 (0.0%)	0.005
No	24 (85.7%)	72 (100.0%)	
Total	28 (100.0%)	72 (100.0%)	

DISCUSSION

Among the various cardiac surgical procedures, CABG is most frequently performed procedure with an estimated rate of 400,000 procedures per annum and 62 procedures per 100,000 inhabitants in US and Europe.[17]

As in any other surgical procedure, post-operative morbidity and mortality remains a serious concern after CABG and research in the past few decades have focused on perioperative medications as well as development in instrumentation and techniques to decrease the likelihood of complications after CABG making it safer and effective.

Among the various post-operative complications of CABG, in adult patients, AKI is a frequently encountered and clinically significant complication.[3] Postoperative AKI is independently linked to higher short-term morbidity and increased treatment costs while long-term mortality.[6] Therefore measures which can reduce the occurrence of AKI and its severity are of paramount importance in clinical practice.[3,5,6]

The frequency of diabetes in patients undergoing CABG surgery continues to increase. During cardiac surgeries hyperglycemia occurs in perioperative period, has been reported to have strong relationship with increased morbidity and mortality.[12,13,4] HbA1c levels serve as an indicator of adequate glycemic control i.e. <7%. Perioperative hyperglycemia is also an independent predictor of post-operative acute kidney injury.[3,10]

Thus it appears that there is high risk of AKI when cardiac surgery is performed in a diabetic patient. Recently there was evidence that not only diabetes but poor glycemic control was related with increased risk of AKI after cardiac surgeries proposing potential role of glycemic control in the risk stratification of such patients.[6] Due to the limited available evidence and the lack of local published studies, this research was deemed necessary.

The aims of this research were to compare the incidence of acute kidney injury in diabetic patients with HbAlc ≥7% and HbA1c< 7% who underwent CABG surgery and to identify the severity of AKI and adverse outcome in diabetic patients who underwent CABG surgery.

In this study, the average age of CABG patients was 51.5±7.4 years. Our finding is in conformity with[18] who noted the same average age of 51.3±5.7 years in patients undergoing CABG at Chaudhary Pervaiz Elahi Institute of Cardiology, Multan. In another local study[19] reported similar mean age of 51.6±10.3 years among such patients undergoing CABG at Punjab Institute of Cardiology, Lahore. Similar mean age has already been reported in a number of other local studies where[29,20,21] observed it to be 53.6±10.2 years, 55.3±9.6 years and 54.5±3.4 years respectively. A comparable mean age has been observed in Indian patients undergoing CABG where[22] reported it to be 52.±11.2 years and[23] reported it to be 53.7**±9.5 years. A** similar trial in Bangladesh[24] reported comparable mean age of 54.8±2.5 years while[25] reported it to be 53.4±8.9 years in Nepal.

This observed mean age in the present study matches with statistics reported by other studies conducted in local as well as other populations in South-East Asia. However in comparison with western population, this mean age is quite younger where[26] in UK and[27] in USA observed much higher mean age at the time of CABG and reported it to be 67.1±10.1 years and 66.1±9.9 years respectively. Another study[28] also reported higher mean age of 67.3±9.1 years among Chinese such patients. This difference in the mean age can be attributable to geographical as well as life style and genetic factors associated with coronary artery disease. It implies public health measures in this regard to increase public awareness about this aspect to reduce the burden of disease and delay its development as

much as possible.

We observed a male predominance (M:F; 7.3:1) in patients undergoing CABG surgery. In another similar study[29] conducted at Punjab Institute of Cardiology, Lahore, reported alike predominance of males with male to female ratio of 7.2:1. Findings of this study agree with another study[30], as they also mentioned similar predominance of males with male to female ratio of 6.2:1 among CABG patients at Rahim Yar Khan.A notable male predominance was evident, with a male-to-female ratio of 6.2:1 has also been reported by another study[20] at Chaudhary Pervaiz Elahi Institute of Cardiology Multan. Other studies[22,23] described comparable predominance of male patients with male to female ratio of 7.1:1 and 7.9:1 respectively in Indian CABG patients. Another study[31] observed it to be 7.3:1 among Italian such patients.

We observed that following cardiac surgery, in patients with poor glycemic control the frequency of post-operative AKI (44.0% vs. 12.0%; p-value<0.001) and mortality (8.0% vs. 0.0%; p-value=0.041) was significantly high.

Our results in line with the parent study where[6] evaluated AKI and mortality in 300 German patients undergoing CABG surgery. The author took cut-off value of HbA1c ≥6.0 % to define good and poor glycemic control. The author reported similar significantly higher frequency of AKI (56.5% vs. 41.0%; p-value=0.008) and mortality (3.3% vs. 0.0%; p-value<0.05) in patients with poor glycemic control undergoing CABG surgery.

Our observation is also in line with a similar study[32] conducted over 202 Turkish patients undergoing CABG surgery. The author reported AKI in 10.5% patients and mortality in 1.8% patients. When compared patients with low and high HbA1c, the author reported similar higher frequency of AKI (16.7% vs. 3.6%; p-value=0.002) and mortality (6.7% vs. 1.8%; p-value=0.036) in patients with poor glycemic control. In another Turkish study[33] studied 60 patients with good glycemic control matched with another 60 patients having poor glycemic control undergoing CABG surgery. They too reported similar significantly higher frequency of AKI (25.0% vs. 10.0%; p-value=0.031) and mortality (8.3% vs. 0.0%; p-value=0.046) in patients with poor glycemic control. Still another Turkish study[34] described similarly higher rate of mortality in patients undergoing CABG surgery with high HbA1c in the pre-operative workup (21.4% vs 0.0%; p-value=0.005).

Similar results have also been reported by an Egyptian study[35] evaluated results of CABG surgery in 40 patients with good versus poor glycemic control. The author reported similar significantly increased frequency of AKI (45.0% vs. 10.0%; p-value=0.034) in patients with poor glycemic control prior to surgery (HbA1c ≥6.5%).

However, it is clear that pre-operative poor glycemic control may lead to post operative AKI and mortality in diabetics which highlights the significance of glycemic control as well as potential role of HbA1c in the risk stratification. We also observed that increased duration of surgery was also an important determining factor of acute kidney injury as the frequency of AKI was lower when the duration of surgery was ≤5 hours as compared to when it was >5 hours (23.7% vs. 34.1%; p-value=0.254). This association between duration of surgery and acute kidney injury can be explained by increase surgical stress, tissue trauma and exposure to anesthetic and other medications as well as derangements in hemodynamics with prolongation of operative time which are established risk factors of acute kidney injury.[3] In the light of this evidence, it is advocated that duration of surgery should be reduced to minimum in this population.

This trial is the first of its type in local population and contributes to the already available published international evidence on the subject. A large sample size of 100 patients was strength of this study besides strict exclusion criteria. A major and strong limitation to the current study was that we didn't take into account the role of peri-operative insulin therapy and ideal glycemic control in the management of such patients and its impact on the development of AKI, its severity and overall mortality which would have fixed the place of glycemic control in managing such patients more clearly. It is a crucial study and one which is greatly to be suggested in

future clinical studies.

CONCLUSION

Preoperative poor glycemic control was found to be a strong link with acute kidney injury and mortality in diabetics undergoing CABG. This capitalizes the significance of glycemic management and the potential role of HbA1c in risk stratification for optimizing patient care.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Riaz ul Haq:** Data collection, analyzing references.
2	**Muhammad Mujahid:** Data entry, critical revision.
3	**Muhammad Farooq Ahmad:** Data collection.
4	**Muhammad Hussnain Raza:** Proof reading.
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ORIGINAL ARTICLE

Efficacy of Valsartan versus enalapril in lowering Proteinuria in patients with diabetic nephropathy.

Awais Asghar[1], Naila Unbreen[2], Muhammad Owais Fazal[3], Ghulam Abbas Tahir[4], Muhammad Usman Musharraf[5]

ABSTRACT… Objective: To compare the effectiveness of valsartan and enalapril in reducing proteinuria in diabetic nephropathy patients. **Study Design:** Randomized Controlled Trial. **Setting:** Medical Floor, Allied Hospital. **Period:** January 3, 2024, to January 9, 2024 (Six Months). **Methods:** The study involved patients enrolled after approval from the Institutional Ethical Review Committee at Punjab Medical College, Faisalabad. Participants were randomly divided into two groups: Group A received valsartan 80mg daily, and Group B received enalapril 10mg daily for 3 months. Patients were monitored for efficacy after 3 months. **Results:** This study show no significant difference between the efficacy of the two drugs, but validation through multicenter studies is needed. **Conclusion:** We concluded that the efficacy of valsartan and enalapril in lowering proteinuria in patients with diabetic nephropathy is equal, and no significant difference is found; however, our results require validation through other multicentre studies.

Key words: Diabetic Nephropathy, Enalapril, Efficacy, Proteinuria, Valsartan.

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INTRODUCTION

Macroalbuminuria, or excretion of more than 300 mg of albumin in a 24-hour collection, or macroalbuminuria coupled with abnormal renal function, as indicated by an abnormality in serum creatinine, calculated creatinine clearance, or glomerular filtration rate (GFR), are the usual criteria used to diagnose diabetic nephropathy (DN). A steady rise in proteinuria, a decline in GFR, hypertension, and a high risk of cardiovascular morbidity and death are the hallmarks of diabetic nephropathy. More than 44% of new occurrences of kidney failure are caused by diabetes, making it the most prevalent cause. Chronic hyperglycaemia is a major risk factor for the development of diabetic nephropathy.[1,2]

The glomerular basement membrane thickening and matrix material buildup in the mesangium are the pathological first alterations that occur concurrently with the development of microalbuminuria. Nodular deposits are then typical, and as high proteinuria develops, glomerulosclerosis gets worse until glomeruli are gradually destroyed and renal function declines. Usually, it develops gradually over the years.[3]

Diabetic nephropathy is the most common cause of ESKD and is a serious complication that affects approximately One-fourth of American adults who have diabetes.[4] ACE inhibitors have been shown in certain trials to have a specialized function in lowering intraglomerular pressure in addition to lowering systemic hypertension. In patients with normotensive diabetes, an ACE inhibitor slows the growth of proteinuria and stops the albumin excretion rate from rising. Improved glycaemic management, strict blood pressure control, and the administration of an ACE inhibitor or ARB are interventions that are effective in reducing the progression of albuminuria.[5]

Enalapril and losartan alone were found to reduce proteinuria by 33% in the literature ($p < 0.05$).[6] Another study shows the mean percentage reduction in proteinuria was 25.68 ± 21.40 with enalapril.[7] while the mean percentage reduction in proteinuria with valsartan is 33% (27-38%) (33 ± 21.4).[8]

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Some studies show that enalapril and valsartan have equal efficacy in reducing proteinuria, i.e., 33%.[7,9] Others, however, demonstrate that enalapril is less effective, with a reduction of only 25%. The rationale for my study is that if recent studies indicate that valsartan is more effective in our population, which is genetically and geographically different from other populations, then future recommendations could favour using valsartan, as it may be more cost-effective and avoid side effects like a dry cough.

OPERATIONAL DEFINITION

Efficacy

- Diabetic nephropathy was diagnosed by ACR (Albumin to creatinine ratio) >20mg/mmol.
- Efficacy was measured by monitoring ACR at 3 months.

The drug was considered effective if the ACR became less than 10 mg/mmol

HYPOTHESIS

Null Hypothesis

Two medications are equally effective at reducing proteinuria in diabetic nephropathy patients.

Alternative Hypothesis:

- There is a difference in the efficacies of two drugs

METHODS

This randomised controlled trial was conducted at Medical OPD, Allied Hospital, Faisalabad from January 3, 2024, to January 9, 2024 (six months) following ERC clearance, vide letter No. 48.ERC/FMU/2023-24/412, Dated: 06/08/24.

The WHO sample size calculator for two means was used to determine the sample size. The population mean test value was 33.[7] The population was expected to be 25.68[9] The pooled standard deviation is 21.4%. The study power was 80%. Level of significance 5%. Sample size was 204 (102 in each group).

The Sampling Technique used was Non-probability consecutive sampling.

Inclusion Criteria

- Patients of both genders aged 35-70yr years old
- Fasting blood sugar >126mg dl or on treatment for diabetes
- Patients with BP >= 120/80

Exclusion Criteria

1. Patients having Diabetes Mellitus Type I.
2. Patients having nephropathy due to
   a. bladder outlet obstruction
   b. Interstitial nephritis
   c. chronic glomerulonephritis
3. Patients with UTI, i.e., pus cells >10/HPF, confirmed on medical record

Data Collection Procedure

Following institutional ethical review board permission, the study was done in Faisalabad Medical University, screening of the participants with pre-decided criteria, and consent was taken from each participant. In the study. All the participants were randomly divided into two groups. Group A was given valsartan 80mg single dose daily, & group B was given enalapril 10mg as a single dose daily using computer computer-generated random number table for 3 months. 1st dose of the drug was supervised, and BP was checked after 1 hour to avoid 1st dose hypotension. Patients were followed after 3 months for efficacy by monitoring albuminuria as mentioned in the operational definition. All the information was recorded on a pre-designed form by the researcher.

Data Analysis

Version 20 of SPSS software was utilized for data entry and analysis. For quantitative data such as age, blood glucose levels, ACR, and the length of diabetes, the mean and standard deviation were computed. Gender and efficacy were examples of qualitative variables for which frequency and percentage were computed. To use According to the chi-square test, $p < 0.05$ was considered significant. Stratification was used to control for variables such as age, gender, and length of diabetes. The post-stratification chi-square test was used to determine that a p-value (< 0.05).

RESULTS

To assess the effectiveness of valsartan versus enalapril in reducing proteinuria in patients with diabetic nephropathy, 204 participants (102 in each

group) who met the selection criteria were included.

In Group-A, 42.16% (n=43) and Group-B, 45.10% (n=46), were between the ages of 35 and 50, while Group-A's 57.84% (n=59) and Group-B's 54.90% (n=56) were between the ages of 51 and 70. Group A's mean+sd was 51.06+8.42 years, whereas Group B's was 50.73+8.06 years. (Table-I)

The gender distribution shows that 31.37% (n=32) of Group-A and 35.29% (n=36) of Group-B were female, while 68.63% (n=70) of Group-A and 64.71% (n=66) of Group-B were male. (Table-II)

In Group A, the mean duration of diabetes was 6.57+2.99 years, while in Group B, it was 6.52+3.01 years. (Table-III)

Mean blood glucose levels in Group A were 139.31+7.69 and 141.20+7.42 in Group B. (Table-IV)

Mean ACR levels in Group A were 24.72+2.19 and 24.57+2.04 in Group B. (Table-V)

Comparison of efficacy of valsartan vs enalapril in lowering proteinuria in patients with diabetic nephropathy" shows that in Group-A, 37.25% (n=38) and 28.43% (n=29) in Group-B, while 62.75% (n=64) in Group-A and 71.57% (n=73) in Group-B had no efficacy, p value was 0.17. (Table-VI)

Stratification was used to adjust for variables such as age, gender, and length of diabetes. To apply the post-stratification chi-square test, $p < 0.05$ was considered significant. (Table-VII)

TABLE-I

Distribution of age (n=204)

Age (in years)	Group-A (n=102)		Group-B (n=102)	
	No. of Patients	%	No. of Patients	%
35-50	43	42.16	46	45.10
51-70	59	57.84	56	54.90
Total	102	100	102	100
Mean+SD	51.06+8.42		50.73+8.06	

TABLE-II

Distribution of gender (n=204)

Gender	Group-A (n=102)		Group-B (n=102)	
	No. of patients	%	No. of patients	%
Male	70	68.63	66	64.71
Female	32	31.37	36	35.29
Total	102	100	102	100

TABLE-III

Mean duration of diabetes (n=204)

Duration of Diabetes (Years)	Group-A (n=102)		Group-B (n=102)	
	Mean	SD	Mean	SD
	6.57	2.99	6.52	3.01

TABLE-IV

Mean blood glucose levels (n=204)

Blood Glucose Levels	Group-A (n=102)		Group-B (n=102)	
	Mean	SD	Mean	SD
	139.31	7.69	141.20	7.42

TABLE-V

Mean ACR (n=204)

ACR Levels	Group-A (n=102)		Group-B (n=102)	
	Mean	SD	Mean	SD
	24.72	2.19	24.57	2.04

TABLE-VI

Comparison of efficacy of Valsartan Vs Enalapril in lowering proteinuria in patients with diabetic nephropathy" (n=204)

Efficacy	Group-A (n=102)		Group-B (n=102)	
	No. of Patients	%	No. of Patients	%
Yes	38	37.25	29	28.43
No	64	62.75	73	71.57
Total	102	100	102	100

P value: 0.17

TABLE-VII

Stratification of efficacy with respect to age, gender, and duration of diabetes. (n=204)

Parameter/ Group (n=204)	Efficacy		P-Value
Age 35-50 years	**Yes**	**No**	
A	19	24	0.006
B	8	38	
Age 51-70 years			
A	19	40	.55
B	21	35	
Gender			
Male			
A	29	41	0.17
B	20	46	
Female			
A	9	23	
B	9	102	
Duration of Diabetes			
5 YEARS			
A	16	23	0.06
B	9	32	
➢ **5 Years**			
A	12	3	0.02
B	20	41	

DISCUSSION

DM-II raises the risk of renal and cardiovascular conditions when micro-albuminuria develops. among many parts of the world, the prevalence of end-stage renal disease among people with DM-II has increased. There is mounting evidence that one of the main therapy objectives for renal and perhaps cardiovascular protection is the reduction and normalization of proteinuria. ACE inhibitors have been shown in certain trials to have a specialized function in lowering intraglomerular pressure in addition to lowering systemic hypertension. In patients with normotensive diabetes, an ACE inhibitor slows the growth of proteinuria and stops the albumin excretion rate from rising. Improved glycaemic management, perfect blood pressure control, and the administration of an ACE inhibitor or ARB are interventions that are effective in reducing the course of albuminuria.

Some of the studies reveal equal efficacy of enalapril and valsartan in reducing proteinuria, i.e, 33%.[10,11] While others show comparatively less efficacy of enalapril in reducing proteinuria, i.e, 25%[12] The rationale of my study is that if recent studies showed more efficacy of valsartan in our population, which is genetically and geographically different from other populations, then future recommendations could be formulated to use valsartan as it would be more cost-effective, and side effects like dry cough could be avoided.

We found that, of the 204 cases (102 in each group), 42.16% (n=43) in Group A and 45.10% (n=46) in Group B were between the ages of 35 and 50, while 57.84% (n=59) in Group A and 54.90% (n=56) in Group B were between the ages of 51 and 70. The mean+sd was 51.06+8.42 in Group A and 50.73+8.06 years in Group B. Of these, 68.63% (n=70) in Group A and 64.71% (n=66) were male, while 31.37% (n=32) in Group A and 35.29% (n=36) were female. When valsartan and enalapril are compared for their ability to reduce proteinuria in patients with diabetic nephropathy, Group A experienced 37.25% (n=38) and 28.43% (n=29) efficacy, whereas Group B experienced 62.75% (n=64) and 71.57% (n=73) ineffectiveness; the p-value was 0.17.

Enalapril and losartan by themselves were found to reduce proteinuria by 33% ($p < 0.05$).[7] Another study shows the mean percentage reduction in proteinuria was 25.68 ± 21.40 with enalapril.[13] while the mean percentage reduction in proteinuria with valsartan is 33% (27-38%) (33 ± 21.4)[14].

Some studies show equal efficacy of enalapril and valsartan in reducing proteinuria, i.e, 33%.[15,16] While others show comparatively less efficacy of enalapril in reducing proteinuria, i.e, 25%.[17] Our findings are in agreement with this study reveals that enalapril had a lower rate of efficacy; however, the difference was not statistically significant.

Giancarlo Viberti and associates report that 332 individuals with microalbuminuria and DM-II, with or without High blood pressure, were assigned randomly to receive 80 mg/d valsartan or 5 mg/d amlodipine for 24 weeks. A blood pressure target of 135/85 mmHg was achieved by doubling the dose,

with doxazosin and bendrofluazide added as necessary. The outcome measure, primarily, was the percentage change in UAER (urine albumin excretion) between baseline and 24 weeks. There was a highly significant between-group effect (P<0.001) at 24 weeks, with the UAER being 56% (95% CI, 49.6 to 63.0) of baseline with valsartan and 92% (95% CI, 81.7 to 103.7) of baseline with amlodipine. In both the hypertensive and normotensive groups, valsartan comparably reduced UAER. When taking valsartan, more people saw a return to normoalbuminuria (29.9% versus 14.5%; P=0.001). In whole of the whole study period, the two treatments' BP reductions were similar (valsartan's systolic/diastolic was 11.2/6.6 mm Hg, amlodipine's was 11.6/6.5 mm Hg), and there was never a statistically significant difference between the groups in blood pressure readings in the normotensive or hypertensive subgroups.

They found that in individuals with DM-II and microalbuminuria, including the subgroup with baseline normotension, valsartan reduced UAER more efficiently than amlodipine at the same level of achieved BP and the same degree of BP decrease. This suggests that valsartan has an antiproteinuric action that is independent of blood pressure. Enalapril and losartan by themselves were found to reduce proteinuria by 33% ($p < 0.05$).[18]

However, considering the cost-effectiveness of Valsartan, we are of the view that this drug may be used, while enalapril has no significantly higher efficacy. The results of this study prove our hypothesis that "there is no difference in the efficacy of two drugs in lowering proteinuria among patients of diabetic nephropathy". Our results are required to be validated through some other multicentre studies.

CONCLUSION

We concluded that the efficacy of valsartan and enalapril in lowering proteinuria in patients with diabetic nephropathy is equal, and no significant difference is found; however, our results require validation through other multicentre studies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Awais Asghar:** Conception of idea, data collection.
2	**Naila Unbreen:** Manuscript writing.
3	**Muhammad Owais Fazal:** Data analysis.
4	**Ghulam Abbas Tahir:** Data collection.
5	**Muhammad Usman Musharraf:** Results.

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ORIGINAL ARTICLE

Etiological spectrum of non-celiac malabsorption in pediatric population in a tertiary care hospital.

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ABSTRACT… Objective: To determine the etiological spectrum of non-celiac malabsorption in pediatric population at a tertiary care hospital. **Study Design:** Analytical, cross-sectional study. **Setting:** Department of Gastroenterology, National Institute of Child Health (NICH), Karachi, Pakistan. **Period:** July 2025 to November 2025. **Methods:** Children aged 2–10 years presenting with symptoms of malabsorption for more than two weeks were enrolled through consecutive sampling. Stool analysis were performed to confirm etiology. Data were analyzed using SPSS version 26.0. **Results:** In a total of 220 children, 124 (56.4%) were males, and median age of 6.0 years (IQR 4.0–8.0). Chronic diarrhea 194 (88.2%) and steatorrhea 107 (48.6%) were the most common clinical manifestations. Giardiasis was the most frequent etiology 72 (32.7%), followed by carbohydrate malabsorption 54 (24.5%), fat malabsorption 41 (18.6%), protein malabsorption 27 (12.3%), and chronic intestinal infection 26 (11.8%). Age (p=0.041), residence (p=0.021), parental education (p=0.029), and hemoglobin levels (p=0.004) showed significant associations with etiology of non-celiac malabsorption. Chronic diarrhea was most frequent in Giardiasis (95.8%) and chronic intestinal infection (96.2%) with a significant association (p=0.032). Steatorrhea was strongly linked to fat malabsorption (87.8%, p<0.001). Fatigue or pallor was more common in infective etiologies, seen in Giardiasis (45.8%) and chronic intestinal infection (42.3%) (p=0.018). **Conclusion:** Infectious causes, particularly Giardiasis, remain the leading etiology of non-celiac malabsorption among children. Infective etiologies were associated with anemia, chronic diarrhea, and nutritional compromise, whereas non-infective causes were linked with specific nutrient malabsorption profiles.

Key words: Children, Diarrhea, Giardiasis, Malabsorption, Steatorrhea.

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INTRODUCTION

Malabsorption is a disorder in which the body fails to absorb nutrients from any point of the gastrointestinal system, resulting in deficiencies and other health problems.[1] Malabsorption can be a result of a variety of small intestinal diseases, as well as pancreatic, biliary tract, liver, and digestive tract diseases.[2] There are several conditions that can lead to malabsorption in children, such as celiac disease, pancreatic insufficiency, bile acid malabsorption and lactose intolerance.[3]

Malabsorption is typically found in underdeveloped countries with limited access to basic healthcare services. Around the world, millions of individuals, including children, suffer from malabsorption. Malabsorption syndromes have several etiologies, which makes it difficult to determine their actual frequency and prevalence.[4,5] In the United States, the cumulative prevalence of malabsorption is 1 in 133, but the prevalence of malabsorption due to Crohn's disease ranges from 20 to 100 per 100,000.[5] In developed countries, the most commonly reported reason behind malabsorption is celiac disease, which affects approximately 1% of the patients.[6,7] In developing countries like Pakistan, the actual burden of malabsorption and its etiology are not fully known.[8]

Different studies from the world reports the celiac disease as the most common cause of malabsorption. A recent study by Baciu et al evaluated the different sign and symptoms and etiologies of malabsorption in children and reported the celiac disease in 51.7% of children as most common cause of malabsorption followed by cystic fibrosis in 31% children, and Cow's milk protein allergy in 17.3% children.[9]

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A recent study from Pakistan by Masood et al also evaluated the different sign and symptoms and risk factors of malabsorption in adults and reported the tuberculosis in 57.14% of adults as most common cause of malabsorption followed by celiac disease in 23.8%.[10]

Early diagnosis is critical for children with malabsorption syndromes, as this maximizes the possibility of the best possible child-specific outcome. The data regarding etiological spectrum of non-celiac malabsorption in children is very limited in Pakistan. Therefore, we will conduct this study to review the various etiologies of non-celiac malabsorption syndromes in children presenting at Gastroenterology Department of NICH Hospital. The results of this study could help developing local data about malabsorption syndromes and their causes in pediatric population and ultimately help physicians to treat patients earlier in order to prevent complications, morbidity and mortality. The aim of this study was to determine the etiological spectrum of non-celiac malabsorption in pediatric population at a tertiary care hospital.

METHODS

This cross-sectional analytical study was conducted at the Department of Gastroenterology, National Institute of Child Health (NICH), Karachi, Pakistan during July 2025 to November 2025 after approval from the Institutional Ethical Review Committee (letter number: IERB-14/2025). The sample size was determined using the OpenEpi online calculator. The prevalence of cow's milk protein allergy as an etiological cause of malabsorption reported by Baciu et al. (17.3%) was taken as the reference proportion[9], with a 95% confidence interval and a 5% margin of error, the calculated sample size was 220 children. Non-probability consecutive sampling was adopted. Children of either gender, aged between 2 and 10 years who presented with symptoms of malabsorption persisting for more than two weeks, such as chronic diarrhea, steatorrhea, abdominal pain, abdominal distension, cramping, or failure to gain weight, were included. Only those children who met the diagnostic confirmation criteria of non-celiac malabsorption, as defined by stool analysis, were enrolled. Exclusion criteria included children previously diagnosed with celiac disease confirmed by positive anti-tissue transglutaminase IgA (>10 U/mL), those who had taken antiparasitic medication in the preceding three months, or those suffering from acute gastroenteritis, chronic pancreatitis, or exocrine pancreatic insufficiency. Children with clinically diagnosed lactose intolerance were also excluded to eliminate potential overlap with other carbohydrate malabsorption disorders. Pediatric malabsorption was defined as the presence of one or more of the following symptoms; chronic diarrhea, steatorrhea, abdominal pain, distension or cramping, and failure to gain weight, with confirmatory stool test findings. Written informed consent was sought from the parents / caregivers of all participants.

Demographic information like age, gender, residence, and parental educational status were noted at the time of enrollment. Height and weight of all children were obtained using standardized equipment. Clinical assessment was performed about the duration and frequency of diarrhea, stool consistency and character, presence of abdominal distension or cramps, vomiting, and signs of failure to thrive or weight loss. Assessment of nutritional status, degree of dehydration, and other systemic manifestations of chronic malabsorption were also performed. Stool samples from each child were collected under aseptic conditions in sterile, wide-mouthed containers, and then immediately transported to the institutional laboratory for analysis regarding pH, presence of fat droplets, and detection of pathogens. Carbohydrate malabsorption was confirmed as stool pH < 5.5, identified using pH indicator paper. Fat malabsorption (steatorrhea) was verified as > 60 fat droplets / hpf on Sudan III staining. Protein malabsorption was verified as the presence of α1-antitrypsin in stool using enzyme-linked immunosorbent assay (ELISA). Parasitic and infective causes were established by microscopic detection of Giardia, Clostridium difficile, or Cryptosporidium species on wet mount preparations and antigen detection methods.

Data entry and analysis were done by IBM-SPSS Statistics, version 26.0. Quantitative variables were summarized as mean±SD or median and interquartile range, depending on the normality distribution of data. Categorical variables were shown as frequencies and percentages. Effect

modifiers including age, gender, residence, and hygiene practices were controlled through stratification. Associations between demographic factors and etiological findings were assessed using a chi-square test or fisher's exact test (whichever was appropriate). Numeric data comparisons were carried out using analysis of variance or Kruskal-Wallis test. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Among a total of 220 children, the median age was 6.0 years (IQR 4.0–8.0). There were 124 (56.4%) male, and 96 (43.6%) female children. In terms of residence, 132 (60.0%) children belonged to rural areas, whereas 88 (40.0%) were from urban settings. With respect to parental education, 57 (25.9%) children had parents with no formal education, 84 (38.2%) had parents with primary education, and 79 (35.9%) had parents who had attained secondary education or above. The median body weight of the participants was 17.0 kg (IQR 14.5–20.0), and the median hemoglobin concentration was 10.1 g/dL (IQR 9.2–11.0), indicating mild to moderate anemia across the study population (Table-I).

TABLE-I

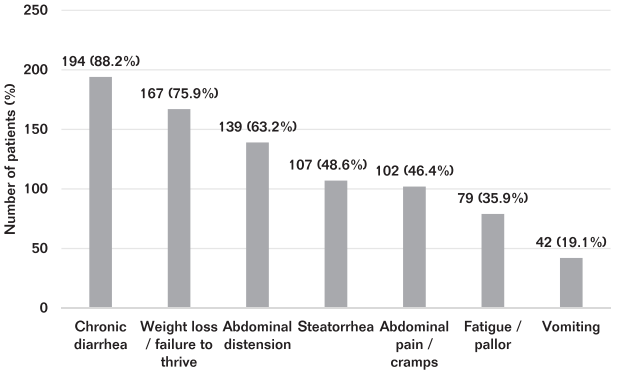
Demographic and baseline characteristics of study population (n=220)

Characteristics		Frequency (%)
Gender	Male	124 (56.4%)
	Female	96 (43.6%)
Age group (years)	2 to 5	94 (42.7%)
	>5 to 10	126 (57.3%)
Residence	Rural	132 (60.0%)
	Urban	88 (40.0%)
Parental education	No formal education	57 (25.9%)
	Primary	84 (38.2%)
	Secondary or above	79 (35.9%)

Among the presenting clinical features (Figure-1), chronic diarrhea was the most frequently observed symptom and was reported in 194 children (88.2%), followed by weight loss or failure to thrive in 167 (75.9%). Abdominal distension was documented in 139 (63.2%) participants, steatorrhea in 107 (48.6%), and abdominal pain or abdominal cramps in 102 (46.4%). Fatigue or pallor suggestive of anemia was noted in 79 (35.9%) cases, whereas vomiting was present in 42 (19.1%).

FIGURE-1

Frequency of clinical manifestations in non-celiac malabsorption (N=220)



Among children with non-celiac malabsorption, Giardiasis was found in 72 (32.7%), carbohydrate malabsorption in 54 (24.5%), fat malabsorption in 41 (18.6%), protein malabsorption in 27 (12.3%), and chronic intestinal infection in 26 (11.8%). Gender distribution did not differ significantly across etiologies (p = 0.412). Age showed a significant association with Giardiasis as it was predominated in children aged 2–5 years (58.3%), while carbohydrate (68.5%), and protein malabsorption (66.7%) were more frequent in those aged >5–10 years (p=0.041). Residence was significantly related to etiology as Giardiasis (65.3%) and chronic intestinal infection (69.2%) were more common in rural areas, whereas carbohydrate (63.0%) and fat malabsorption (56.1%) occurred more often in urban children (p=0.021). Parental education showed significance (p=0.029) as infective causes predominated in children of parents with no or primary education, while carbohydrate malabsorption was frequent in those with higher education (50.0%). Hemoglobin levels varied significantly as Giardiasis and chronic infection had lower median hemoglobin values (9.6 [8.9–10.3] and 9.9 [9.0–10.7] g/dL) compared with higher levels in carbohydrate, fat, and protein malabsorption (10.4, 10.3, and 10.5 g/dL, respectively), indicating greater anemia in infective etiologies (p=0.004). Table-II is showing details about the association of etiology of non-celiac malabsorption with respect to demographic and clinical characteristics.

TABLE-II

Association of etiology of non-celiac malabsorption with respect to demographic and clinical characteristics (N=220)

Characteristics		Giardiasis (n=72)	Carbohydrate Malabsorption (n=54)	Fat Malabsorption (n=41)	Protein Malabsorption (n=27)	Chronic Infection (n=26)	P-Value
Gender	Male	43 (59.7%)	32 (59.3%)	22 (53.7%)	15 (55.6%)	12 (46.2%)	0.412
	Female	29 (40.3%)	22 (40.7%)	19 (46.3%)	12 (44.4%)	14 (53.8%)	
Age group (years)	2 to 5	42 (58.3%)	17 (31.5%)	20 (48.8%)	9 (33.3%)	6 (23.1%)	0.041
	>5 to 10	30 (41.7%)	37 (68.5%)	21 (51.2%)	18 (66.7%)	20 (76.9%)	
Residence	Rural	47 (65.3%)	20 (37.0%)	18 (43.9%)	13 (48.1%)	18 (69.2%)	0.021
	Urban	25 (34.7%)	34 (63.0%)	23 (56.1%)	14 (51.9%)	8 (30.8%)	
Parental education	No formal education	26 (36.1%)	8 (14.8%)	9 (22.0%)	5 (18.5%)	9 (34.6%)	0.029
	Primary	26 (36.1%)	19 (35.2%)	19 (46.3%)	10 (37.0%)	10 (38.5%)	
	Secondary or above	20 (27.8%)	27 (50.0%)	13 (31.7%)	12 (44.5%)	7 (26.9%)	
Hemoglobin in g/dl (median [IQR)		9.6 (8.9-10.3)	10.4 (9.7-11.2)	10.3 (9.4-11.0)	10.5 (9.6-11.5)	9.9 (9.0-10.7)	0.004

TABLE-III

Association of clinical manifestations with respect to etiology of non-celiac malabsorption (N=220)

Clinical Manifestations	Giardiasis (n=72)	Carbohydrate Malabsorption (n=54)	Fat Malabsorption (n=41)	Protein Malabsorption (n=27)	Chronic Infection (n=26)	P-Value
Chronic diarrhea	69 (95.8%)	45 (83.3%)	34 (82.9%)	21 (77.8%)	25 (96.2%)	0.032
Weight loss / failure to thrive	58 (80.6%)	38 (70.4%)	32 (78.0%)	19 (70.4%)	20 (76.9%)	0.241
Abdominal distension	39 (54.2%)	31 (57.4%)	27 (65.9%)	16 (59.3%)	16 (61.5%)	0.326
Steatorrhea	31 (43.1%)	21 (38.9%)	36 (87.8%)	12 (44.4%)	7 (26.9%)	<0.001
Abdominal pain / cramps	31 (43.1%)	24 (44.4%)	20 (48.8%)	16 (59.3%)	14 (53.8%)	0.284
Fatigue / pallor	33 (45.8%)	12 (22.2%)	17 (41.5%)	6 (22.2%)	11 (42.3%)	0.018
Vomiting	13 (18.1%)	9 (16.7%)	7 (17.1%)	5 (18.5%)	8 (30.8%)	0.712

Chronic diarrhea had the highest frequency in Giardiasis (95.8%) and chronic intestinal infection (96.2%), showing a significant association with etiology (p=0.032). Steatorrhea showed a strong association with fat malabsorption, present in 36 of 41 (87.8%) children compared with lower frequencies in other etiologies (p<0.001). Fatigue or pallor was significantly associated with infective etiologies, occurring in 33 of 72 (45.8%) with Giardiasis and 11 of 26 (42.3%) with chronic infection (p = 0.018). Details about the association of clinical manifestations with respect to etiology of non-celiac malabsorption.

DISCUSSION

The present study identified Giardiasis as the leading cause of non-celiac malabsorption in children, accounting for 72 cases (32.7%), followed by carbohydrate malabsorption in 54 (24.5%), fat malabsorption in 41 (18.6%), protein malabsorption in 27 (12.3%), and chronic intestinal infections in 26 (11.8%). Yacha et al.[11], reported parasitic infestations as a significant cause of malabsorption in 15% children, particularly among those above 2 years of age. On the other hand, Baciu et al.[9], demonstrated celiac disease (51%) and cystic fibrosis (32%) as the predominant etiologies.

The disparity reflects the influence of regional, environmental, and socioeconomic factors, where poor sanitation, unsafe drinking water, and inadequate hygiene practices favor infectious etiologies in low- and middle-income countries.[12]

In this study, the predominance of Giardiasis in children aged 2–5 years (58.3%) aligns with the typical epidemiological pattern of Giardia lamblia infection in early childhood. Young children are thought to have relatively higher exposure risks due to poor hand hygiene and contaminated water source.[13] Yacha et al.[11], found parasitic infections predominantly affecting younger cohorts which seems similar to the present findings. In contrast, Nidhya et al., reported structural or autoimmune causes such as celiac disease and tropical sprue, exhibiting that infectious etiologies are less common where sanitation and early screening are well established.[14,15]

The research showed a significant association between residential background and malabsorption etiology (p=0.021) as Giardiasis and chronic intestinal infections were more frequent among rural children, whereas carbohydrate and fat malabsorption were more common among urban residents. Pucinischi et al.[16], highlighted that malabsorption etiologies vary according to socio-economic settings. Rural populations often have environmental risk factors related to reduced access to clean water and healthcare, while among urban children, non-infective causes of malabsorption related to dietary habits are more common. The present data highlight the fact that geographic variations play a crucial role in determining the pattern of etiology for pediatric malabsorption.[17] Education of parents formed the other important determinant of etiology (p=0.029). Baciu et al.[9], suggested a strong association between low parental literacy and late diagnosis of treatable malabsorptive diseases. Low educational status may predispose to late utilization of health services, poor dietary hygiene, and ignorance about certain preventive measures.[18] The data suggest that parental awareness and education are important modifiable variables in minimizing preventable infectious causes of pediatric malabsorption.[19]

The median hemoglobin concentration was lower in infective etiologies: Giardiasis, 9.6 g/dL (IQR 8.9–10.3), and chronic intestinal infection, 9.9 g/dL (IQR 9.0–10.7), compared with non-infective causes, p=0.004. Our findings are supported by Baciu et al.[9], who reported anemia in 45% of cases of pediatric malabsorption. Similarly, Yacha et al.[11], observed anemia and growth failure as the major presenting complications associated with infective diarrhea of protracted duration among children. These facts underscore the need for a routine anemia screening and nutritional rehabilitation in children with infective malabsorption.[20] In this study, chronic diarrhea was significantly associated with Giardiasis and chronic intestinal infection (p=0.032). Similarly, Miller et al.[21], demonstrated the presence of chronic diarrhea and carbohydrate malabsorption in enteric infections among HIV-infected children. The pathophysiology is similar to both conditions consisting of villous atrophy and inflammation of the mucosa, leading to secondary malabsorptive states.[22] Our data confirm that chronic diarrhea should raise suspicion for an infectious and non-celiac etiology for malabsorption.[23]

There was a specific association of steatorrhea with fat malabsorption, identified in 87.8% of children with this etiology (p<0.001). This direct association confirms the diagnostic value of stool fat estimation in distinguishing lipid absorption defects from other forms of malabsorption. Pucinischi et al.[16], similarly reported fat malabsorption as a key symptom of pancreatic or mucosal disease. Tests like Sudan III staining for stool remain simple, inexpensive methods available in developing countries for early detection of fat malabsorption.[24] The repeated finding of infection, anemia, and malnutrition clearly indicates the insidious effect of chronic gastrointestinal infections on growth and development in childhood. Testing for micronutrient deficiency and anemia should, therefore, be included in the workup of all children presenting with chronic symptoms of malabsorption.[25]

This study had several limitations: it was cross-sectional in nature and thus could not establish causality between putative risk factors and malabsorption etiologies; the diagnostics in this study were stool-based, and although sensitive for screening purposes, they may miss more subtle

mucosal abnormalities or enzyme deficiencies detectable through endoscopy or molecular techniques. The single-center design limits the generalizability of findings; multicentric studies across diverse geographical and socioeconomic backgrounds would enhance external validity.

CONCLUSION

Infectious causes, particularly Giardiasis, remain the leading etiology of non-celiac malabsorption among children in low-resource settings. This study underscores the significant influence of age, residence, and parental education on disease pattern and severity. Infective etiologies were associated with anemia, chronic diarrhea, and nutritional compromise, whereas non-infective causes were linked with specific nutrient malabsorption profiles.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Incidence and risk stratification of pediatric acute respiratory distress syndrome in pediatric intensive care unit.

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ABSTRACT… Objective: To determine the incidence and risk stratification of pediatric acute respiratory distress syndrome (PARDS) in mechanically ventilated (MV) patients admitted at the pediatric intensive care unit (PICU). **Study Design:** Prospective Observational study. **Setting:** The PICU of National Institute of Child Health, Karachi, Pakistan. **Period:** April 2024 to March 2025. **Methods:** A total of 200 children aged 1 month to < 18 years admitted to the PICU with PARDS, and undergoing MV were included. Risk stratification was done on the basis of oxygenation index (OI) categorizing as mild (4 ≤ OI < 8), moderate (8 ≤ OI < 16), and severe (OI ≥ 16). Duration of MV, use of inotropes, PICU stay duration, and mortality were documented and compared with respect to PARDS severity using chi-square test, and Kruskal-Wallis test, taking p<0.05 as significant. **Results:** Among 200 children, 111 (55.5%) were female, and overall median age was 8.00 (IQR, 4.00–12.00) years. Regarding PARDS categorizations, 24 (12.0%) had mild, 82 (41.0%) moderate, and 94 (47.0%) severe PARDS. Inotropic support was required in 84 (42.0%) patients. Median duration of MV, and PICU stay were 8.00 (5.00–11.00), and 16.00 (12.00–23.00) days, respectively, increasing significantly with severity (p<0.001). Mortality was highest in severe PARDS (21.3%) compared to moderate (2.4%) and mild cases (4.2%) (p<0.001). **Conclusion:** The PALICC definition and stratification system for PARDS effectively categorize mechanically ventilated pediatric patients into distinct severity groups associated with clinically meaningful differences in ventilator requirements, PICU stay, and mortality.

Key words: Children, Inotropes, Mechanical Ventilation, Mortality, Oxygenation Index.

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) has been long known to clinicians since its early description.[1] Various guidelines had been published in the last three decades to define ARDS, but these were originally adult-derived criteria/definitions, which were then extrapolated for pediatric populations.[2,3] With time, it became apparent that pediatric-specific definitions were strongly needed. Due to numerous anatomic and physiologic differences between adults and children, like incomplete airway cartilage formation, greater increase in resistance with decrease in radius of airways, higher metabolic demand, or greater compliance, infants and children are more prone to serious illness with relatively small insults.[4] To overcome these hurdles, in 2015 a panel of 27 experts constituted the Pediatric Acute Lung Injury Consensus Conference (PALICC) and proposed new pediatric-specific definitions for ARDS.[5]

Wong et al demonstrated the PALICC criteria for stratification of PARDS into mild (23.9%), moderate (39.9%), and severe (36.2%) groups with overall mortality of 30.3%.[6] The largest international prospective study, Pediatric Acute Respiratory Distress Syndrome Incidence and Epidemiology (PARDIE)[7], found that PARDS affects 3% of PICU patients, and mortality exceeds 30% in those with severe hypoxemia. Gupta et al., estimated that the PALICC criteria showed a higher prevalence of PARDS (9.8%) as compared to the Berlin definition (4.2%).[8] Prasertsan et al observed the prevalence and outcome of PARDS according to the PALICC as 7.4% and the mortality rate as 51.1% in a PICU in Thailand.[9] In India, the incidence of PARDS was relatively higher (11.4%), with an overall mortality of 45.2%, as indicated by Bhart et al in their prospective observational study.[10]

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In Pakistan, there is a considerable lack of research exploring PARDS while some researchers have documented the frequency of PARDS to be as high as 15.3% in PICUs.[11] Although researchers used OSI as the labeling criteria for PARDS, invasive procedures are still in use for the assessment of oxygenation, which do not depict the actual burden of the disease among the local pediatric population. The current study was planned with the objective of estimating the incidence and risk stratification of PARDS in mechanically ventilated (MV) patients at PICU using the PALICC criteria.

METHODS

This prospective observational study was performed at the pediatric intensive care unit (PICU) of the National Institute of Child Health, Karachi, Pakistan, from April 2024 to March 2025, after obtaining approval from the Institutional Ethical Review Board (letter number: IERB-35/2023, dated: 14-12-2023). A sample size of 200 was calculated as per the WHO sample size calculator, taking the expected prevalence of RDS in the PICU as 15.3%[11], setting the confidence level at 95%, and the margin of error at 5%. Children aged between 1 month to < 18 years and admitted to the PICU due to ARDS defined in the PALICC were included. Only those who were mechanically ventilated were included. The exclusion criteria were patients with active perinatal disease or those with preparation/recovery from cardiac intervention. ARDS was labeled on the basis of hypoxemia caused by non-cardiogenic pulmonary edema developed acutely in the context of severe systemic illness. The partial pressure of oxygen (PaO_2) in the arterial blood <80 mm of Hg was considered hypoxemia. A non-probability consecutive sampling technique was followed for sample selection. Informed written consent from parents/caregivers of patients was obtained.

Cases meeting the eligibility criteria went through documentation of their demographics and clinical parameters. The history of the onset of symptoms of the patients was recorded. An X-ray chest was done for each patient and reviewed with a radiologist for the presence of infiltrates. Information regarding ventilator settings and the use of inotrope support was also gathered. Oxygenation index (OI) was calculated for all patients, and risk stratification was done on the basis of OI values, considering the PALICC. Risk stratification followed as mild (4 ≤ OI < 8), moderate (8 ≤ OI < 16), and severe (OI ≥ 16), calculated using mean airway pressure (MAP) X fraction of inspired oxygen (FiO_2) / PaO_2 X 100.[12] All the patients were followed for the disease outcome. A specifically predesigned proforma was utilized for the collection of relevant data.

Data were analyzed using IBM SPSS Statistics version 26.0. Categorical variables were summarized as frequencies and percentages, while continuous variables were presented as median and interquartile ranges (IQR) after assessing normality with the Shapiro-Wilk test. Comparisons across PARDS severity were performed using the Chi-square test for categorical variables, and the Kruskal-Wallis test for continuous variables, taking $p<0.05$ as significant. Survival analysis was conducted using Kaplan-Meier curves with log-rank (Mantel-Cox) test.

RESULTS

In a total of 200 mechanically ventilated children diagnosed with PARDS, 111 (55.5%) were female. The median (IQR) age was 8.00 (4.00-12.00) years. According to PALICC criteria, PARDS was classified into mild 24 (12.0%), moderate 82 (41.0%), and severe 94 (47.0%) categories. The male-to-female distribution was comparable across PALICC classification of PARDS ($p=0.955$) (Table 1). The median age was statistically similar among children of different PALICC categories ($p=0.797$). Median weight also did not significantly differ ($p=0.752$). Bilateral pulmonary infiltrates were significantly more frequent in moderate and severe PARDS compared to mild cases ($p=0.019$) (Table-I).

Inotropes were used among 84 (42.0%) children during PICU stay. Mortality was reported in 23 (11.5%) cases. The median duration of MV, and PICU stay were 8.00 (5.00-11.00) days, and 16.00 (12.00-23.00) days, respectively. The median duration of MV progressively increased with PARDS severity ($p<0.001$). The requirement for inotropic support was significantly higher in severe PARDS ($p<0.001$). The median PICU stay increased with severity, from 8.00 days (IQR, 7.00–9.75) in mild to 14.00 days (IQR, 12.00–17.25) in moderate,

and 23.00 days (IQR, 15.00–24.25) in severe cases (p<0.001). Mortality was significantly higher in severe PARDS (21.3%) compared to moderate (2.4%) or mild (4.2%) (p<0.001). Table-II is showing comparison of various outcomes according to PARDS as per PALICC classification.

The Kaplan-Meier survival analysis demonstrated a significant difference in cumulative survival across severity groups (log-rank test, p=0.011), with the lowest survival observed among patients with severe PARDS (Figure-1).

DISCUSSION

This study demonstrated that according to PALICC classification, severe PARDS was the most common category (47%), followed by moderate (41%) and mild (12%) cases. Judith et al.[6] reported an approximately balanced distribution among mild (27.3%), moderate (36.4%), and severe (36.4%) PARDS in their prospective study, although the proportion of mild PARDS was comparatively higher than that observed in the present cohort.

FIGURE-1

Survival analysis with respect to pediatric acute respiratory distress syndrome severity

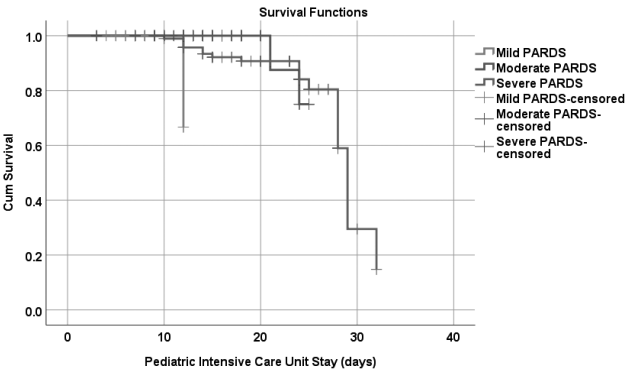

TABLE-I

Characteristics of children according to PARDS classification

Characteristics		Total (%) Mild (n=24)	Severity of PARDS		P-Value
			Moderate (n=82)	Severe (n=94)	
Gender	Male	89 (44.5%)	14 (58.3%)	45 (54.9%)	52 (55.3%)	0.955*
	Female	111 (55.5%)	10 (41.7%)	37 (45.1%)	42 (44.7%)	
Age (years)#		8.00 (4.00-12.00)	8.00 (4.00-12.00)	8.50 (3.75-13.00)	8.00 (4.00-12.00)	0.797^
Weight (kg)#		23.36 (12.00-35.00)	20.50 (9.75-35.75)	23.00 (11.2-35.00)	24.00 (12.00-35.00)	0.752^
Radiological findings	Bilateral	144 (72.0%)	12 (50.0%)	58 (70.7%)	74 (78.7%)	0.019*
	Unilateral	56 (28.0%)	12 (50.0%)	24 (29.3%)	20 (21.3%)	

Kg: kilogram; PARDS: pediatric acute respiratory distress syndrome;
*Chi-square test applied; ^Kruskal-Wallis test applied
#Presented as median and interquartile range

TABLE-II

Comparison of outcomes according to PARDC classification

Outcomes	Total	Severity of PARDS			P- value
		Mild (n=24)	Moderate (n=82)	Severe (n=94)	
Duration of mechanical ventilation (days)#	8.00 (5.00-11.00)	4.00 (2.00-5.00)	7.50 (5.00-9.00)	9.50 (6.00-13.00)	<0.001^
Use of inotropes	84 (42.0%)	4 (16.7%)	24 (29.3%)	56 (59.6%)	<0.001*
Duration of PICU stay (days)#	16.00 (12.00-23.00)	8.00 (7.00-9.75)	14.00 (12.00-17.25)	23.00 (15.00-24.25)	<0.001^
Mortality	23 (11.5%)	1 (4.2%)	2 (2.4%)	20 (21.3%)	<0.001*

PARDS: pediatric acute respiratory distress syndrome
*Chi-square test applied; ^Kruskal-Wallis test applied
#Presented as median and interquartile range

Wong et al.[6], in a multicenter study across Asia, found that 23.9%, 39.9%, and 36.2% of patients had mild, moderate, and severe PARDS, respectively, aligning closely with the current findings where moderate and severe cases predominated. The higher proportion of severe PARDS cases in the present study may be attributed to referral bias, as NICH serves as a tertiary referral center receiving critically ill patients from across the region, many of whom present late in their disease course.

Mortality in the current study was 11.5%, which increased significantly with PARDS severity, reaching 21.3% among severe cases. This graded increase in mortality with disease severity is consistent with the survival curves and outcomes described by Khemani et al.[7], where severe PARDS was associated with a mortality rate of approximately 33%. Ju-Ming et al. reported a 30.3% overall PICU mortality rate among PARDS patients, and a 100-day mortality of 39.7%, with risk increasing progressively from mild to severe PARDS.[2] These data affirm the prognostic validity of the PALICC stratification system, as higher OI thresholds correspond to worsened outcomes.[14,15]

The association between bilateral infiltrates and worse outcomes observed in this study is corroborated by findings from Rudolph et al.[16], who demonstrated significantly increased mortality among patients with bilateral consolidations (26.3% versus 9.3% for unilateral disease, p=0.025). In this study, bilateral infiltrates were present in 72% of cases and were significantly more prevalent in moderate and severe disease (p=0.019). These finding reinforce the importance of incorporating radiological assessment into early risk stratification protocols in suspected PARDS.[17]

This study found that duration of MV, and PICU stay increased significantly with respect to PARDS severity. Judith et al.[13], demonstrated that time to resolution of oxygenation defect progressively lengthened from mild to severe PARDS (p<0.001). The duration of PICU stay emphasizes the substantial resource burden posed by severe PARDS.[18] The findings from Liang et al.[19], highlight the importance of using dynamic OI measurements to refine prognostication. Liang et al.[19], documented that the worst OI within 72 hours after diagnosis better stratified outcomes, with mortality rates closely aligned to severity definitions. Dynamic assessment offers a practical and valuable tool for clinicians in resource-limited settings where advanced biomarkers or imaging modalities may not be readily available.[20]

The single-center nature of the study may limit generalizability. The study design did not allow for longitudinal reassessment of oxygenation indices. The study did not collect detailed comorbidity data, nutritional status, or severity of illness scores such as PRISM III or PELOD-2. The recent PALICC-2 guidelines have emphasized not only refining diagnostic criteria but also addressing the morbidity burden and resource limitations globally.[21]

CONCLUSION

The PALICC stratification system for PARDS effectively categorize MV pediatric patients into distinct severity groups associated with clinically meaningful differences in ventilator requirements, PICU stay, and mortality. Severe PARDS remains a major clinical challenge with significant resource utilization and mortality. Early identification and aggressive management of moderate and severe cases are critical.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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4	**Zaiba Anwar:** Data analysis.
5	**Uzma Siddique:** Data collection.
6	**Ghazala Jamal:** Critical revision, data analysis.

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ORIGINAL ARTICLE

Short-term beneficial effect of Zinc Supplement in preterm neonates having neonatal sepsis.

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ABSTRACT… Objective: To assess the short-term effect of oral zinc supplementation on mortality in preterm neonates with bacterial sepsis. **Study Design:** Randomized Controlled Trial. **Setting:** The Neonatal Unit of Sharif Medical City Hospital, Lahore. **Period:** December 20, 2021 to June 20, 2022. **Methods:** A total of 250 preterm neonates with gestational age between 28–36 weeks and diagnosed with sepsis were enrolled using non-probability consecutive sampling technique. They were randomly distributed into two groups. Group A received zinc supplementation orally (3 mg/kg twice daily), while Group B received distilled water as a placebo. Both groups received standard antibiotic treatment. Neonates were monitored in the NICU until discharge or death, and 7-day mortality was recorded. Chi-square test was applied to associate mortality rates. The p value of ≤ 0.05 was considered statistically significant. **Results:** The mean age of neonates in Group A was 41.19 ± 19.10 hours, while in Group B, it was slightly lower at 39.24 ± 19.63 hours. Group A had a significantly lower 7-day mortality rate of 9(7.2%) compared to Group B at 26(20.8%) (p = 0.002). No deaths occurred in the 6–18 hour age subgroup of Group A, while Group B had 8(6.4%) deaths (p = 0.005). Mortality was significantly lower in Group A among neonates with higher birth weights: 3(2.4%) vs. 12(9.6%), (p = 0.007) and gestational ages of 31–33 weeks: 5(4.0%) vs. 19(15.2%), (p < 0.001). **Conclusion:** Oral zinc supplementation significantly decreased short-term mortality in preterm neonates with sepsis. Zinc may serve as an effective adjunct therapy in managing neonatal sepsis.

Key words: Mortality, Neonatal Sepsis, Preterm Infants, Zinc Supplements.

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INTRODUCTION

Sepsis remains one of the major contributors to illness and death in newborns and young infants.[1] In 2017, nearly half of all sepsis cases worldwide occurred in children, with approximately 20 million reported cases and 2.9 million expiries in those below the age of five years.[2] According to the Global Burden of Disease (GBD) Study 2016/2017, there are a projected 1.3 million new cases of neonatal sepsis annually (95% CI: 0.8 to 2.3 million), leading to around 203,000 deaths (95% CI: 178,700 to 267,100) directly attributed to sepsis.[3,4] The impact is particularly severe in low- and middle-income countries (LMICs), where infection related illnesses are more common and healthcare services with sufficient equipment and workers are not readily available.[5,6]

Neonatal sepsis is typically categorized into early-onset sepsis (EOS) and late-onset sepsis, depending on the beginning of symptoms. EOS is primarily transmitted vertically from the mother during childbirth, whereas late-onset sepsis is often developed from the hospital environment or the community. Key risk factors for neonatal sepsis are prematurity and low birth weight.[7] Specific risk factors associated with EOS include maternal infections during labor, multiple pregnancies, prolonged labor, premature rupture of membranes, and meconium aspiration syndrome.[8] Research indicates that prompt introduction of antibiotic treatment in neonates with expected sepsis significantly lowers both morbidity and mortality rates.[9]

Zinc, recognized by the World Health Organization as a cost-effective public health intervention through supplementation and fortification, possess a vital role in supporting immune system, growth, and reproductive health.[10] It is particularly vital for immune system regulation, cognitive development, and motor functions.

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Zinc contributes to the functioning of T-cells and the adaptive immune response while also exhibiting antioxidant and anti-inflammatory properties.[11]

Oral zinc supplementation during neonatal sepsis has been demonstrated to reduce both the severity and duration of the illness. Preterm infants are particularly vulnerable due to their significantly lower zinc reserves compared to term neonates, as approximately 60% of fetal zinc accumulation occurs in the third trimester. Furthermore, preterm babies have a limited capacity to absorb and preserve zinc necessary for growth. Therefore, their zinc intake must be increased by two to three times the standard maintenance requirements.[12]

Extensive evidence supports that additional zinc supplementation helps to lower the morbidity and mortality rates and promotes better growth in both preterm and term neonates.[12] Timely diagnosis and treatment of neonatal sepsis are crucial for successful clinical outcomes.[7] Given that Pakistan is a region with widespread zinc deficiency, enteral zinc supplementation is widely recommended for neonatal care. Few studies reported no significant difference in mean hospital stay between zinc (142.85 ± 69.41 hours) and placebo groups (147.99 ± 73.13 hours), with mortality rates of 9.77% and 7.8%, respectively ($p > 0.05$).[13,14] However, another study found a statistically significant decrease in hospital stay ($p < 0.01$).[15]

To ensure sufficient zinc levels in newborns, maternal nutrition must be prioritized. Poor maternal zinc status has been related with adverse pregnancy consequences like low birth weight, intrauterine growth restriction, and preterm birth.[16] Reduced maternal plasma zinc levels may impair placental zinc transport, thereby limiting fetal zinc availability. In response, the United Nations Children's Fund (UNICEF) commends that all pregnant women in developing nations must receive multiple micronutrient supplements, containing zinc.[17]
Elevated serum zinc concentrations have been linked to enhanced immune function and superior clinical results in neonatal sepsis.[18] However, findings from randomized controlled trials and literature review have yielded inconsistent results regarding the impact of zinc on sepsis-related consequences in neonates.[19-21] Notably, a review by Tang et al. included overlapping data from multiple studies conducted at a single site[22], which may have compromised the accuracy of the pooled effect estimates.[23]

Neonatal sepsis remains a main reason of morbidity and mortality, particularly in preterm infants due to their underdeveloped immune systems. Despite standard antibiotic therapy, outcomes often remain suboptimal. Zinc, an important trace element, shows a critical role in immune function, inflammation control, and tissue repair. Previous research has suggested that zinc supplementation may diminish the severity and duration of infections in pediatric populations. However, limited data exist regarding its role specifically in preterm neonates with bacterial sepsis. Therefore, the study aims to compare the outcome of oral zinc supplementation versus placebo in preterm infants receiving standard treatment for bacterial sepsis to evaluate its potential as an adjunct therapy for improving short-term survival and clinical outcomes.

METHODS

This randomized controlled trial was performed at the Neonatal Unit, Department of Pediatrics, Sharif Medical City Hospital, Lahore, over a six-month period from December 20, 2021 to June 20, 2022, using a non-probability, consecutive sampling technique. The ethical approval (SMDC/SMRC/218-21) was taken from the ethical review committee of the concerned hospital. The sample size was estimated using 80% power of the test, 5% level of significance, and previously reported mortality rates of 17.6% in neonatal sepsis.[24] A total of 250 preterm neonates with a gestational age between 28 and 36 weeks diagnosed with sepsis were included, with 125 neonates randomly distributed to each of the two study groups: Group A (zinc supplementation) and Group B (placebo). On the other hand, neonates already receiving treatment for sepsis, with an Apgar score less than 6 at 5 minutes, or those with congenital anomalies were excluded from the study.

After obtaining ethical approval and informed parental consent, demographic and clinical data for instance gender, age, gestational age, and birth

weight were recorded. Neonates were randomly assigned to either group using the lottery method to ensure allocation concealment. Group A received oral zinc supplementation at a dosage of 3 mg/kg twice daily, while Group B received distilled water as a placebo. Both groups continued to receive standard antibiotic treatment for neonatal sepsis as per hospital protocol. All neonates were managed in the neonatal intensive care unit and monitored daily. Criteria for discharge included clinical stability, normalization of vital signs, adequate feeding, and improvement in laboratory parameters for example white blood cell count, platelet count, blood culture results, and C-reactive protein levels.

Data was analyzed using SPSS version 25.0. Quantitative variables like age, birth weight, and gestational age were documented as means and standard deviations, whereas categorical variables such as gender and mortality were expressed as frequencies and percentages. The chi-square test was used to compare mortality rates between the two groups. Stratification was done for potential confounding factors, including age, birth weight, gestational age, and mortality, which was compared within each stratum applying the chi-square test. A p-value of ≤ 0.05 was considered as statistically significant.

RESULTS

The study included 250 preterm neonates diagnosed with neonatal sepsis, equally divided into two groups: Group A (zinc supplement group, n=125) and Group B (placebo group, n=125). The mean age of neonates in Group A was 41.19 ± 19.10 hours, while in Group B, it was slightly lower at 39.24 ± 19.63 hours. In terms of gender distribution, Group A comprised 65(52.0%) males and 60(48.0%) females, whereas Group B included 68(54.4%) males and 57(45.6%) females, showing a relatively balanced gender distribution in both groups. The mean gestational age of neonates receiving zinc supplementation (Group A) was 33.16 ± 3.38 weeks, which was comparable to the placebo group (Group B) with a gestational age of 33.63 ± 2.62 weeks. The average birth weight of neonates in Group A was 2.46 ± 0.73 kg, slightly higher than that of Group B, which was 2.39 ± 0.50 kg, as presented in Table-I.

The short-term (within 7 days) mortality in the study groups revealed a significantly lower mortality rate in the zinc-supplemented group (Group A), with 9(7.2%) neonates dying, compared to 26(20.8%) neonates in the placebo group (Group B) (p = 0.002). When mortality was further stratified by age groups, no deaths were observed in the 6–18 hour age subgroup of Group A, whereas Group B had 8(6.4%) deaths, showing a statistically significant association (p = 0.005). In the 19–36 hour age group, mortality was low in both groups (2(1.6%) deaths in Group A and 4(3.2%) in Group B), with an insignificant association (p = 0.413). Similarly, in the 37–55 hour subgroup, 6(4.8%) neonates in Group A and 8(6.4%) in Group B died, also without statistical significance (p = 0.480). However, in neonates older than 55 hours, mortality was notably lower in the zinc group 1(0.8%) in comparison to the placebo group 6(4.8%), with the statistically significant difference (p = 0.032), as presented in Table-II.

Stratification of mortality by birth weight and gestational age revealed that notable differences were observed among the zinc-supplemented group (Group A) and the placebo group (Group B). Among neonates with a birth weight of 1.3–2.30 kg, mortality was lower in Group A 6(4.8%) in comparison to Group B 14(11.2%), with the statistically insignificant association (p = 0.094). However, in the higher birth weight category of 2.31–3.50 kg, mortality was significantly lower in the zinc group 3(2.4%) contrasted with the placebo group 12(9.6%), with a statistically significant difference (p = 0.007). Stratification by gestational age revealed that in the 26–30 weeks subgroup, there was no mortality in Group A compared to one death 1(0.8%) in Group B (p = 0.202). In contrast, among neonates with a gestational age of 31–33 weeks, a significantly lower mortality rate was observed in the zinc group 5(4.0%) than the placebo group 19(15.2%) (p < 0.001). In the 34–36 week subgroup, mortality rates were similar between Group A 4(3.2%) and Group B 6(4.8%), showing no significant difference (p = 0.696), as presented in Table-III.

TABLE-I

Age of neonates in the two group (n=250)

Variables		Group-A (Zinc) (n=125)	Group-B (Placebo) (n=125)
Age of neonates in hours		41.19 ± 19.10	39.24 ± 19.63
Gender	Male	65(52.0%)	68(54.4%)
	Female	60(48.0%)	57(45.6%)
Gestational Age (weeks)		33.16 ± 3.38	33.63 ± 2.62
Birth Weight of neonates (kg)		2.46 ± 0.73	2.39 ± 0.50

TABLE-II

Mortality in study groups stratified for age of neonates.

Variables			Group-A (Zinc) (n=125)	Group-B (Placebo) (n=125)	P-Value
Mortality (within 7 days)		Yes	9 (7.2%)	26 (20.8%)	0.002
		No	116 (92.8%)	99 (79.2%)	
Age of neonates (hours)	6-18	Yes	0 (0.0%)	8 (6.4%)	0.005
		No	22 (17.6%)	19 (15.2%)	
	19-36	Yes	2 (1.6%)	4 (3.2%)	0.413
		No	25 (20.0%)	24 (19.2%)	
	37-55	Yes	6 (4.8%)	8 (6.4%)	0.480
		No	32 (25.6%)	28 (22.4%)	
	>55	Yes	1 (0.8%)	6 (4.8%)	0.032
		No	37 (29.6%)	28 (22.4%)	

DISCUSSION

Sepsis is recognized as a major contributor to illness and death among newborns.[25] A deficiency in zinc may result in impaired immune function, developmental delays in cognition and movement, more vulnerable to infections, and stunted growth.[26] Low levels of zinc have been detected in the bloodstream of low birth weight (LBW) infants. Preterm infants, in particular, have relatively higher nutritional needs for zinc, partly because around 55% of a fetus's zinc accumulation occurs in the third trimester of pregnancy.[27]

The present study assessed the effect of zinc supplementation on short-term mortality among preterm neonates diagnosed with sepsis. The zinc-supplemented group (Group A) showed a significantly lower mortality rate of 9(7.2%) compared to the placebo group 26(20.8%), with a (p= 0.002), highlighting a strong association between zinc administration and improved survival. Additionally, stratification by birth weight revealed that neonates in the 2.31–3.50 kg range experienced significantly reduced mortality with zinc supplementation 3(2.4%) vs. 12(9.6%), (p = 0.007). A comparable trend was seen in neonates with a gestational age between 31–33 weeks, where the zinc group had a fatality rate of 5(4.0%) versus 19(15.2%) in the placebo group (p < 0.001). These results are consistent with the meta-analysis by Tang et al., which included four RCTs with 986 neonates and demonstrated that zinc supplementation significantly declined mortality (RR = 0.48; 95% CI = 0.25–0.94; p = 0.03) and

TABLE-III

Mortality in study groups stratified for birth weight and gestational age of neonates.

Mortality Within 7 Days			Group-A (Zinc) (n=125)	Group-B (Placebo) (n=125)	P-Value
Birth weight of neonates (kg)	1.3-2.30	Yes	6(4.8%)	14(11.2%)	0.094
		No	49(39.2%)	48(38.4%)	
	2.31-3.50	Yes	3(2.4%)	12(9.6%)	0.007
		No	67(53.6%)	51(40.8%)	
Gestational age (weeks)	26-30	Yes	0(0.0%)	1(0.8%)	0.202
		No	14(11.2%)	8(6.4%)	
	31-33	Yes	5(4.0%)	19(15.2%)	<0.001
		No	38(30.4%)	17(13.6%)	
	34-36	Yes	4(3.2%)	6(4.8%)	0.696
		No	64(51.2%)	74(59.2%)	

increased serum zinc levels. While Tang's review found no significant influence on hospitalization or the number of deceased patients as a separate outcome.[22]

A study by Irfan et al. also stated that zinc supplementation in infants under 4 months led to a significant decline in treatment failure (RR = 0.61) and mortality rate, specifically at a dose of 3 mg/kg two times a day, similar to the dosage used in the present study.[28] This supports the notion that both dosage and patient characteristics such as preterm status are key determinants of treatment success.

The results of the present study, which demonstrated a significant decrease in short-term mortality among preterm neonates with sepsis receiving zinc supplementation 9(7.2%) in the zinc group vs. 26(20.8%) in the placebo group; (p = 0.002), are in strong agreement with several previous studies highlighting zinc's protective role in early-onset neonatal sepsis. A randomized controlled trial by Banupriya et al. indicated that neonates' not receiving zinc had a significantly higher mortality rate (13%) as compared to those who received zinc (5%) (p = 0.04), further reinforcing zinc's beneficial role.[29] Likewise, in another trial, the same group observed that zinc supplementation significantly reduced inflammatory markers like calprotectin and IL-6, although mortality differences did not reach statistical significance.[20] Additionally, prior research has shown that zinc supplementation is especially valuable in preterm and exceedingly low birth weight neonates[30], which is consistent with the present study's subgroup analysis indicating significantly lower mortality in neonates with birth weights of 2.31–3.50 kg and gestational ages of 31–33 weeks.

In the present study, zinc supplementation was found to significantly reduce short-term (within 7 days) mortality, particularly in subgroups based on age (>55 hours), birth weight (2.31–3.50 kg), and gestational age (31–33 weeks). The overall mortality was notably lesser in the zinc group 9(7.2%) as compared to the placebo group 26(20.8%) (p = 0.002). These findings are partially consistent with the results presented by Newton B et al., who conducted a similar RCT administering 3 mg/kg of zinc sulfate twice daily for 10 days in septic neonates. Whereas Newton's study observed a statistically insignificant reduction in mortality (4.5% in the zinc group as compared to 13.6% in controls; p = 0.27), they did find that zinc supplementation led to improved neurological outcomes at one month of age (p = 0.02).[19] Similarly, a study by Heba et al. concluded that zinc significantly reduced both morbidity and mortality in neonates, further supporting the importance of zinc in enhancing immunity and survival.[31]

Zinc is an essential micronutrient that offers a cost-effective and safe option when provided through supplementation or food fortification, making it a valuable addition to current infant and young child health and nourishment initiatives.[10] Moreover, preterm infants are particularly prone to developing zinc insufficiency. The findings of the present study demonstrated a statistically significant decrease in short-term mortality among preterm neonates with sepsis receiving zinc supplementation, align with earlier studies reporting the preventive efficacy of zinc in this populace.[32-34] In contrast, a research by Bhatnagar et al. observed a protective effect of zinc supplementation, noting a reduced need for ICU admission or escalation of antibiotic therapy. Although their study showed a comparable decline in all-cause mortality, it did not report statistically significant mortality reduction, possibly due to differences in sample size or study design.[35] Similarly, another additional study on preventive zinc supplementation in preterm neonates also reported enhanced mortality outcomes, supporting the biological rationale that preterm infants, who miss out on substantial transplacental zinc transfer during the third trimester and have immature gastrointestinal absorption, stand to benefit most from zinc supplementation.[36] Furthermore, another trial concluded that zinc supplementation did not significantly alter the incidence of bacterial sepsis when used preventively.[13]

This study was limited by its short follow-up period of 7 days, which did not allow assessment of long-term outcomes or potential adverse effects of zinc supplementation. Additionally, the sample size, though adequate for short-term mortality analysis, may not have been sufficient to detect differences across all subgroups. Future large-scale, multicenter

trials with extended follow-up are recommended to validate these findings, assess long-lasting benefits, and establish standardized guidelines for zinc use in preterm neonates with sepsis.

CONCLUSION

The study concluded that zinc supplementation in preterm neonates with neonatal sepsis significantly decreased 7-day mortality as compared to placebo. This useful effect was more pronounced in neonates with birth weights between 2.31–3.50 kg and those with a gestational age of 31–33 weeks. Although differences in mortality were not statistically significant in all subgroups, the overall trend supports the prospective role of zinc as an adjunctive therapy to improve short-term survival outcomes in preterm neonates suffering from sepsis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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7	**Waseem Asif:** Critical review.

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ORIGINAL ARTICLE

Medical thoracoscopy: An effective tool for diagnosis of pleural tuberculosis.

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ABSTRACT… Objective: To assess the diagnostic yield, safety, and outcomes of medical thoracoscopy in patients with suspected pleural tuberculosis. **Study Design:** Cross sectional study. **Setting:** Department of Pulmonology, Shaikh Zayed FPGMI, Lahore. **Period:** January 2015 and December 2024. **Methods:** This is a retrospective study. A total of 119 patients who underwent medical thoracoscopy for suspected pleural tuberculosis between January 2015 and December 2024 were included. Data were analyzed using descriptive statistics. **Results:** Tuberculosis was confirmed in the majority of cases, demonstrating a high diagnostic yield. Pleural adhesions were seen in over half of the patients; most were managed successfully during thoracoscopy, while a few required additional interventions. No major complications occurred. Minor events included post-procedural pain (35.3%), surgical emphysema (4.2%), air leak (4.2%), and wound site infection (0.8%). Three patients required surgical referral. **Conclusion:** Medical thoracoscopy is a safe, reliable, and effective procedure for diagnosing pleural tuberculosis, with minimal complications and added therapeutic benefit in managing pleural adhesions.

Key words: Medical Thoracoscopy, Pleural Tuberculosis.

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INTRODUCTION

Tuberculosis (TB) remains a serious worldwide health issue, and pleural TB is among the most common extrapulmonary manifestations. Its diagnosis is frequently difficult due to nonspecific presenting features and the paucibacillary nature of the pleural fluid.[1,2] Traditional techniques such as pleural fluid examination, cytology, and closed pleural biopsy have inconstant yields. Closed pleural biopsy can make a diagnosis in 60–80% of diagnoses, but it is operator- and sampling-dependent in accuracy.[3]

Medical thoracoscopy, or pleuroscopy, is a minimally invasive technique which facilitates direct visualization of the pleural space and biopsies of specific areas. It has been found to have a substantial increase in diagnostic yield, with yields greater than 90% in pleural TB.[4,5] It compares favorably to blind pleural biopsy, as it provides larger and more representative tissue samples and offers a safer profile.[6]

Apart from its diagnostic application, thoracoscopy also facilitates therapeutic procedures like adhesiolysis and pleurodesis, specifically beneficial in complicated pleural effusions.[7] Due to its superior diagnostic yield, safety, and therapeutic value, medical thoracoscopy has become widely accepted as a useful instrument in the diagnosis and treatment of pleural tuberculosis, particularly in resource-limited countries with high burden.[1,6]

In spite of its established benefits, medical thoracoscopy is currently underutilized in most resource-constrained high TB burden nations. Local clinical practice assessment of its efficacy can inform on its contribution to early and accurate pleural TB diagnosis.

METHODS

This cross-sectional study was conducted in the Department of Pulmonology, Shaikh Zayed Hospital, FPGMI, Lahore. Retrospective data from 119 patients who underwent medical thoracoscopy for suspected pleural tuberculosis between January 2015 and December 2024 were included.

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Ethical approval was obtained from the Institutional Review and Research Advisory Board of Shaikh Zayed FPGMI, Lahore (Ref: 02-TERC/NHRC-SZH/INT-SC/868, dated: 12-09-2025). Data were entered and analyzed using SPSS version 20. Descriptive statistics, including frequencies and percentages, were applied, and the results were presented in the form of tables and pie chart.

RESULTS

During the study period, 119 patients underwent medical thoracoscopy with suspicion of pleural tuberculosis. A definitive diagnosis of pleural tuberculosis was achieved in 114 cases (95.8%), whereas 5 patients (4.2%) remained undiagnosed.

Among the study population, 81 patients (68.1%) were male and 38 (31.9%) were female, yielding a male-to-female ratio of roughly 2:1. With regard to age distribution, 31 patients (26.0%) were younger than 25 years, 31 (26.0%) were between 26–50 years, and 57 (47.9%) were older than 50 years.

The right pleural space was affected in 70 patients (58.8%), the left side in 48 patients (40.3%), while bilateral disease was seen in only 1 case (0.8%).

Chest radiographs showed varied presentations: opaque hemithorax in 11 patients (9.2%), large pleural effusion in 24 (20.2%), moderate effusion in 62 (52.1%), mild effusion in 9 (7.6%), hydropneumothorax in 8 (6.7%), and pneumothorax in 5 (4.2%) cases.

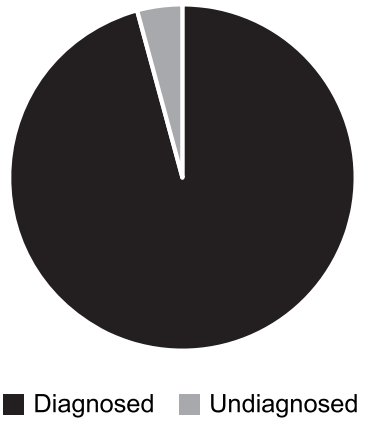
Thoracoscopic examination most frequently revealed gritty and inflamed pleura in 64 patients (53.8%). Pleural nodules were detected in 30 cases (25.2%), while a combination of nodules with inflamed pleura was observed in 25 cases (21.0%). Pleural adhesions were identified in 68 patients (57.1%).

Of the 68 patients with adhesions, 54 (79.4%) underwent successful adhesiolysis during thoracoscopy. The remaining 14 patients (20.6%) required additional interventions post-procedure, such as external suction and intrapleural streptokinase. Despite these measures, 3 patients (4.4% of those with adhesions) eventually required surgical referral.

No significant complications were encountered in the study population. The most common minor event was post-procedural pain, noted in 42 patients (35.3%). Surgical emphysema and air leak were each seen in 5 patients (4.2%), while wound site infection occurred in one patient (0.8%).

FIGURE-1

Diagnostic yield of Medical thoracoscopy



DISCUSSION

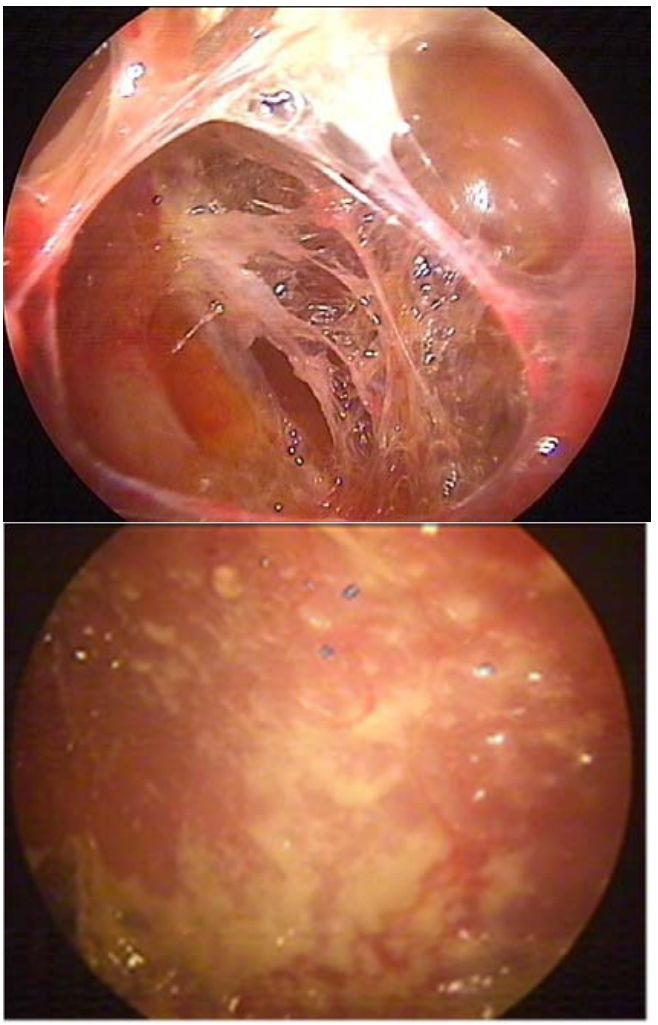
In the present study, medical thoracoscopy established a diagnosis in 114 out of 119 patients with suspected pleural tuberculosis, yielding a diagnostic accuracy of 95.8%. This success rate is comparable to earlier reports, where diagnostic yields ranged from 85% to 95% (1,4,8,9). Loddenkemper and colleagues emphasized that thoracoscopy remains the most sensitive minimally invasive method for evaluating pleural tuberculosis[1], and similar results have been documented in studies from India, China, and the Middle East.[9,10]

Most of our patients were male (68%), with a male-to-female ratio of approximately 2:1. This finding is consistent with regional data, where pleural TB is more frequently observed in men.[10,11] Nearly half of our patients were older than 50 years, which differs slightly from some series where younger adults predominate.[12] This variation may reflect differences in local epidemiology, delayed health-seeking behavior, or the presence of comorbidities in older patients. Right-sided effusion was more

common than left, a pattern also noted in other reports, though laterality is generally not considered diagnostically significant.

FIGURE-2

Thoracoscopic image, pleural adhesions Fig: 3 Thoracoscopic image, gritty pleura & parietal pleural nodules



Moderate effusion was the most frequent radiographic presentation (52.1%), followed by large effusion and opaque hemithorax. Less common findings included hydropneumothorax (6.7%) and pneumothorax (4.2%). These patterns are consistent with the study by Dixit et al., who reported that moderate to large effusions represent the majority of pleural TB cases, whereas hydropneumothorax and pneumothorax are uncommon but recognized manifestations.[13]

TABLE-I

General characteristics of study population		
Total number of cases N=119		
Gender Distribution		
Male	81	68.1%
Female	38	31.9%
Age Distribution		
Less than 25 years	31	26.0%
26 to 50 years	31	26.0%
More than 50 years	57	48.0%
Side Involved		
Right	70	58.8%
Left	48	40.3%
Both	01	0.08%
X- Ray Findings		
Opaque Hemithorax	11	9.2%
Large pleural effusion	24	20.2%
Moderate pleural effusion	62	52.1%
Mild pleural effusion	09	7.6%
Hydropneumothorax	08	6.7%
Pneumothorax	05	4.2%
Thoracoscopy Findings		
Pleural Nodules	30	53.8%
Gritty & Inflamed pleura	64	25.2%
Pleural Nodules & Gritty & Inflamed pleura	25	21.0%
Adhesions	68	57.1%

Thoracoscopic evaluation demonstrated gritty inflamed pleura in more than half of the cases, pleural nodules in one-fourth, and a combination of both in another one-fifth of patients. Pleural adhesions were observed in 68 patients (57.1%). These macroscopic features correspond with classical descriptions of tuberculous pleuritis, including diffuse inflammation, nodularity, and fibrous adhesions.[2] Such findings allow targeted biopsies from diseased areas, which explains the high diagnostic yield obtained.

A notable observation from our study was the therapeutic role of thoracoscopy. Of the 68 patients with adhesions, 54 (79.4%) underwent successful adhesiolysis during the procedure. Fourteen required additional interventions such as external suction or intrapleural streptokinase, while only three

ultimately needed surgical management. These results indicate that early thoracoscopy not only facilitates diagnosis but also prevents progression to more invasive surgery. Lee and Colt similarly reported that thoracoscopic adhesiolysis improves drainage and reduces the need for thoracotomy or decortication[7], while studies from TB-endemic regions have emphasized its cost-effectiveness as both a diagnostic and therapeutic tool.[14,15]

The strengths of this study include the relatively large number of patients and comprehensive reporting of demographic, radiological, and thoracoscopic findings. However, being a single-center study without long-term follow-up, its generalizability is limited.

CONCLUSION

Overall, our findings confirm that medical thoracoscopy is a safe, accurate, and versatile procedure in the evaluation of pleural tuberculosis. In addition to providing diagnostic clarity in the vast majority of cases, it allows effective adhesiolysis, thereby reducing the burden of surgical intervention in complicated effusions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

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2	**Talha Mahmud:** critical review.
3	**Muhammad Naeem Akhtar:** Statistical analysis.
4	**Abdul Saeed Khan:** Study Design.

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ORIGINAL ARTICLE

Evaluation of intraocular pressure changes following Nd: YAG laser posterior capsulotomy.

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ABSTRACT… Objective: To evaluate the change in intraocular pressure (IOP) one week after Nd: YAG laser posterior capsulotomy in patients with posterior capsular opacification. **Study Design:** Quasi-experimental study. **Setting:** LRBT Free Eye Hospital, Lahore. **Period:** 5th August 2025 to 5th November 2025. **Methods:** Using purposive sampling, 110 pseudophakic patients aged 40–85 years with visually significant PCO were included. Pre-laser IOP was recorded, Nd: YAG capsulotomy was performed using standard protocols, and post-laser IOP was reassessed one week after the procedure. Data were analyzed with SPSS v23, using chi-square testing with $p < 0.05$. **Results:** The mean age of participants was 63.2 ± 10.1 years. The average IOP increased from 15.12 ± 2.45 mmHg pre-laser to 16.98 ± 3.28 mmHg post-laser, reflecting a mean rise of 1.86 ± 1.52 mmHg (12.31% ± 8.17%). Younger patients (<60 years) showed a significantly higher incidence of IOP elevation greater than 5 mmHg compared to older individuals (38.9% vs. 17.6%; $p = 0.0085$). Male patients also exhibited significantly greater IOP increases compared to females (33.9% vs. 13.7%; $p = 0.023$). **Conclusion:** Nd: YAG laser posterior capsulotomy is associated with a measurable increase in intraocular pressure, with younger age and male gender serving as significant predictors of larger IOP elevation. Routine monitoring of post-laser IOP is recommended, particularly in high-risk groups, to prevent potential optic nerve damage.

Key words: Cataract Surgery, Intraocular Pressure, Nd: YAG Capsulotomy, Ophthalmology Pseudophakia, Posterior Capsular Opacification.

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INTRODUCTION

Following a smooth cataract procedure with intraocular lens (IOL) implantation, posterior capsular opacification (PCO) is a common delayed complication.[1-2] Approximately 20% to 25% of cases have this condition. Third Mechanism: After cataract extraction, lens epithelial cells that have remained inside the capsular bag proliferate, which is what causes it.

Types are: 1. Pearl-type vacuolation 2. PCO of fibrosis type.[3] A somber ring. A capsular bag is created using the contemporary method of cataract extraction, which includes both the entire posterior capsule and a portion of the anterior capsule.[4]

PCO complications include decreased visual acuity, impaired contrast sensitivity, glare disability, and monocular diplopia, all of which call for further treatment.[5] Serious side effects, like endophthalmitis, vitreous loss, and IOL displacement or decentration, can result from surgical capsulotomy. The modern Nd: YAG laser posterior capsulotomy, which is less expensive, non-invasive, safe, and an extremely successful outpatient department procedure, has taken its place.[6]

Complications of Nd:YAG: The effect of Nd: YAG laser posterior capsulotomy on IOP, as well as other ocular parameters such as best-corrected visual acuity (BCVA), anterior chamber depth (AGO), and macular thickness, risk of retinal tear/detachment remains a subject of debate.[5] While some studies suggest an increase in IOP following the procedure[7], others report no significant change or even a decrease in IOP.[8]

Complications of Nd:YAG: The impact of Nd: YAG laser posterior capsulotomy on IOP, other ocular variables, including best-corrected visual acuity (BCVA), anterior chamber depth (AGO), and macular thickness, risk of retinal tear/detachment

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is a controversial issue.[5] Some studies indicate an elevation of IOP after the operation[7], others report no significant change or even a reduction in IOP.

A previous study[9] assessed the alterations in Intraocular Pressure (IOP) following Nd-YAG Laser Posterior Capsulotomy (LPC) of PCO and found out 70% of the patients had an increase in IOP, i.e.,> 5mmHg with respect to baseline. Conversely, similar results were found in 24.44 percent of the cases in another study.[6]

This study was rationale-based on the need to examine the effect of Nd: YAG laser posterior capsulotomy on intraocular pressure (IOP). The already available literature on this topic demonstrates a significant discrepancy in its results and requires thorough investigation to clarify the possible impact of this procedure on IOP. Therefore, it is urgently required to comprehend the implications of Nd: YAG laser posterior capsulotomy on IOP to influence practices and require prescribing IOP-lowering drugs. This proactive concept not only fills the existing gap in the research results but also has a strong clinical implication for our particular group of people. So this study aimed to find the percentage change in IOP after Nd: YAG laser posterior capsulotomy on patients undergoing cataract surgery.

METHODS

The quasi-experimental study was performed in the Layton Rahmatullah Benevolent Trust (LRBT) Free Eye Hospital, Multan Road, Lahore, Pakistan, during a duration 5th August 2025 to 5th November 2025 after the approval from ethical committee (No. 122/Admin/LRBT-2025) Dated: 04-08-2025. The sample was sampled using a non-probability purposive sampling method and a sample size of 110 patients was calculated with a 95% confidence interval, 8% margin of error and an expected percentage of 24.44% increase in intraocular pressure (IOP) one week following Nd: YAG laser posterior capsulotomy of patients who had it in the eyes of an artificial opaque lens (PC-IOL), instead of the natural posterior chamber.[6] The patients had to have reduced vision, not less than two lines on the Snellen chart as a result of PCO, as well as a baseline intraocular pressure of 10-20 mmHg. Clinical exclusion was made of diabetic retinopathy, retinal detachment, corneal disease, inflammatory eye disease, glaucoma, trabeculectomy, or maculopathy. The participants who had a history of complicated cataract removal or long-term corticosteroid intake, which were established according to medical history and records, were also not allowed to participate in the study.

One hundred ten patients who fit the inclusion criteria were recruited in the Outdoor Clinic of the Layton Rahmatullah Benevolent Trust (LRBT) Free Eye and Cancer Hospital, Multan Road, Lahore. All subjects to be subjected to Nd: YAG laser posterior capsulotomy gave informed consent, and socio-demographic data were taken in a structured proforma (name, age, gender, address, contact number). The pre-laser intraocular pressure (IOP) was recorded, and then the intervention proceeded. The process involved the use of 1% tropicamide to dilate the pupil, and topical anesthesia was applied using proparacaine hydrochloride. An Nd: YAG laser (Quantum Switched VISULAS YAG III, Carl Zeiss, Germany) was used with an Abraham capsulotomy lens applied. A 3.0- 4.0 mm hole was made at the posterior capsule, starting with an energy of 1.013 mJ per pulse and modifying the energy depending on the capsule thickness. NSAID eye drops were also recommended three times per day for one week after capsulotomy. One week after the procedure, intraocular pressure was again measured to determine the changes relative to the baseline.

Analysis of data was done using SPSS version 23. The data on quantitative variables, including age, pre- and post-laser IOP, were in the form of mean, standard deviation, whereas the data of qualitative variables, including gender and change in IOP percentage, were in the form of frequencies and percentages. The data were stratified by age and gender to evaluate the effect modification, and then a chi-square test was performed. A p-value of below 0.05 was deemed to be statistically significant.

RESULTS

The study included 110 participants with a mean age of 63.2 ± 10.1 years. The average pre-laser intraocular pressure (IOP) was 15.12 ± 2.45 mmHg, which increased to 16.98 ± 3.28 mmHg one week

after the Nd: YAG laser posterior capsulotomy, reflecting a mean rise of 1.86 ± 1.52 mmHg and an overall percentage increase of 12.31% ± 8.17%. Among the participants, 53.6% were male and 46.4% were female. When stratified by age, a significantly higher proportion of younger patients (<60 years) experienced an IOP rise greater than 5 mmHg compared to older patients (38.9% vs. 17.6%, p = 0.0085). Similarly, gender-based analysis showed that males demonstrated a significantly greater tendency toward higher IOP elevation, with 33.9% experiencing an increase of more than 5 mmHg compared to only 13.7% of females (p = 0.023). Overall, these findings indicate that Nd: YAG capsulotomy is associated with a measurable rise in IOP, with younger age and male gender emerging as significant predictors of a larger post-procedural increase.

TABLE-I

Summary of data

Variable	Value
Age (years)	63.2 ± 10.1
Pre-laser IOP (mmHg)	15.12 ± 2.45
Post-laser IOP (mmHg)	16.98 ± 3.28
Difference in IOP (mmHg)	1.86 ± 1.52
% Change in IOP	12.31% ± 8.17%

TABLE-II

Frequency distribution of qualitative variables

Variable	n (%)
Gender	
Male	59 (53.6%)
Female	51 (46.4%)

DISCUSSION

The current study shows that in pseudophakic patients with posterior capsular opacification (PCO), intraocular pressure (IOP) increased statistically significantly one week following Nd: YAG laser posterior capsulotomy. Although the extent and duration of this rise vary throughout the literature, this finding is consistent with a number of earlier studies that documented a brief increase in intraocular pressure after the procedure.[6-9]

Multiple studies have documented a significant, though often transient, rise in IOP after Nd: YAG capsulotomy. Mehmood et al. observed a mean IOP increase from 15.40 ± 2.71 mmHg pre-procedure to 19.04 ± 3.50 mmHg post-procedure, with 24.44% of patients experiencing a notable IOP elevation.[6] Similarly, Shams et al. reported a mean IOP spike at two hours post-laser, which generally returned to baseline by one week.[10,11] Varghese et al. also found that while IOP increased immediately after the procedure, it typically normalized within a week.[12] These results are consistent with the current study's observation of a mean IOP rise of 1.86 ± 1.52 mmHg (12.31% ± 8.17%) at one week.

However, some studies have reported minimal or no significant IOP changes post-capsulotomy, particularly when lower laser energies are used or when prophylactic IOP-lowering medications are administered.[13-15] Ansari et al. found that IOP increases were more pronounced with higher energy levels, but generally returned to baseline within a week, suggesting that energy settings and patient selection are important factors.[14,15]

TABLE-III

Chi-square test applied; p < 0.05 considered significant.

IOP Change Category	Age <60 Years (n=36)	Age ≥60 Years (n=74)	P-Value (Age)	Male (n=59)	Female (n=51)	P-Value (Gender)
>5 mmHg increase	14 (38.9%)	13 (17.6%)		20 (33.9%)	7 (13.7%)	
3–5 mmHg increase	15 (41.7%)	23 (31.1%)	0.0085	22 (37.3%)	16 (31.4%)	0.023
<3 mmHg increase	6 (16.7%)	27 (36.5%)		13 (22.0%)	20 (39.2%)	
No change/decrease	1 (2.8%)	11 (14.9%)		4 (6.8%)	8 (15.7%)	
Total	36 (100%)	74 (100%)		59 (100%)	51 (100%)	

The current study identified younger age and male gender as significant predictors of greater IOP elevation post-capsulotomy. While most prior research has focused on the role of pre-existing ocular comorbidities (e.g., glaucoma, diabetes), the influence of demographic factors such as age and gender has been less frequently explored. The observed higher risk in younger and male patients may reflect differences in ocular anatomy, inflammatory response, or trabecular meshwork function, but further research is needed to clarify these mechanisms.[16-19]

Given that a subset of patients—particularly younger and male individuals—are at higher risk for significant IOP elevation, routine post-procedure IOP monitoring is warranted. This is especially important for patients with additional risk factors for glaucoma or optic nerve damage. The findings also support the use of the lowest effective laser energy and consideration of prophylactic IOP-lowering medications in high-risk cases.[8,17-20]

This study's quasi-experimental design and single-center setting may limit generalizability. The follow-up period was limited to one week; longer-term IOP trends and late complications were not assessed. Additionally, the exclusion of patients with pre-existing glaucoma or other ocular pathologies may underestimate the risk in the general population.

Further multicenter, randomized studies with longer follow-up are needed to better define the risk profile for IOP elevation post-Nd: YAG capsulotomy and to establish optimal monitoring and prophylactic strategies, particularly in high-risk subgroups.

CONCLUSION

The present study demonstrates that Nd: YAG laser posterior capsulotomy leads to a statistically significant rise in intraocular pressure one week post-procedure in pseudophakic patients with posterior capsular opacification. The mean IOP increased by 1.86 ± 1.52 mmHg, corresponding to a 12.31% ± 8.17% rise from baseline. Younger patients (<60 years) and male patients were significantly more likely to experience a clinically relevant IOP elevation (>5 mmHg). These findings indicate that while Nd: YAG capsulotomy is generally safe, careful post-procedure monitoring of IOP is warranted, particularly in younger and male patients, to prevent potential complications such as optic nerve damage.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	**Ali Hashim Zubair:** Data entry, critical revision.
3	**Momina Malik:** Data collection.
4	**Amtul Mussawar Sami:** Proof reading.
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ORIGINAL ARTICLE

Evaluation of hearing outcomes in ossicular chain reconstruction: A comparison between total and partial ossicular replacement prostheses.

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ABSTRACT… Objective: To evaluate and compare postoperative hearing outcomes in patients who have undergone ossicular chain reconstruction using partial and total ossicular replacement prostheses. **Study Design:** Prospective Non-randomized Clinical study. **Setting:** Department of Otorhinolaryngology, Shifa International Hospital, Islamabad. **Period:** April 2024 to April 2025. **Methods:** Patients undergoing ossiculoplasty were enrolled consecutively and categorized into two groups based on prosthesis used: total ossicular replacement prosthesis (TORP) and partial ossicular replacement prosthesis (PORP). The selection of prosthesis was determined intraoperatively based on extent of ossicular chain damage. All patients were followed post-operatively. Pre-operative and post-operative hearing thresholds were assessed using pure tone audiometry. **Results:** The TORP group had a higher preoperative air-bone gap (ABG) at 31.77 ± 10.05 dB, compared to the PORP group at 26.31 ± 10.67 dB. After surgery, ABG improved in both groups, reaching 17.54 ± 10.83 dB in the TORP group and 19.69 ± 10.34 dB in the PORP group. Both results met the criteria for successful ossiculoplasty. The analysis within the TORP group showed significant hearing improvement, with a p-value of less than 0.01. This group had a mean ABG gain of 14.23 dB and a large effect size. In contrast, the PORP group showed a moderate improvement of 6.62 dB, with a p-value of 0.05. However, the differences between the two groups were not statistically significant, with a p-value of 0.185 and a Hedges' g effect size of -0.519 favoring TORP. **Conclusion:** Both TORP and PORP effectively treat conductive hearing loss. TORP may provide more benefit for patients with severe preoperative hearing loss or significant ossicular damage. Choosing a prosthesis should depend on what is found during the operation instead of past practices.

Kew words: Chronic Suppurative Otitis Media (CSOM), Conductive Hearing Loss, Ossiculoplasty, Partial Ossicular Replacement Prosthesis (PORP), Total Ossicular Replacement Prosthesis (TORP).

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INTRODUCTION

Ossicular chain disruption results in conductive hearing loss, which may be secondary to a number of aetiologies, including chronic suppurative otitis media (CSOM), cholesteatoma, malignancies, trauma, and congenital diseases (Deklerck et. al, 2014).[1] For those patients where the incus is completely absent, synthetic ossicular prostheses can be useful. There are two main options – total ossicular replacement prosthesis (TORP) and partial ossicular replacement prosthesis (PORP), both of which are commonly used in the conditions mentioned above (Vassbotn et. al, 2007).[2] The choice of which of the two surgeries to perform is generally down to whether the stapes is intact – in which case a PORP is more suitable – or if there is only a footplate, so that a TORP is a better option (Schmerber et. al, 2006).[3] However, the option of TORP with intact stapes suprastructure has been shown to be an effective alternative with good hearing results (Baker et. al, 2015).[4]

As regards the effectiveness of both types of surgeries, results have varied greatly and have often been conflicting. Better results of TORP have been reported in some studies (Murugasu et. al, 2005; Vincent et. al, 2011)[5,6] while PORP has been more effective in others (Brackmann, 1993; Yu et. al, 2013).[7,8] PORP has also been reported to be more stable in long term follow-up (Yu et. al, 2013).[8] There have even been studies where no significant difference was found in efficacy (Faramarzi et. al, 2023).[9] It has also been seen that staged ossicular reconstruction yields the best results as opposed to unstaged (Kim et. al, 2006; Shelton & Sheehy, 1990).[10,11]

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The purpose of this research is to compare the effectiveness of PORP and TORP in the Pakistani population, which has not been explored in detail before. The global literature on the subject is obviously quite controversial, and we aim to add our latest findings to shed more light on the matter. Our objective was to evaluate improvement in conductive hearing levels in an equal number of patients who had undergone either TORP or PORP.

METHODS

This non-randomised clinical trial was conducted at Department of Otorhinolaryngology, Shifa International Hospital, Islamabad from April 2024 to April 2025 after approval from the ethical committee (IRB. No. 141-24). Patients who underwent ossicular chain reconstruction at our centre were enrolled in the prospective database. All patients with chronic suppurative otitis media (CSOM), regardless of the presence of cholesteatoma or history of previous ear surgery, were included in our study. Demographic information and baseline clinical characteristics including patient sex, laterality, stapes status, malleus status, indication of surgery, staged vs unstaged, revision ear surgery, extrusion of prosthesis and surgical technique were recorded.

The pre-operative and post-operative pure tone audiometric data were recorded. Guidelines issued by American Academy of otolaryngology - Head and Neck Cancer Surgery (AAO-HNS)[12] were followed. Pre-operative and post-operative air conduction threshold (AC) and bone conduction threshold (BC) were recorded as the average of four-tone pure-tone at 0.5, 1, 2 and 3 kHz. Pre-operative and post-operative air bone gap (ABG) was reported as air conduction (AC) threshold minus bone conduction threshold (BC). Closure of the air-bone gap (Δ ABG) was calculated as pre-operative ABG minus post-operative ABG.

The main outcome of interest was air bone gap and change in air bone gap. AAO-HNS recommend documenting mean and standard deviation of post operative air-bone gap and number of decibels of change in air bone gap (Δ ABG). The number of patients achieving post-operative air bone gap < 20 dB was also recorded.

Surgical approaches whether trans-canal or combined approach tympanoplasty were included. After disease clearance in CSOM usually for hearing reconstruction a TORP is used when supra-structure is absent and a PORP is used when supra-structure is present. All of our patients had a footplate present and mobile confirmed pre-operatively. In both TORP and PORP the length of the prosthesis is adjusted so it just touches the tympanic membrane. Cartilage augmented tympanoplasty is then done with a piece of cartilage placed in between the head of titanium prosthesis and tympanic membrane. Gel foam is placed within the middle ear cleft and over the tympanic membrane to stabilize the prosthesis, graft and flap.

Statistical analysis using IBM SPSS 23.0 (IBM Corporation, Armonk, NY, U.S.A). The categorical variables were summed together using percentages and frequency. The range and mean +/- standard deviation were used to describe continuous variables as needed. The data was parametric, and the Shapiro-Wilk test was used to evaluate the normality of all continuous variables. The t-test was used for group comparison. Paired sample t-test when comparing pre-operative and post-operative air bone gap within one group and independent sample t-test when comparing two groups. A p-value of less than 0.05 was deemed significant for statistical analyses. This study was authorized by Shifa International Hospital's Institutional Review Board.

RESULTS

A total of 36 ossiculoplasties were done by the senior author. Out of which 26 fulfilled the inclusion criteria, came for routine follow ups, and had adequate pre & post operative pure tone audiogram data. Out of 26 patients included, 13 patients underwent TORP and 13 underwent PORP. Baseline clinical characteristics and demographic data is summarized in Table-I. The mean age of patients in the TORP group was 39.2 while it was 37.6 in the PORP group. For gender and laterality, an equal half and half split between male-female and right-left. Diagnoses were categorized as mucosal disease with presence of tympanic membrane perforation (46.2%), squamous disease with presence of cholesteatoma (50%) and tympansclerosis (3.8%). The percentage of staged

ossiculoplasties was higher in the TORP group as compared to the PORP group (23.1% and 7.7% respectively). In contrast, the percentage of revision cases was higher in the PORP group as compared to the TORP group (15.4 % and 7.7 % respectively). The percentage of presence of malleus at the time of ossiculoplasty in the TORP group was 84.6 % while 61.5 % in the PORP group. The percentage of prosthesis extrusion in both the groups was similar i.e. 7.7 %.

The preoperative air-bone gap (ABG) was higher in the TORP group than in the PORP group, i.e. measuring 31.77 ± 10.05 dB in TORP group compared to 26.31 ± 10.67 dB in the PORP group. Postoperatively, the mean ABG improved to 17.54 ± 10.83 dB in the TORP group and 19.69 ± 10.34 dB in the PORP group. Both groups achieved a mean postoperative ABG below 20 dB, which meets common criteria for successful ossiculoplasty.

Within-group analysis showed that TORP significantly improved conductive hearing loss (p value < 0.01) with a large effect size. The PORP group also showed improvement that was close to statistical significance (p = 0.05), linked with a moderate effect size. The mean ABG improvement was 14.23 dB in the TORP group and 6.62 dB in the PORP group. This finding indicates a greater gain in hearing after TORP placement.

Table-III shows results of an independent sample t-test run to compare effectiveness of TORP vs PORP. Results were not found to be significantly different in-terms of effectiveness (p=0.185). Hedges'g effect size was -0.519 for TORP vs PORP.

TABLE-I

Characteristic of demography in both groups.

Characteristic		All Patients (n = 26)	TORP (n = 13)	PORP (n = 13)
Age yrs [mean (range)]		38.4 (12-65)	39.2 (12-65)	37.6 (17-65)
Sex	Male	13 (50%)	7 (53.8%)	6 (46.2%)
	Female	13 (50%)	6 (46.2%)	7 (53.8%)
Side	Right	13 (50%)	7 (53.8%)	6 (46.2%)
	Left	13 (50%)	6 (46.2%)	7 (53.8%)
Surgery indication	Mucosal disease	12 (46.2%)	4 (30.8%)	8 (61.5%)
	Squamous disease	13 (50%)	8 (61.5%)	5 (38.5%)
	Tympanosclerosis	1 (3.8%)	1 (7.7%)	0
Malleus status	Present	19 (73.1%)	11 (84.6%)	8 (61.5%)
	Absent	7 (26.9%)	2 (15.4%)	5 (38.5%)
Staged	Yes	4 (15.4%)	3 (23.1%)	1 (7.7%)
	No	22 (84.6%)	10 (76.9%)	12 (92.3%)
Revision surgery	Yes	3 (11.5%)	1 (7.7%)	2 (15.4%)
	No	23 (88.5%)	12 (92.3%)	11 (84.6%)
Prosthesis extrusion	Yes	2 (7.7%)	1 (7.7%)	1 (7.7%)
	No	24 (92.3%)	12 (92.3%)	12 (92.3%)

TABLE-II

Surgery	Timepoint	Mean ABG (SD)	Mean Difference	t (df)	p-value	Effect size (Hedges' g)
TORP	Pre-op	31.77 (10.05)				
	Post-op	17.54 (10.83)				
			14.23	3.42 (12)	0.003	0.889
PORP	Pre-op	26.31 (10.67)				
	Post-op	19.69 (10.34)				
			6.62	1.78 (12)	0.05	0.462

TABLE-I				
Group	Mean Difference (SD) [Post – Pre]	t (df)	P-value (two-sided)	Effect Size (Hedges' g)
TORP	14.23 (14.98)	3.42 (12)		
PORP	6.62 (13.41)	1.78 (12)		
TORP - PORP	-7.62 (5.58)	-1.37 (24)	0.185	-0.519

DISCUSSION

For many years, ossiculoplasty has been carried out using various materials and techniques. Titanium's low mass, dependability, and biocompatibility have made it a popular material. Numerous studies showing the results of these titanium prosthesis have been published. No research articles comparing the effectiveness of TORP and PORP in the Pakistani population have yet been published.

The present study evaluated hearing outcomes following ossiculoplasty using PORP and TORP prostheses, with particular emphasis on postoperative air–bone gap (ABG) closure. Both prosthesis types resulted in a mean postoperative ABG below 20 dB (TORP: 17.54 ± 10.83 dB; PORP: 19.69 ± 10.34 dB), meeting the widely accepted benchmark for surgical success. These findings are consistent with previously published literature, where mean ABG closures typically ranged between 10–20 dB following ossiculoplasty (Dornhoffer, 1998[13]; Yung, 2006.[14]

Interestingly, while some studies (e.g., Dornhoffer, 1998[13] reported 69% of PORP cases and 35% of TORP cases had excellent hearing results (< or = 10 dB PTA-ABG), whereas 31% and 50% of PORP and TORP cases had good results (11 to 20 dB PTA-ABG), our results suggest that TORP can be equally or more effective, particularly in patients with larger preoperative ABGs — a trend observed in our study where the TORP group had a higher baseline ABG (31.11 ± 1.05 dB) than the PORP group (26.31 ± 1.67 dB). This difference may account for the greater hearing gain observed in the TORP group, as patients with more severe conductive deficits may benefit more from total ossicular replacement.

The most recent meta analysis published in February 2023 on this subject concludes an average improvement in air-bone gap (ABG) of about 12 dB following titanium PORP placement and 17 dB with TORP placement. It also states that a greater proportion of patients receiving PORP placements achieve a "successful" postoperative ABG of less than 20 Db.[15] Our results are comparable with an average improvement in ABG in the PORP group of 6.62 dB and in the TORP group of 14.23 dB. All our patients fall under the 20 dB ABG window post operative. It is important to note here that our PORP patients had a lower pre-operative air bone gap of 26.31 as compared to 31.77 of the TORP group, reflecting less room for improvement.

In our study TORP significantly improved conductive hearing loss (p value < 0.01). Although the difference between TORP and PORP did not reach statistical significance, the moderate effect size (Hedges' g = -0.519) suggests that TORP may be more effective in reducing the air–bone gap. This trend might become statistically significant with a larger sample size, warranting further investigation in larger, prospective studies.

Several studies have evaluated hearing outcomes following ossiculoplasty, with particular focus on air-bone gap (ABG) closure and post-operative air-bone gap less than 20 dB as an indicator of surgical success. The type of prosthesis used, integrity of the middle ear structures, and surgical technique are all key factors affecting outcomes. In our study, both TORP and PORP achieved mean post-operative ABG values below 20 dB, but TORP showed a larger mean ABG improvement with 14.2 dB.

Our study possesses notable strengths that enhance the reliability of our results and conclusions drawn from them, particularly as it adds to the limited literature available in this area of clinical practice. Along with being one of the first comparisons between the two prostheses in Pakistan and providing novel regional data, it also contributes on the global scale by utilizing standardized, internationally accepted ways of outcome measures. While other similar

studies have cited high variability in the surgical procedures as a limitation, our study minimized variability by having all the procedures performed by the same senior surgeon. This aimed to maintain uniformity in the surgical technique and handling of the prosthesis while reducing inconsistencies introduced by differing levels of surgical expertise. This approach allowed a more thorough comparison of the outcomes with minimal influence of external factors that could have brought forth unanticipated differences in hearing results.

Despite having several strengths, one of the limitations worth noting is that, as a single-center study, our results may not be a complete representation of the outcomes across other surgical settings in Pakistan. Nevertheless, a controlled environment with unvarying surgical and audiometric protocol was crucial to conduct our research to adequately compare TORP and PORP. Another limitation was keeping the follow-ups limited to short-term, which may have not allowed us to record long-term complications but it was necessary in our case. This was primarily due to limitations relating to the academic timeline of the degree program, which required the studies and the manuscript to be completed and submitted within a certain timeframe. As a result, the long-term outcomes were not able to be assessed. Future research with longer follow up periods are necessary to better understand the long-term effects and sustainability of the results.

This study lays a foundation for future research to further expand through multi-center trials and longer follow-up periods. Such studies would better satisfy the demands to represent general surgical settings across Pakistan and lead to a more comprehensive evaluation of long-term outcomes. The insights from our work may eventually allow evidence-based refinement in ossicular reconstruction, aiming to reduce complication rates and improve the patients' postoperative quality of life.

CONCLUSION

As our research indicates, both procedures improve conductive hearing loss, though in select patients, primarily those with more severe preoperative hearing loss, TORP appears to be, on average, more advantageous.

According to this study, both PORP and TORP are viable ossicular reconstruction options, though the latter seems especially beneficial in patients with substantial ossicular chain damage.TORP seems especially beneficial in patients with advanced ossicular chain damage. We recommend that the choice of prosthesis be made based on the operative findings on the continuity of the ossicular chain, stapes mobility, and the middle ear anatomy, rather than on the historical biases pertaining to PORP and TORP. Surgeons must take preoperative hearing loss into account and should provide patients with realistic expectations based on the anticipated outcomes of surgical intervention for their specific middle ear disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Significance of hemogram and peripheral smear in diagnosis of suspected cases of thalassemia.

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ABSTRACT… Objective: To estimate the significance of hemogram and peripheral smear in diagnosis of suspected cases of thalassemia presented to the Farooq Hospital Lahore. **Study Design:** Cross-sectional study. **Setting:** Department of Pathology, Farooq Hospital, Westwood Lahore. **Period:** December 2023 to December 2024. **Methods:** Patients from all branches of Farooq hospital Lahore visiting for hemoglobin electrophoresis testing were included. Complete blood count was performed on automated hematology analyzer and blood smears were examined by Hematologist. The hemoglobin electrophoresis was performed on electrophoresis automated system. The IBM SPSS version 27.0 software used to analyze the collected data. **Results:** From total (n=473), majority of the patients were females (73.78%) then males (26.21%). The mean age was 19.99+14.731. The beta thalassemia trait was the most prevalent among the other variants. A substantial number of patients exhibited low MCV levels and moderate hemoglobin deficiency, as well as microcytic hypochromic, anisocytosis, poikilocytosis, and target cells. The beta thalassemia trait was associated with statistically significant red blood cells (p=0.024), poikilocytosis (p=0.001), and target cells (p=0.001). **Conclusion:** These results emphasize the significance of peripheral smear and hemogram in the diagnosis of thalassemia. This study also underscores the importance of targeted screening and diagnostic strategies to effectively identify carriers and manage affected individuals, particularly in light of the high female representation and young mean age of patients.

Key words: Beta thalassemia Major, Beta thalassemia Trait, Hemogram, Hemoglobin Variants, Peripheral Smear.

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INTRODUCTION

Around the world, there are more than forty million people who are carriers of hemoglobinopathies. Thalassemia is the most prevalent form of a single gene disorder that affects people all over the world. It is a serious genetic disease.[1] Alpha thalassemia and beta thalassemia are the two principal varieties of thalassemia. These two types of thalassemia are distinguished by the component of the globin chain that is formed in smaller amounts.[2] There are four genes that make up the alpha globin chain. A reduction in alpha globin chain synthesis is the defining characteristic of alpha thalassemia. This decrease is caused by the deletion or mutation of one or more of the four alpha globin genes that are located on chromosome 16. Mild alpha-thalassemia is another name for this condition. Examples of mild alpha-thalassemia are distinguished by the lack of two alpha-globin genes in the affected individual. Patients who have this disorder do not appear to be experiencing any symptoms; yet, they do have a low red blood cell count and moderate anemia when they are examined. They seem and feel normal, but routine checks may indicate that there is a problem with their health. It is also known as hemoglobin H disease. There was a lack of three alpha globin genes in these affected individuals. Because of the extreme anemia that they suffer from, those who are affected by the disorder typically need blood transfusions in order to continue living.[3]

Beta thalassemia is a hereditary disorder that is extremely prevalent in Pakistan.[4] It has been determined that more than two hundred mutations in the beta globin gene are responsible for the development of beta thalassemia all over the world. A mutation that was found on chromosome 11 is the root cause of beta thalassemia.[5] This disease is quite prevalent along the coast of the Arabian Sea, particularly in the provinces of South and Khyber Pakhtunkhwa, which are located close to the border with Afghanistan.[3]

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Beta thalassemia can result in a wide range of clinical manifestations, such as asymptomatic microcytic hypochromic red cells in the heterozygous state (also known as beta thalassemia trait) and severe anemia in the homozygous state (also known as beta thalassemia major), which can be fatal in the first few years of life if regular blood transfusions are not administered.[6]

According to the findings of studies, the incidence of this specific genetic problem is increased by a number of factors, including poverty, consanguinity, and ignorance of the genetic condition. There are between 90,000 and 100,000 persons in the United States who are affected by this condition. The number of younger patients is growing on a daily basis as a result of the growing burden of disease, but the number of older patients is decreasing as a result of the decreased life expectancy.[7] Some research indicated that low resources and lack of awareness also contribute to the disorder's rising prevalence. Social factors such as consanguineous marriages and marrying within ethnic groups contribute to the disease's increasing prevalence.[8] In a developing country like Pakistan, where many people suffer from beta thalassemia the cost of establishing treatment programs is too expensive. So, the alternate long-term strategy would be able to reduce the number of patients by education, couple screening before marriage, prenatal screening and genetic counseling.[9] The present study was conducted to estimate the significance of hemogram and peripheral smear in diagnosis of suspected cases of thalassemia presented to the Farooq Hospitals of Lahore.

METHODS

The Pathology department at Farooq Hospital in Westwood and the College of Allied Health Sciences at Akhtar Saeed Medical and Dental College in Lahore conducted this cross-sectional study and was carried out during the months of December 2023 and December 2024. The study was approved by the institutional review board (CAHS-10/2024-MLT-86). The non-probability convenient sampling technique was used. In this study, four hundred and seventy three patients were enrolled. Patients from all branches of Farooq Hospital Lahore (Farooq Hospital Westwood, Akhter Saeed Trust Hospital EME, Farooq Hospital DHA, and Farooq Hospital Iqbal Town) for hemoglobin electrophoresis testing (advised by the physician) were included in this study. A performa was designed to collect data from every patient. After obtaining verbal informed consent, about 03 ml of whole blood was collected from every patient in EDTA vaccutainer.

The complete blood count (CBC) was performed on MINDRAY (BC-5000) automated hematology analyzer. The blood smears of every patient were examined by the consultant Hematologist. The hemoglobin electrophoresis was performed on MINIPHOR-08 electrophoresis automated system, which follows the principle of separating electrically charged biomolecules in a solution. This instrument quantified the levels of hemoglobin A, hemoglobin A2, hemoglobin F, hemoglobin S/D, and hemoglobin H. To further differentiate between hemoglobin S and hemoglobin D, capillary electrophoresis was performed. The polymerase chain reaction (PCR) was advised for the confirmation of hemoglobin H.

The information collected was entered into an Excel spreadsheet and analyzed using Statistical Package for the Social Sciences (IBM SPSS) version 27.0. The mean and percentages were computed. The chi-square test and multivariate analysis were performed to ascertain statistically significant associations. A p-value of $p<0.05$ was deemed statistically significant.

RESULTS

In this study, the majority of patients were female (n=349, 73.78%) compared to male patients (n=124, 26.21%). The average age (± standard deviation) of the patients was 19.99 ± 14.731. The age range was three months to eighty-five years. The patients were categorized into five age categories. The participating patients were sourced from four branches of Farooq Hospital (Table-I). The majority of patients were from the outdoor (n=257, 54.33%), while others were admitted to the medical unit (n=179, 37.84%), pediatrics (n=30, 6.34%), gynecology (n=5, 1.05%), and the critical care unit (n=2, 0.42%), respectively.

TABLE-I

Characteristics and frequency of different study variables

Study Variables	Frequency (%)
Mean age (+ standard deviation)	19.99+14.731
Age groups	
• Infant (3–12 months old)	53 (11.20%)
• Toddler (1–3 years old)	71 (15.01%)
• Preschool (3-5 years old)	19 (4.01%)
School age (6–12 years old)	16 (3.38%)
Adolescents & Adults (12 to onward years old)	314 (66.38%)
Gender	
Males	124 (26.21%)
Females	349 (73.78%)
Referral branch	
Farooq Hospital Westwood	162 (34.20%)
Farooq Hospital Iqbal Town	67 (14.20%)
Akhter Saeed Trust Hospital	217 (45.90%)
Farooq Hospital DHA	27 (5.70%)
Department	
Outdoor patient	257 (54.33%)
Medical unit	179 (37.84%)
Peads	30 (6.34%)
Gynecology	05 (1.05%)
Intensive care unit	02 (0.42%)

The analysis of the CBC revealed that the mean (± standard deviation) of total red blood cells, hemoglobin, mean corpuscular volume (MCV), and red cell distribution width-standard deviation (RDW-SD) were 4.061 ± 1.931, 8.063 ± 2.863, 67.646 ± 13.044, and 47.216 ± 10.235, respectively. The CBC variables were assessed in patients in accordance with the standard ranges (Table-II). The mean (± standard deviation) values for hemoglobin A, hemoglobin A2, hemoglobin F, hemoglobin H, and hemoglobin D were 94.153 ± 15.543, 2.70 ± 1.88, 1.99 ± 13.51, 0.064 ± 1.40, and 0.77 ± 5.96, respectively.

According to the results of hemoglobin electrophoresis, the majority of patients had normal hemoglobin electrophoresis (n=420, 88.79%). The prevalence of beta thalassemia trait was determined to be 6.97% (n=33), whereas 2.11% (n=10) exhibited beta thalassemia major. 1.90% (n=9) of patients had hemoglobin D disease, while only 0.21% (n=1) had hemoglobin H disease (Figure-1).

Multivariate analysis was employed to identify the statistically significant correlation between CBC variables and total hemoglobin electrophoresis (Figure-2). Hemoglobin (p=0.001), MCV (p=0.004), and RDW-SD (p=0.016) were shown to be statistically significant.

The majority of patients had microcytic hypochromic red blood cells (n=383, 80.97%). Additional morphologies of red blood cells observed in patients are presented as well (Table-II). The chi-square test was utilized to determine the correlation between red blood cell and total hemoglobin electrophoresis. Microcytic hypochromia (p=0.003), anisocytosis (p=0.003), poikilocytosis (p=0.001), target cells (p=0.001), pencil cells (p=0.001), and tear drop cells (p=0.001) were identified as statistically significant. The chi-square test was utilized to determine the relationship of study variables with beta thalassemia major and beta thalassemia trait. Red blood cells (p=0.024), poikilocytosis (p=0.001), and target cells (p=0.001) were statistically significant in relation to beta thalassemia trait (Table-III).

FIGURE-1.

Estimation of hemoglobin electrophoresis in study patients

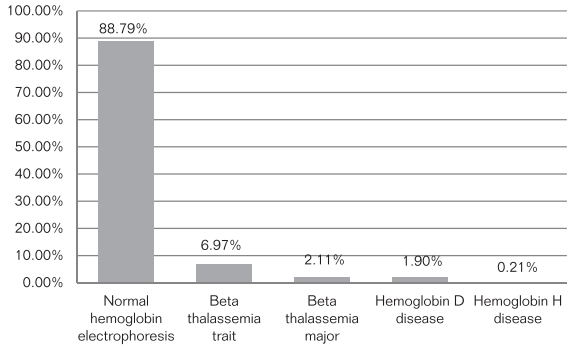

FIGURE-2

Estimated marginal means of complete blood count variables and hemoglobin electrophoresis

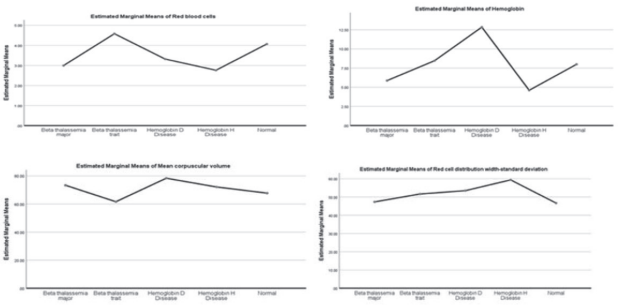

TABLE-II

Frequency and association of clinical variables in overall hemoglobin electrophoresis

Clinical Variables	Frequency (%)	P-Value
Total red blood cells (4.1-5.3 x10^6/uL)		
Normal total red blood cells (4.1-5.3 x10^6/uL)	356 (75.26%)	0.124
Low total red blood cells (< 4.1 x10^6/uL)	95 (20.08%)	
High total red blood cells (> 5.3 x10^6/uL)	22 (4.65%)	
Hemoglobin (12.0-16.0 g/dL)		
Normal hemoglobin levels (12.0-16.0 g/dL)	18 (3.80%)	0.001*
Mild deficiency (10.0-11.9 g/dL)	76 (16.06%)	
Moderate deficiency (6.1-9.9 g/dL)	286 (60.46%)	
Severe deficiency (< 6.0 g/dL)	169 (35.72%)	
Mean corpuscular volume (75-95 fL)		
Normal MCV (75-95 fL)	88 (18.60%)	0.004*
Low MCV (< 75 fL)	385 (81.39%)	
Red cell distribution width-standard deviation (39–46 fL)		
Normal RDW-SD (39–46 fL)	212 (44.82%)	0.016*
Low RDW-SD (< 39 fL)	68 (14.37%)	
High RDW-SD (> 46 fL)	193 (40.80%)	
Red blood cell morphology		
Microcytic hypochromia	383 (80.97%)	0.003*
Anisocytosis	381 (80.54%)	0.003*
Poikilocytosis	56 (11.83%)	0.001*
Target cells	51 (10.78%)	0.001*
Pencil cells	42 (8.90%)	0.001*
Tear drop	17 (3.6%)	0.001*
Macrocytic hypochromia	03 (0.63%)	1.00

*Significant p-value

DISCUSSION

Beta thalassemia, an autosomal recessive hemoglobinopathy, is one of the most common genetically transmitted disorders in the world.[10] Annually, between 5,000 to 9,000 children are born with beta thalassemia, despite lack of a documented registry in Pakistan. The projected carrier rate ranges from 5-7%, with 9.8 million carriers in the entire population.[11] In present study more females (73.78%) were tested for hemoglobin electrophoresis as compared to males (26.21%). The mean age of the patients was 19.99+14.731. The majority (66.38%) of patients were adults (12 to onward years old). The study of Aziz et al. showed male predominance, with 54.0% males and 46.0% females. The patients' ages ranged from 2 to 21 years, with a mean age of 8.33. More patients (36%) were between 6-10 years of age.[12] Another study by Faizan et al. represented more males (51%) than females (49%) with age range from 1 year to 10 years.[3] The difference in these findings represents population difference.

From total (n=10), thalassemia major patients, (80%) were males and (20%) females. The more patients (40%) were 3-12 months old. The findings of Khan et al. study are in consistent with the present study showing the male predominance (56%). The majority of beta thalassemia major patients were within the age range of 5-11 years (70%), with a smaller but significant proportion aged between 12-18 years (30%).[13] The study of Siddiqui et al. represented more males (47.8%) than females (52.2%). The average age was 11±5.2 years.[14]

TABLE-III

Frequency and association of variables in beta thalassemia major and beta thalassemia trait

Variables	Beta thalassemia Major n=10	P-Value	Beta thalassemia Trait n=33	P-Value
Age groups				
• Infant (3–12 months old)	04 (40%)	0.591	-	0.122
• Toddler (1–3 years old)	03 (30%)		06 (18.18%)	
• Preschool (3-5 years old)	-		02 (6.06%)	
School age (6–12 years old)	-		01 (3.03%)	
Adolescents & Adults (12 to onward years old)	03 (30%)		24 (72.72%)	
Gender				
Males	08 (80%)	0.800	07 (21.21%)	0.635
Females	02 (20%)		26 (78.78%)	
Hemoglobin				
Normal hemoglobin levels	-	0.591	01 (3.03%)	0.173
Mild deficiency	-		06 (18.18%)	
Moderate deficiency	02 (20%)		20 (60.60%)	
Severe deficiency	08 (80%)		06 (18.18%)	
Total red blood cells				
Normal total red blood cells	03 (30%)	0.700	18 (54.54%)	0.024*
Low total red blood cells	07 (70%)		10 (30.30%)	
High total red blood cells	-		05 (15.15%)	
Mean corpuscular volume				
Normal MCV	04 (40%)	0.483	01 (3.03%)	0.162
Low MCV	06 (60%)		32 (96.96%)	
Red cell distribution width-standard deviation				
Normal RDW-SD	07 (70%)	0.689	08 (24.24%)	0.194
Low RDW-SD	-		09 (27.27%)	
High RDW-SD	03 (30%)		16 (48.48%)	
Red blood cell morphology				
Microcytic hypochromia	07 (70%)	0.300	32 (96.96%)	0.273
Anisocytosis	07 (70%)	0.300	32 (96.96%)	0.273
Poikilocytosis	06 (60%)	0.600	26 (78.78%)	0.001*
Target cells	06 (60%)	0.600	26 (78.78%)	0.001*
Pencil cells	-	-	07 (21.21%)	0.081
Tear drop	03 (30%)	0.700	01 (3.03%)	0.273
Macrocytic hypochromia	-	-	-	-

*Significant p-value

In thalassemia trait patients of present study (n=33), more females (78.78%) were observed as compared to males (21.21%) and more (72.72%) adult (12 years to onward) patients. The study of Shakoor et al. had same findings of beta thalassemia trait representing more females (59.54%) than males (40.46%) with more patients (25.95%) belonging to 21–30 years age group.[15]

In present study, the frequency of beta thalassemia

major was found to be 2.11% while the frequency of beta thalassemia trait was 6.97%. Shakoor et al. conducted study on 805 suspected cases and found that 131 patients (16.27%) were diagnosed with beta thalassemia trait.[15] According to Mansoor et al. overall hemoglobinopathies was observed in 14.5% patients. The frequency of beta thalassemia major was 42.4% while beta thalassemia trait was observed in 57.6% of patients.[16] The frequency of hemoglobin D and hemoglobin H was 1.90% and 0.21% respectively in present study. According to Kamil et al. findings, 21.5% of patients had hemoglobin disorders. Out of 708 carriers, 19.6% showed traits of thalassemia minor, 0.36% showed Hb S trait, 1.30% showed Hb D trait, and 0.21% showed Hb E trait.[17] The study of Mansoor et al. reported the frequency of hemoglobin D of 1.2%.[16] The present study found fewer frequencies of beta thalassemia major and beta thalassemia trait as compared to the previous studies. This may suggest regional differences, ethnicity difference, and the status of consanguineous marriages, as the present study did not estimate these factors.

The present study described the significance of hemogram and peripheral smear in diagnosis of suspected cases of thalassemia presented at Hospital. The MCV and hemoglobin levels are used in the preliminary identification of microcytic anemia, which is a characteristic of beta thalassemia. The present study estimated the overall mean of total red blood cells, hemoglobin, MCV, RDW-SD were 4.061+1.931, 8.063+2.863, 67.646+13.044, and 47.216+10.235 respectively. The majority of patients had low MCV (81.39%), moderate deficiency of hemoglobin (60.46%), normal RDW-SD (44.82%), and normal total red blood cells (75.26%). The findings of present study are in consistent with Khanzada et al. study. They also presented that the (41.7%) patients had low MCV, with (46.3%) low MCH. These findings are consistent with typical characteristics of beta thalassemia trait, including a decrease in MCV and MCH due to reduced hemoglobin synthesis and the presence of unpaired globin chains in red blood cells.[18]

In present study, the red blood cells (p=0.024), poikilocytosis (p=0.001), and target cells (p=0.001) were found statistically significant with beta thalassemia trait. In study of Kamil et al. the mean hemoglobin level was 10.3 ± 2.3 in thalassemia minor, 9.3 ± 2.3 in HbS trait, 10.3 ± 3.2 in HbD trait, and 9.3 ± 2.0 in HbE trait. The mean RBC value in thalassemia was 5.1 ± 1.1, while Hb S, HbD, and HbE had values of 4.1 ± 0.9, 4.6 ± 1, and 4.3 ± 0.6. The average MCV was 65.3 ± 8.5 in thalassemia carriers, 71 ± 10.8 in HbS, 72.8 ± 14 in HbD, and 70.4 ± 9.5 in HbE.[17] In the present study, the overall mean of hemoglobin A, hemoglobin A2, hemoglobin F, hemoglobin H, and hemoglobin D was 94.153+15.543, 2.70+1.88, 1.99+13.51, 0.064+1.40, and 0.77+5.96 respectively. According to Kamil et al. the average HbA2 levels for thalassemia minor, HbS trait, HbD trait, and HbE trait were 5 ± 1.5, 2.5 ± 0.9, 1.9 ± 0.4, and 0.9 ± 1.6, respectively.[17]

The present study shows (70%) microcytic hypochromia, (70%) anisocytosis, (60%) poikilocytosis, (60%) target cells, and (30%) tear drop cells seen in thalassemia major patients. The study of Nurjanah et al. demonstrated 100% microcytic anemia, 100% hypochromic, 100% poikilocytosis dominating target cells, and 85% basophil stippling in beta thalassemia major patients.[19] The present study also shows (96.96%) microcytic hypochromia, (96.96%) anisocytosis, (78.78%) poikilocytosis, (78.78%) target cells, (21.21%) pencil cells, and (3.03%) tear drop cells seen in thalassemia trait patients. The findings of Bhabhor et al. study are relevant with the present study findings represented (100%) microcytic hypochromia, poikilocytosis, and target cells seen in beta thalassemia trait patients.[20] The frequency rates and morphological findings of present study align with global and regional trends but also highlight some differences, such as the absence of rare hemoglobin variants. The sample size is limited, and the study is single-centered, involving participants from a tertiary care hospital, therefore the generalizability of the results is constrained. More studies with relevant large sample size and more comprehensive approaches are recommended.

CONCLUSION

The present study highlights the frequency of hemoglobin variants and significance of hemogram and peripheral smear in diagnosis of beta

thalassemia. Beta thalassemia trait was the highest among other variants in present study population. A significant proportion of patients represented moderate hemoglobin deficiency and low MCV levels with microcytic hypochromia, anisocytosis, poikilocytosis and target cells. These findings underscore the importance of targeted screening and diagnostic strategies to identify carriers and manage affected individuals effectively, particularly given the high female representation and young mean age of patients. Enhanced awareness, early detection, and comprehensive care are essential for reducing the burden of beta thalassemia in our population.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Clinicohematological profile and treatment outcomes of Hodgkin's Lymphoma- a single center experience from Pakistan.

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ABSTRACT… Objective: To evaluate the epidemiological and clinical characteristics, along with treatment outcomes of Hodgkin's lymphoma patients in Pakistan. **Study Design:** Prospective Cross Sectional study. **Setting:** National Institute of Blood Diseases and Bone Marrow Transplantation (NIBD), Karachi, Pakistan. **Period:** January to December 2024. **Methods:** This was a cross sectional study comprising 22 patients diagnosed with HL as per WHO Classification who presented at National Institute of Blood Diseases and BMT Karachi Pakistan from January to December 2024. The quantitative variables were represented as mean (SD), while nominal variables were presented as frequency and percentages by using SPSS 25 version and STATA 15 version. The Kaplan Meier analysis and log rank test was done for survival analysis. **Results:** A total of 22 HL patients were included in the study. The mean age of the study participants was 31.7±18.7 years. In the study, 63.6% of the patients were male, while 36.4% were female. B symptoms were present in 86.4% of the patients. Hepatomegaly, was noted in 27.3, while splenomegaly, was observed in 45.5% of patients. The Hb level in the cohort was above 10.5 g/dl in the majority (63.7%), while 36.3% had anemia. LDH is a marker of tissue damage, and in this cohort, 63.7% of patients had LDH levels higher than 220 U/L, indicating ongoing cellular breakdown or tissue damage. The site of tissue diagnosis in the study primarily involved cervical lymph nodes (72.8%), followed by Axillary (13.7%) and inguinal (9.1%) lymph nodes. The 90 months overall survival in 22 patients was 73.5%. **Conclusion:** The present study revealed the detailed clinical hematological and treatment outcome of HL patients in Pakistan. However, multicenter studies with larger sample size are needed to validate the findings and enhance treatment strategy especially for relapse patients.

Key words: Clinico-hematological Characteristics, Hodgkin's Lymphoma (HL), Overall Survival, Treatment.

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INTRODUCTION

Hodgkin's lymphoma (HL) is a rare malignancy accounting for 0.4% of newly diagnosed cancer cases and 0.2% cancer related deaths worldwide annually.[1] However, in the recent years there has been a rise in the incidence rates and a shift in epidemiological trends with increasing rates observed among females, younger patients and the Asian population.[2]

Remarkable variations in the incidence, histological subtypes, and mortality rates have been reported across different geographical regions. While higher incidence rates are noted in developed countries, contrarily, mortality rates are higher in Asian countries.[2,3] Several etiological and prognostic factors have been implicated in the pathogenesis and clinical diversity of the disease including genetic factors, environmental influences, and/or the interaction of these two elements.

Genome wide association studies have identified human leukocyte antigen (HLA) and non-HLA loci associated with the risk of developing HL and have also proposed immune dysregulation and infections as key regulators in the pathogenesis.[4,5] Viral infections such as Epstein-Barr virus (EBV) and human immunodeficiency virus (HIV) are associated with the development of HL by causing deoxyribonucleic acid (DNA) damage. Environmental determinants of disease burden include exposure to ionizing radiation, alcohol use, obesity, hypertension, smoking as well as socioeconomic status.[2,6,7] While these factors have been extensively studied in western populations, there is still a need for further research in developing countries.

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With the recent advancements in treatment strategies and introduction of new drugs such as check point inhibitors there has been substantial improvement in the treatment outcomes.[8,9] However due to disease heterogeneity, differing patient characteristics and, the challenges faced in low socioeconomic countries such as Pakistan, treatment outcomes are not as favorable as in the developed world. Additionally, there is limited published data on the clinico-pathological features and treatment outcomes of HL patients in our country.

This study was aimed to evaluate the epidemiological and clinical characteristics, along with treatment outcomes of Hodgkin's lymphoma patients presenting at one of referral hematology center in Pakistan, in order to highlight the disease characteristics indigenous to our population.

METHODS

This was a cross sectional study comprising patients diagnosed with HL as per WHO Classification, including both newly diagnosed and relapse/ refractory cases who presented at National Institute of Blood Diseases and Bone Marrow Transplantation (NIBD-BMT), Karachi Pakistan from January to December 2024 after institutional review board approval (NIBD/IRB- 281/01-2025). A total of 22 patients (aged 12 years and above) were enrolled, including 13 treatment-naive, and 9 with relapse/ refractory disease (who had received primary treatment from some other center at Pakistan). The study was approved by the hospital institutional review board. Demographic variables like age, gender, Eastern Cooperative Oncology Group (ECOG) performance status (PS), physical examination, fever (>38.6°C), weight loss (>10% of body weight in 6 months), Ann Arbor stage, and existing comorbidities were documented.

Imaging was performed using whole-body fluorodeoxyglucose (FDG) positron emission tomography (PET) preferentially or computerized tomography (CT) neck, chest, abdomen and pelvis with contrast in cases of non availability of PET imaging. Bone marrow (BM) biopsy was performed in patients who had CT imaging instead of PET scan. Baseline complete blood count (CBC), renal, hepatic profile, lactate Dehydrogenase (LDH), viral markers, Echo and pulmonary function tests (PFTs) were performed as part of pre treatment evaluation.

The disease staging and prognostication was performed as per British journal of hematology (BJH) guidelines into early stage (Stage I and II) and advanced stage (Stage III and IV) disease. Early stage was further classified into favorable and unfavorable risk group as per European organization for research and treatment for cancer (EORTC). The Hodgkin International Prognostic Index [IPI] on the basis of the following criteria [i.e., Hemoglobin (Hb), age, gender, disease stage, white blood counts (WBC), absolute lymphocyte count(ALC), and serum albumin were calculated for patients with advanced stage disease.

All treatment naïve patients received 6 cycles of ABVD (Adriamycin, bleomycin, vinblastine, and dacarbazine) as the standard regimen. None of the patient received radiotherapy due to non availability at the institute. Relapse/ refractory patients were offered salvage regimen (ICE/DHAP/BV-B) as per availability and patients who underwent remission were consolidated with autologous stem cell transplant (ASCT). Response assessment was done via PET scan at two time points, interim imaging (after 2 cycles) and end of treatment. Patients were then followed up 6 monthly via CT imaging. Comprehensive physical examination and blood counts were performed on follow-up visits every 3 months.

Statistical Analysis

The quantitative variables were represented as mean, standard deviation (SD), while nominal variables were presented as frequency and percentages. The Shapiro-wilk test for normality evaluation of quantitative variable was utilized. To evaluate the differences in alive and dead patients two independent sample t-test for numeric variables Fisher Exact test for nominal variables were applied. Kaplan Meier curves and log rank test was done for survival analysis. SPSS 25 version and STATA 15 version were utilized for statistical test and presentation of data. The p-value equal or <0.05 was considered statistically significant.

RESULTS

A total of 22 HL patients were included in the study. The mean age of the study participants was 31.7±18.7 years. In the study, 63.6% of the patients were male, while 36.4% were female. Co-morbidities were present in 18.1% of the participants. The mean (SD) follow up was 29 (24) months. The most commonly affected region by lymphadenopathy was the cervical region, with 77.3% of patients presenting with cervical lymphadenopathy. With respect to infection at the time of presentation, 91% of the cohort did not present with an infection, however 9% of patients had infection at presentation. B symptoms were present in 86.4% of the patients. Hepatomegaly, was noted in 27.3, while splenomegaly, was observed in 45.5% of patients.

The Hb level in the cohort was above 10.5 g/dl in the majority (63.7%), while 36.3% had anemia. LDH is a marker of tissue damage, and in this cohort, 63.7% of patients had LDH levels higher than 220 U/L, indicating ongoing cellular breakdown or tissue damage. The site of tissue diagnosis in the study primarily involved cervical lymph nodes (72.8%), followed by axillary (13.7%) and inguinal (9.1%) lymph nodes. The various clinical characteristics at disease presentation are depicted in Table-I and Figure-1.

(%): Percentage, BM: Bone Marrow, cHL: Classical Hodgkin's Lymphoma, CT: computed tomography, LDH Lactate Dehydrogenase, LTF: Lost to follow up, MCHL: Mixed Cellularity-Hodgkin's Lymphoma, N/A:Not Available, n:Number, NSHL: Nodular Sclerosis Hodgkin's Lymphoma, PET-CT: Positron Emission Tomography-Computed Tomography, WBC: White Cells Counts

The demographics, hematological characteristics and diagnosis methods were compared in dead and alive patients but no significant results were established. (Table-II)

FIGURE-1.

Flow chart showing outcome of patients with HL.

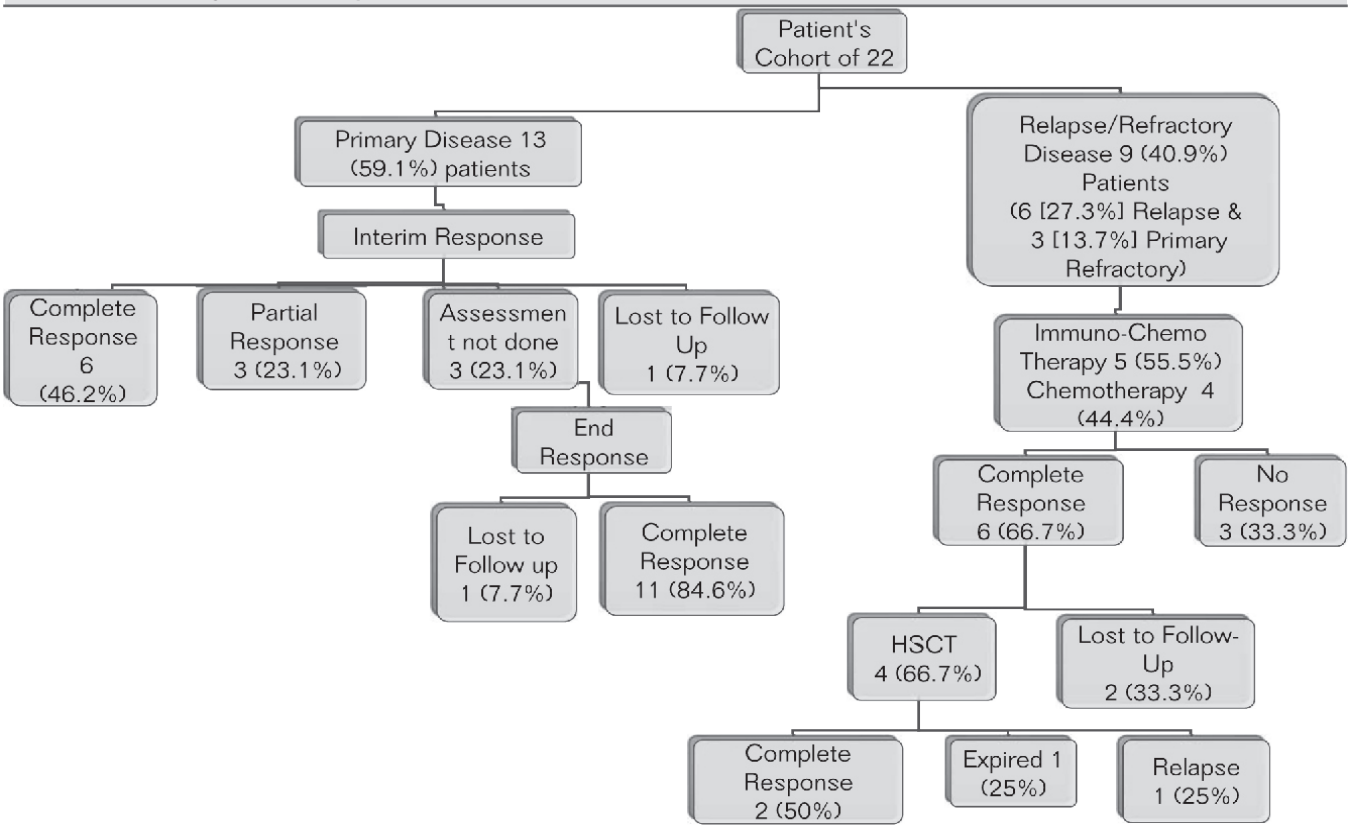


TABLE-I		
Clinical characteristics of HL patients at presentation, treatment and response:		
Age	Mean (SD)	31.7 (18.7)
Gender	Female, n(%)	8 (36.4)
	Male, n(%)	14 (63.6)
Co- Morbidity	No n(%)	18 (81.9)
	Yes n(%)	4 (18.1)
Physical Examination lymphadenopathy	Inguinal lymph node n(%)	1 (4.6)
	Cervical lymph node n(%)	17 (77.3)
	Cervical lymph node, inguinal lymph node n(%)	1 (4.6)
	Axillary lymph node, cervical lymph node n(%)	1 (4.6)
	Axillary lymph node n(%)	1 (4.6)
	Axillary, inguinal, cervical n(%)	1 (4.6)
Infection at presentation	No n(%)	20 (91)
	Yes n(%)	2 (9)
B symptoms	No n(%)	3 (13.7)
	Yes n(%)	19 (86.4)
Hepatomegaly	No n(%)	16 (72.8)
	Yes n(%)	6 (27.3)
Splenomegaly	No n(%)	12 (54.6)
	Yes n(%)	10 (45.5)
Hemoglobin (g/dl)	<10.5 n(%)	8 (36.4)
	>10.5 n(%)	14 (63.7)
WBC (10^9/L)	<15 n(%)	21 (95.5)
	>15 n(%)	1 (4.6)
Platelet (10^9/L)	<150 n(%)	2 (9.1)
	>150 n(%)	20 (91)
LDH	N/A	6 (27.3)
	<220 n(%)	2 (9.1)
	>220 n(%)	14 (63.7)
Urea	<50 n(%)	20 (91)
	>50 n(%)	2 (9.1)
Creatinine	<1.2 n(%)	22 (100)
	>1.2 n(%)	0 (0)
Liver function	Normal n(%)	21 (95.5)
	Abnormal n(%)	1 (4.6)
Site of tissue diagnosis	Axillary lymph node n(%)	3 (13.7)
	Cervical lymph node n(%)	16 (72.8)
	Inguinal lymph node n(%)	2 (9.1)
	Mediastinal lymph node n(%)	1 (4.6)
cHL subtype	N/A n(%)	9 (41)
	MCHL n(%)	4 (18.2)
	NSHL n(%)	9 (40.9)
BM biopsy	Not done n(%)	15 (68.2)
	Done n(%)	7 (31.9)
BM involvement biopsy (n=7)	No n(%)	4 (18.2)
	Yes n(%)	3 (13.7)
Ann-Arbor Stage	2B n(%)	4 (18.2)
	3A n(%)	2 (9.1)
	3B n(%)	11 (50)
	4B n(%)	5 (22.8)
Status at the time of 1st visit	Primary disease n(%)	13 (59.1)
	Relapse n(%)	6 (27.3)
	Primary refractory n(%)	3 (13.7)
Primary Disease (n=13)		
End of Treatment Response Assessment by (n=13)	PET-CT n(%)	11 (84.7)
	CT n(%)	1 (7.7)
	LTF n(%)	1 (7.7)
Relapse	Yes n(%)	2 (15.4)
	No n(%)	7 (53.8)
	LTF n(%)	4 (30.8)
Final Outcome	Alive n(%)	19 (86.4)
	Death n(%)	3 (13.6)

TABLE-II

Comparison of HL patients' characteristics and final outcome:

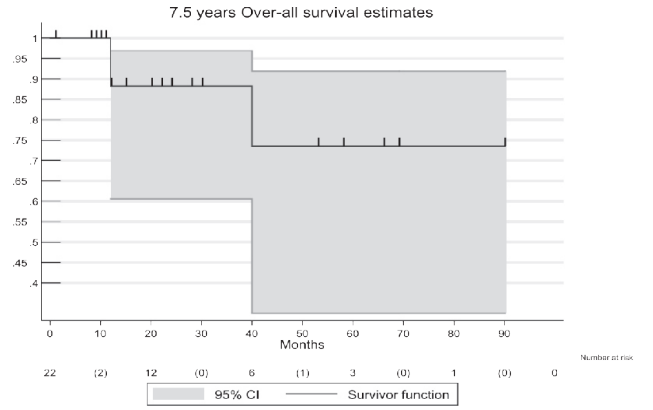
Parameters		Alive (n=19)	Died (n=3)	P-Value
		N (%)	N (%)	
Age	Mean (SD)	31.58 (19.07)	32.67 (20.3)	0.77
Follow up		30 (25)	21 (16)	0.74
Gender	Female	8 (42.1)	0 (0)	0.27
	Male	11 (57.9)	3 (100)	
Co- Morbidity	No	15 (78.9)	3 (100)	1.00
	Yes	4 (21.1)	0 (0)	
Platelets (10^9/L)	<150	2 (10.5)	0 (0)	1.00
	>150	17 (89.5)	3 (100)	
LDH	not available	5 (26.3)	1 (33.3)	1.00
	<220	2 (10.5)	0 (0)	
	>220	12 (63.2)	2 (66.7)	
Urea	<50	17 (89.5)	3 (100)	1.00
	>50	2 (10.5)	0 (0)	
Creatinine	<1.2	19 (100)	3 (100)	1.00
	>1.2	0 (0)	0 (0)	
Liver functions	Normal	19 (100)	2 (66.7)	0.14
	Abnormal	0 (0)	1 (33.3)	
B symptoms	No	3 (15.8)	0 (0)	1.00
	Yes	16 (84.2)	3 (100)	
Infection(s)at presentation	No	18 (94.7)	2 (66.7)	0.26
	Yes	1 (5.3)	1 (33.3)	
Physical Examination lymphadenopathy	Inguinal lymph node	1 (5.3)	0 (0)	0.56
	Cervical lymph node	15 (78.9)	2 (66.7)	
	Cervical lymph node, Inguinal lymph node	1 (5.3)	0 (0)	
	Axillary lymph node, cervical lymph node	1 (5.3)	0 (0)	
	Axillary lymph node	1 (5.3)	0 (0)	
	Axillary, inguinal, cervical lymph nodes	0 (0)	1 (33.3)	
Hepatomegaly	No	14 (73.7)	2 (66.7)	1.00
	Yes	5 (26.3)	1 (33.3)	
Splenomegaly	No	9 (47.4)	3 (100)	0.20
	Yes	10 (52.6)	0 (0)	
Hemoglobin (g/dl)	<10.5	8 (42.1)	0 (0)	0.27
	>10.5	11 (57.9)	3 (100)	
WBC (10^9/L)	<15	18 (94.7)	3 (100)	1.00
	>15	1 (5.3)	0 (0)	
cHL subtype	Not available	9 (47.4)	0 (0)	0.36
	MCHL	3 (15.8)	1 (33.3)	
	NSHL	7 (36.8)	2 (66.7)	
Site of tissue diagnosis	Axillary Lymph node	2 (10.5)	1 (33.3)	0.64
	Cervical lymph node	14 (73.7)	2 (66.7)	
	inguinal lymph node	2 (10.5)	0 (0)	
	Mediastinal lymph node	1 (5.3)	0 (0)	
Status at the time of 1st visit	De novo primary disease	13 (68.4)	0 (0)	0.08
	Relapse	4 (21.1)	2 (66.7)	
	Primary refractory	2 (10.5)	1 (33.3)	

(%): Percentage, cHL: Classical Hodgkin's Lymphoma, LDH Lactate Dehydrogenase, LTF: Lost to follow up, MCHL: Mixed Cellularity Hodgkin's Lymphoma, N/A:Not Available, n:Number, NSHL: Nodular Sclerosis Hodgkin's Lymphoma.

The 90 months overall survival in 22 patients is 73.5%. (Figure-2)

FIGURE-2

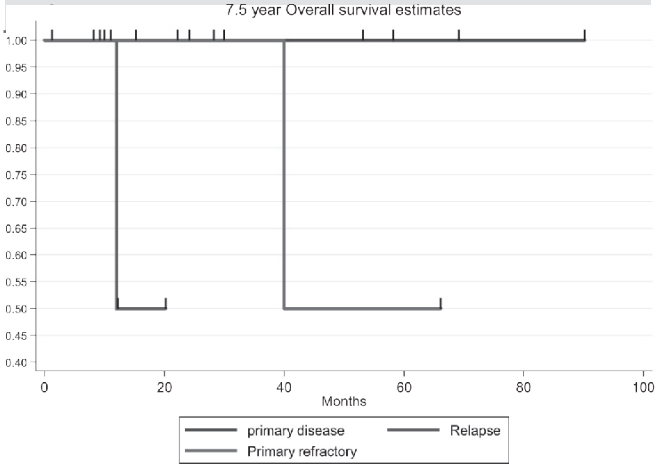
The overall survival of HL patients (n=22).



The 90 months overall survival in primary disease patients was 100%, as 13 (100%) patients were alive at the time of end of the study, while in relapse and refractory group median survival was 12 months and 44 months respectively. (Figure-3) This difference was statistically significant, (log rank test p-value 0.02).

FIGURE-3

The overall survival of relapse/refractory and primary HL



In Relapse/Refractory patients, survival was 0% with a median survival of 12 months in males, while the female patients' consistently demonstrated 100% survival across all groups with a p-value of 0.09. (Table-III)

TABLE-III

Comparison of OS and RFS:

Characteristics		OS (n=22)	P-Value	RFS (n=13)	P-Value	Relapse/Refractory Patients OS (n=9)	P-Value
Gender	Male	53.30%	0.12	80%	0.4	0% (Median=12 Months)	0.09
	Female	100%		0% (Median=Ninety Months)		100%	
B- Symptoms	No	100%	0.6	0% (Median=Ninety Months)	0.7	100% (11 Months Follow Up)	-
	Yes	70%		86%		35.70%	
LDH	<220	100%	0.8	0% (Median=Ninety Months)	0.74	66%	0.8
	>220	68.20%		80%		37.50%	
IPI Score	1			0% (Median=Ninety Months)	0.8		
	3			67%			
Albumin	<4			0% (Median=Ninety Months)	0.48		
	>4			100%			
Stage	Early			100%	0.56		
	Advanced			0% (Median=Ninety Months)			

DISCUSSION

HL is a rare hematological neoplasm, with a diverse clinical and pathological profile depicting variation in the incidence, age, gender distribution and morphology subtypes across the globe. There is a varying age distribution with a documented bimodal peak reported in the western population.[10-12] The first peak is usually around 15-30 years, whereas second peak is around the age of 50-60 years. However, most of the studies done in Asian population reported increased incidence in the younger population.[13,14] Similarly, our study also reported an increased incidence among the younger population.

The reason could be the reduced average life expectancy in this region and socioeconomic and environmental factors, being the reason of this variation from developed world. The gender distribution as reported from the regional data corresponds with increase male to female ratio.[15,16] In this study, we also reported similar finding of male predominance. This could be attributed to the gender discrimination still being prevalent in this part of world and lack of proper care and medical facilities for female population of our society.

The subtype of CHL reported in studies from Pakistan revealed mixed cellularity (MCHL) as a major subtype.[17] Similar findings were reported from India, with MCHL entity in their cohort.[18] Nodular sclerosis (NSHL), being the predominant histological variant in the USA and Europe. Our study population reports an increase incidence of NSHL, which is in contrast with the local data. One of the possibilities of this difference could be the unavailability of histological sub typing in nearly half of our patients.

A pivotal aspect in disease management is accurate staging and prognostication, which guides towards a better disease management plan. Our study population incorporates imaging via PET CT scan and bone marrow biopsy was done in patients who underwent CT imaging instead of PET (i.e. 31.9%).

Our study demonstrates an increased incidence of advanced stage disease (53.8%).Literature have reported similar findings of higher advanced stage diseases prevalence in multiple cohorts.[19,20] The high prevalence of tuberculosis in our region contributes to the misdiagnosis and delayed referral of these patients highlighting the importance of timely diagnosis with proper excision biopsy, and need for the incorporation of better primary care facilities and robust referral system.

ABVD and Escalated BEACOPP have been two chemotherapeutics options utilized in frontline setting for the management of HL worldwide.[21] For limited stage disease, 2-4 cycles of ABVD as per EORTC H10 approach whereas Escalated BEACOPP x 2 plus ABVD X 2 can be used according to GHSG HD17 approach. Number of cycles is guided on the basis of Interim PET imaging. For Advanced stage disease, RATHL approach, starting with ABVD 2 cycles followed by Interim imaging and decision to step down treatment with omission of bleomycin (AVD x 4) or escalation to Escalated BEACOPP is planned. HD 18 approach utilizes Escalated BEACOPP in frontline. Recent updated guidelines from NCCN and American Journal hematology have recommended Brentuximab Vedotin - AVD / Nivolumab – AVD in front line setting for advanced stage disease.[22] Our institutional practice favors ABVD in frontline setting due to familiarity with regimen, good tolerance and mostly outpatient management. In relapse/refractory setting in our cohort, nearly half of our patients receive platinum based regimen, and half of them were able to get immune chemotherapy combinations. We were able to arrange immunotherapy in collaboration with a patient access program, therefore financial burden was minimized. Such programs hold crucial importance as they provide an opportunity for under privileged patients to have an access to recommended line of treatment strategies.

In our cohort, the overall survival (OS) was found to be 73.5%. The 90 months OS in patients who presented with primary disease patients was 100% as all the patients were alive at the time of end of the study. However, in patients with relapse and refractory disease, the OS was 0 % with median survival of 12 months and 44months respectively. The OS reported in our study was comparable to reported national and regional data.[14,23,24] Majority of patients presenting with de novo primary disease were young to middle age which could be the reason

for better OS. A major determinant of better reported outcome could be the absence of infection at disease presentation, as the infection is associated with poor outcomes; its absence allows patients to have better tolerance of treatment. Nevertheless, the poor OS in relapse/refractory patients is in concordance with dismal outcome reported previously. Moreover, we compared different prognostic factor's impact on OS and RFS but none of them was found to have a significant p value. The standard of care for relapse and refractory disease is salvage chemotherapy followed by autologous stem cell transplant (ASCT). In majority of patients, ASCT was hampered on account of financial constraints, limited number of transplant centers in the country and delayed referrals. Therefore, the key lies in early identification of relapse and provision of salvage regimen, and ASCT as soon as remission is achieved.

The study highlights the outcome of HL from a single center in a developing country. However, our study had certain limitations including cross sectional study design from single center, small sample size and unavailability of radiotherapy. Nevertheless, the study demonstrated treatment outcomes at one of the referral hematology center. Previous national studies have reported the demographic characteristics of the disease, however, scarce literature is available on the treatment outcomes and relapse/refractory cases from our region and therefore this was one of the study's strength.

Careful selection of primary treatment regimen keeping in view patient and disease related factors and provision of timely referral system in case of relapse/refractory disease to hematologists is pivotal for definitive management in HL. This requires awareness and collaborative strategies between hematologists, oncologists and referring physicians on the national level. Moreover, in future larger prospective multicenter studies are needed to highlight disease biology and its treatment implications in our part of the world.

CONCLUSION

The study demonstrates the clinical features, demographics and treatment outcomes of HL highlighting the need for careful patient and treatment selection at disease presentation. For relapse/refractory disease timely referral to the hematologist and transplant center is crucial to improve treatment and disease outcomes. In future, larger multicenter national collaborative studies are needed to establish robust outcome inference at national scale.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of NIBD Research Ethics Committee. (NIBD/IRB- 281/01-2025).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Ayaz Asghar:** Manuscript writing.
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3	**Rabeea Munawar Ali:** Critical review.
4	**Aisha Arshad:** Editing.
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6	**Laraib Majeed:** Data collection.
7	**Aisha Jamal:** Writing.
8	**Nida Anwar:** Concept of study, final approval.

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ORIGINAL ARTICLE

The outcome of Sublay vs Onlay mesh hernioplasty in obstructed paraumbilical hernia.

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ABSTRACT… Objective: To compare the results of sublay mesh repair vs onlay mesh repair in patients with obstructed paraumbilical hernia in terms of post operative pain, wound infection and recurrence rates after 2 years. **Study Design:** Comparative prospective study. **Period:** 3 years from 1st January 2022 to 30th December 2024. **Setting:** department of General Surgery of CMA teaching and research hospital which is teaching hospital of Azra Naheed Medical College Lahore Pakistan. **Methods:** Sample size of this study is 112 patients and patients were divided into 2 groups Group A and Group B with 56 patients in each group. Inclusion criteria include all the patients with age between 18 years and 70 years diagnosed with obstructed paraumbilical hernia. Outcomes were measured in terms of post operative pain, wound infection, seroma hematoma formation and recurrence of hernia after 1 and 2 years. All the data was entered and processed by using SPSS 26. **Results:** The most common age group who presented with obstructed paraumbilical hernia is 40 to 49 years of age. post operative pain 24 hours surgery, wound infection after 48 hours of surgery, seroma/hematoma formation 24 hours of surgery and recurrence of hernia after 1 and 2 years is significantly higher in patients who underwent onlay mesh hernioplasty. Post operative pain has no significant relation with diabetic or BMI of patient while wound infection was more in diabetic patients. **Conclusion:** Sublay mesh hernioplasty is superior even for obstructed paraumbilical hernia as compared to onlay mesh repair.

Key words: Hernia, Infection, Onlay, Pain, Recurrence, Sublay.

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INTRODUCTION

Hernia is a common surgical condition characterized by the protrusion of an organ or tissue through an abnormal opening in the body.[1] Among the various types of hernias, paraumbilical hernias, which occur near the navel or umbilicus, are very common, especially in adults. The choice of surgical technique is critical, as it can influence postoperative outcomes, including pain, recurrence rates, and overall patient satisfaction.[2] Two prominent surgical approaches for the repair of paraumbilical hernias are sublay and onlay mesh hernioplasty.

The sublay technique involves the placement of mesh in a retro-muscular position, which is situated behind the rectus abdominis muscle. This approach provides several theoretical benefits, including reduced tension on the abdominal wall, decreased risk of nerve injury, and improved integration of the mesh with the surrounding tissues.[3] Conversely, the onlay technique entails placing the mesh directly on the abdominal wall, above the muscle layer. While this approach is often simpler and quicker to perform, it may also carry a higher risk of complications, such as seroma formation, infection, and increased postoperative pain.[4]

Recent studies have sought to compare the outcomes of sublay and onlay techniques for hernia repair, particularly in the context of obstructed paraumbilical hernias. The use of mesh in the repair of obstructed hernias has frequently been controversial due to the possibility of infections from prosthetic materials. Recent research has proven that biomaterials offer acceptable materials for performing urgent hernia repair. While some research exclusively suggests mesh repair in situations where bowel resection is not necessary, other studies also suggest mesh repair for patients who need colon resection.[5,6]

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Moreover, the impact of patient-related factors, such as body mass index (BMI), comorbidities, and the size of the hernia defect also play important role in the outcomes.[7]

In this study we are going to compare the results of sublay and only mesh hernioplasties exclusively in obstructed paraumbilical hernias in terms of post operative pain, infection and recurrence rates.

METHODS

The general surgery department of CMA Teaching and Research Hospital, a teaching hospital of Azra Naheed Medical College in Lahore, Pakistan, conducted this comparative prospective study. The study ran for three years, from January 1, 2022, to December 30, 2024. With a 90% test power and a 5% level of significance, the sample size of 112 patients (56 in each group) was determined. The mean operative time for the onlay group was 4.4 ± 2.1, while the sublay group's was 3.2 ± 1.4.[8] The formula used was n = Z2 1-α/2 {P1 (1 – P1) + P2 (1 – P2)} / d2. Where Z2 1-α/2 = confidence level 90% = 1.6, P1 = population proportion 1 = 4.4 ± 2.1 and P2 = population proportion 2 = 3.2 ± 1.4 and d = absolute precision = 5.

The sample was gathered using non-convenience probability sampling from among those admitted through the surgical emergency department of CMA Teaching and Research Hospital Lahore, Pakistan, following approval by the Azra Naheed Medical College/CMA Teaching and Research Hospital Institutional Review Board (IRB/ANMC/2021/77-5-8-21). All patients between the ages of 18 and 70 who have been diagnosed with an obstructed paraumbilical hernia by a doctor with more than three years of emergency department experience are eligible to be included. Paraumbilical hernia is defined as presence of swelling in the paraumbilical region distorting the shape of umbilicus. Obstruction is defined clinically as signs of constipation, vomiting, abdominal distension or para umbilical pain with or without fever. Ultrasound abdomen was done in all included patients to assess the size of defect in abdominal wall and contents of hernia sac. All those patients were included in the study in whom small intestine was observed in hernia defect on exploration. Depending upon the condition of small gut, decision of resection of involved gut or reduction of gut back to abdomen was done. Exclusion criteria include patients who were unfit for general anesthesia, recurrent umbilical hernia, non-obstructive paraumbilical hernia and age more than 70 years.

Informed consent of patients was obtained from all the included patients for this study. Basic demographic information of each patient (name, age, sex) was noted.

Patients were divided into 2 groups, Group A and Group B by using lottery method.

Group A patients underwent sublay hernia repair while Group B patients underwent onlay hernia repair. All hernia repair were done by consultant surgeons who had experience of more than 5 years in doing hernia surgeries under general anesthesia. The technique of sublay mesh hernia repair is described by Rhemtulla et al and the technique of onlay mesh hernia repair is described by Kockerling et al.[9,10] Body Mass Index (BMI) was calculated by dividing weight of patient in kilograms by height of patient in meters. HbA1c levels of all patients were done and patients were labelled as Diabetic if their HbA1c levels are more than 6%. Wound infection was defined as developed of skin redness, fever above 100F, pain or purulent discharge from the wound. Recurrence of hernia is defined as development of bulge over the previous hernia site, confirmed by positive cough impulse on standing position and finding of defect in rectus sheath on abdominal ultrasound. Seroma and hematoma formation is the development of fluid collection under the incision site.

The outcomes parameters were measured by post-graduate residents of general surgery who were blinded about group allocation. Intra surgery time was measured in minutes from skin incision till skin closure. Patients were discharged from hospital when hemodynamically stable. Post operative pain was calculated by visual analogue score (VAS) 24 hours after surgery.[11] Patients were discharged from hospital once they were hemodynamically stable with no active compliant after oral diet. Patient were followed after 2 weeks for removal of

skin stiches and then again contacted after 1 year and 2 years for development of any swelling over the incision. Patients who complained regarding any swelling over the incision were called for follow-up and assessed clinically for incisional hernia and further confirmed by abdominal ultrasound to see the defect size.

All the data was entered and processed by using SPSS 26. Quantitative variables like age, intra-operative time and pain score were described by using Mean ± S.D. Gender and development of incisional hernia was described by using frequencies and percentages. Comparison of two groups was done by apply independent sample t-test. A p-value of ≤ 0.05 was considered significant.

RESULTS

Out of total 112 patients included in this study, 83 were females and 29 were male with male to female ratio of 2.8:1. The most common age group who presented with obstructed paraumbilical hernia is 40 to 49 years of age with mean age of patients was 44.7 years with standard deviation of ± 7.8 years. It is clear from Table-I that post operative pain 24 hours surgery, wound infection after 48 hours of surgery, seroma/hematoma formation 24 hours of surgery and recurrence of hernia after 1 and 2 years is significantly higher in patients who underwent onlay mesh hernioplasty. Post operative pain has no significant relation with diabetic or BMI of patient while wound infection was more in diabetic patients while seroma/hematoma formation and recurrence of hernia was more in patients with BMI more than 30.

DISCUSSION

The management of paraumbilical hernias, particularly in the context of obstruction, remains a significant challenge in surgical practice. This study aimed to evaluate the outcomes of two prevalent surgical techniques—sublay and onlay mesh hernioplasty—in patients presenting with obstructed paraumbilical hernias at a tertiary care hospital in Pakistan.

The majority of research in the literature demonstrated that sublay repair was superior to onlay repair in terms of recurrence rates, post-operative pain, and wound infection; however, there are other studies that found no discernible difference in the results of paraumbilical hernias repaired using the sublay or onlay techniques. Both approaches are safe, effective, and associated with comparable rates of complications and recurrence when treating simple paraumbilical hernias, according to a research by Bessa et al.[12]

TABLE-I

Showing number of patients with post operative pain, wound infection, seroma/hematoma formation, recurrence rates after 1 and 2 years. The number and frequency of diabetic patients and patients with increased BMI is also mentioned in this table.

	Group A (Sublay Mesh) (N = 56)	Group B (Onlay Mesh) (N = 56)	P-Value
Post-Operative Pain	7 (12.5%)	12 (21.4%)	
Diabetic	1	2	0.01
BMI > 30	2	3	
Wound Infection	3 (5.35%)	7 (12.5%)	
Diabetic	2	5	0.04
BMI > 30	0	1	
Seroma/Hematoma Formation	2 (3.57%)	9 (16.0%)	
Diabetic	0	2	0.01
BMI > 30	2	5	
Recurrence After 1 Year	0 (0.00%)	4 (7.14%)	
Diabetic	-	0	0.01
BMI> 30	-	3	
Recurrence After 2 Years	2 (3.57%)	3 (5.35%)	
Diabetic	-	-	0.00
BMI> 30	2	3	

Obstructed paraumbilical hernias present unique challenges in surgical management. These hernias are characterized by the incarceration or strangulation of abdominal contents, leading to compromised blood supply and the potential for bowel necrosis.[13] Given the urgency of treating obstructed hernias, the surgical technique must be carefully considered because it can have a substantial impact on patient outcomes. In this particular situation, comparing the safety and efficacy of sublay versus onlay mesh hernioplasty is essential since surgical technique variations may affect the procedure's overall outcome and the incidence of complications.

According to our study's findings, obstructed paraumbilical hernias can be effectively managed using both sublay and onlay procedures, each of which has unique benefits and drawbacks. Postoperative problems like seroma and wound infection were less common with the sublay approach, which places the mesh underneath the fascia. This result is consistent with previous research indicating that sublay hernioplasty may provide superior results because of less strain on the wound and improved mesh integration with surrounding tissues.[14]

The sublay approach's lower complication rate is especially relevant in our setting, where postoperative complications can have a substantial impact on patient outcomes and healthcare expenses, and healthcare resources are frequently few.

Conversely, the onlay technique, characterized by the placement of mesh above the fascia, was associated with a shorter operative time and quicker recovery in our cohort. This finding is consistent with previous studies that have reported similar advantages of onlay hernioplasty.[15] The onlay approach's less intrusive nature, which can enable earlier mobilization and discharge, may be the reason for the faster recovery period. This benefit, though, has to be balanced against the higher risk of complications, including infection, which was noticeably higher in our study's onlay hernioplasty patients. The need for a customized strategy that takes into consideration the risk variables of each patient as well as the particular clinical situation is highlighted by the trade-off between operational time and complication rates.

Furthermore, the surgeon's preference and experience may also have an impact on the surgical procedure selection. It is commonly known that depending on the operating surgeon's competence and experience, surgical results might differ greatly.[16] As a result, it is crucial to take into account each technique's learning curve as well as any potential effects on patient outcomes. In order to reduce complications and maximize recovery, surgeons need to be properly trained in the selected technique.

The impact of postoperative care on surgical outcomes is another important factor to take into account. Regardless of the surgical approach used, a study by Sana et al. showed that patients who got comprehensive postoperative treatment, including pain control and early mobilization, had better recovery trajectories.[17] In order to maximize patient outcomes, this research highlights the significance of a multidisciplinary approach to hernia therapy, combining surgical knowledge with nursing and rehabilitative services. Future research should examine how recovery and complication rates are affected by standardized postoperative protocols, especially in high-risk groups.

It is also important to recognize the limitations of our research. First to draw firm conclusions about the relative efficacy of sublay versus onlay hernioplasty in treating obstructed paraumbilical hernias, prospective randomized controlled trials are necessary. Furthermore, our findings may not be as broadly applicable as they may be due to the relatively small sample size. Confirming our findings and clarifying the long-term effects linked to each approach will require further studies with bigger cohorts and longer follow-up times.

CONCLUSION

With this study it is evident that sublay technique is superior to onlay technique for dealing not with simple paraumbilical hernia but also in obstructed paraumbilical hernias in terms of less post-operative pain, wound infections and recurrences of hernia after 2 years. Post operative pain has no significant

relation with diabetic or BMI of patient while wound infection was more in diabetic patients while seroma/ hematoma formation and recurrence of hernia was more in patients with BMI more than 30.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Ahmed Siddique Ammar:** Data collection, analyzing references.
2	**Mahnoor Masood:** Data entry, critical revision.
3	**Imania Khizar Hayat:** Data collection.
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ORIGINAL ARTICLE

Physiological effects of standard versus gradual pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

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ABSTRACT… Objective: To compare the physiological effects of standard versus gradual open pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. **Study Design:** Prospective Comparative study. **Setting:** Operation Room, Tertiary Care Hospital Jizan, Saudi Arabia. **Period:** Sep 2024 to Aug 2025. **Methods:** Hundred patients recruited for study were randomly divided in two Groups. In Group A, a pressure of 14mmHg was achieved by creating open pneumoperitoneum by CO2 in a standard fashion, while in the intervention Group B, pressure of 5, 10, and 14 mmHg was achieved gradually. At different time intervals, BP, heart rate, SpO2 and EtCO2 were measured. **Results:** Mean heart rate in group A and B was 77.66±8.21and 76.41±7.47 respectively (P-value=0.051). Mean systolic BP in group A and B was 117.7±12.13 and 119.14±7.75 respectively (P-value=0.082). Mean diastolic BP in Group A and B was 77.96±6.45 and 77.38 ± 5.01 respectively (P-value=0.023). Mean SpO2 in group A and B was 99.59 ± 0.53 and 99.6±0.76 (P-value=0.8). Mean EtCO2 in group A and B was 36.86±2.38 and 36.6±2.35 respectively (P-value=0.17). Mean VAS score in group A and B was 2.34±0.72 and 2.06±0.24 respectively (P-value=0.01). In Group A, 13 (26%) patients received injection pethidine due to pain while in Group B only 4 (8%) patients received pethidine (P-value=0.017). **Conclusion:** Gradual open pneumoperitoneum results in more stable physiological and hemodynamic parameters compared to standard rapid open insufflation, without compromising surgical conditions. This is particularly beneficial in patients with cardiovascular compromise.

Key words: Gradual Pneumoperitoneum, Laparoscopic Cholecystectomy, Low-pressure Pneumoperitoneum, Pneumoperitoneum, Standard Pressure.

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INTRODUCTION

Laparoscopic cholecystectomy is presently the gold standard treatment for symptomatic cholelithiasis and is among the most performed laparoscopic procedures globally.[1-2] Compared with open cholecystectomy, it is associated with reduced postoperative pain, shorter hospital stays, earlier return to work, and improved cosmetic outcomes.[3] Despite its clear advantages, the procedure needs the creation of a carbon dioxide (CO_2) pneumoperitoneum, which is not without physiologic changes.

The creation of pneumoperitoneum raises intra-abdominal pressure (IAP), producing a cascade of hemodynamic, respiratory, and metabolic consequences. Increased IAP compresses the inferior vena cava, reducing venous return and preload, while simultaneously elevating systemic vascular resistance (SVR) and afterload.[4] In healthy patients, these changes are well tolerated, but in those with cardiovascular comorbidities, they may result in hemodynamic instability.[5-6] Furthermore, increases in mean arterial pressure, pulmonary artery pressures, and heart rate are observed during standard pneumoperitoneum.[7]

Respiratory dynamics are also altered. Elevation of the diaphragm due to raised IAP reduces thoracic compliance, lowers functional residual capacity (FRC), and increases peak airway pressures.[8] These effects may result in ventilation-perfusion mismatch, hypoxemia, and hypercarbia, particularly in patients with high BMI or chronic respiratory disease.[9] The absorption of CO_2 during pneumoperitoneum further increases hypercarbia and myocardial oxygen demand.[10]

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Given these physiological disturbances, strategies to reduce the adverse effects of pneumoperitoneum have been explored. Among these, the use of low-pressure pneumoperitoneum has been shown to decrease postoperative pain and shoulder tip pain, with some evidence suggesting improved cardiopulmonary stability.[11] However, lower pressures may compromise the operative field and increase difficulty due to inadequate exposure. Another promising approach is the gradual or stepwise insufflation of CO_2 to achieve the required IAP. This technique allows the body to adapt gradually to rising intra-abdominal pressures, potentially minimizing abrupt hemodynamic changes and improving respiratory parameters.[12]

Several studies have investigated the comparative effects of standard rapid versus gradual pneumoperitoneum. One group of researchers concluded that gradual insufflation attenuated increases in heart rate and mean arterial pressure compared with standard rapid insufflation, without increasing operative time.[13] Despite these encouraging outcomes, the available evidence remains limited. In addition, most of these studies have been conducted in mixed laparoscopic procedures, and few have specifically studied laparoscopic cholecystectomy, a procedure in which the duration of pneumoperitoneum is relatively short but widely performed across the globe.

Therefore, further research work is warranted to measure the physiological impact of gradual versus standard pneumoperitoneum in laparoscopic cholecystectomy.

The present study was designed to compare the physiological effects of standard rapid versus gradual pneumoperitoneum in patients undergoing laparoscopic cholecystectomy, with emphasis on hemodynamic and respiratory parameters. We hypothesized that gradual pneumoperitoneum decreases adverse cardiovascular and respiratory changes compared to standard insufflation, without compromising operative conditions.

METHODS

This Prospective comparative study conducted at Operation room, Tertiary Care Hospital Jizan, Kingdom of Saudia Arabia. Hundred patients were recruited for study from Sep 2024 to Aug 2025.

Inclusion Criteria

All patients with symptomatic gallstones, aging between 18 to 65 years, undergoing laparoscopic cholecystectomy with ASA class 1 and 2.

Exclusion Criteria

ASA 3 and above, age >65, bronchial asthma, COPD and coagulopathy.

Patients were enrolled after approval by the hospital ethics committee (JAFH240014), and written informed consent was obtained.

Pre-op assessment was done in clinic by consultant, Patient age, gender, comorbidities, preoperative symptoms, previous surgeries were recorded. Patients fulfilling inclusion criteria were admitted on day of surgery in short stay unit, informed written consent was taken, Injection cefazolin 2 gm will be administered 30 min before making skin incision, four port laparoscopic cholecystectomy was performed by consultant surgeon under general anaesthesia. The patients were randomly assigned two Groups, 50 patients in each, A and B, using Balanced Block Randomization. In the control Group, a pressure of 14mmHg was achieved by creating open pneumoperitoneum by CO2 in a standard fashion, while in the intervention Group B, pressure of 5, 10, and 14 mmHg was achieved gradually at interval of 1 minute. Each patient was assigned a number by the supervisor and recorded. At time zero, before the start of insufflation, Systolic blood pressure (SBP), Diastolic blood pressure (DBP) heart rate (HR), arterial oxygen saturation (SpO2) and end-tidal CO2(EtCO2) were measured and recorded. All patients were positioned in the standard American position (30-degree reverse Trendelenburg and 30-degree left tilt). CO2 gas insufflation was performed in three stages with pressure levels of 5, 10, and 14 mmHg, in Group B, each stage lasting 1 minute. In Group A, only a pressure of 14 mmHg was applied to the patient. After each stage, hemodynamic variables were reassessed at 5,20,40 and 60 minutes. Once the surgery was completed and the surgeon desufflated the intra-abdominal gas, hemodynamic parameters were measured again at the time of extuabation.

According to the visual analogue scale (VAS) system, patients were given a pain score during recovery. Injection Pethidine was administered to patients with VAS 3 or above in recovery.

The data was analyzed using SPSS version 31 software. Continuous variables were expressed as mean± standard deviation (SD) and compared using Student t-test or repeated measures Anova as appropriate. Categorical variables were analyzed with chi-square or Fischer's test. A p-value<0.05 was considered statistically significant.

Based on studies conducted in the past a minimum difference of 10 mmHg in mean arterial pressure was considered clinically significant with standard deviation of 12, power of 80% and $\alpha = 0.05$.[14] The required sample size was calculated as 40 patients per Group. To account for potential dropouts, 100 patients were recruited, 50 in each Group.

RESULTS

Mean age of Group A was 44.10±9.17 years, mean age of Group B was 42.08±8.81 years. Mean age of all patients was 43.09±9.0 years. Difference between two Groups was insignificant as p-value was 0.123.

Female to male ratio was 2.4:1. There was no significant difference between two Groups in terms of gender. Detailed comparison is shown in Table-I below.

TABLE-I

Comparison of gender difference

Group	N	Frequency (%)		P-Value
		Male	Female	
Group A	50	16 (32%)	34 (68%)	0.509
Group B	50	13 (26%)	37 (74%)	

The analysis of heart rate, blood pressure, SpO_2, and $EtCO_2$ revealed that the two groups were largely similar throughout most of the procedure.

No statistically significant differences were found between Group A and Group B in terms of heart rate at any measured time point (all p-values > 0.05).

A single, statistically significant difference in systolic BP was observed at the 5-minute mark, where Group B had a higher mean systolic blood pressure than Group A ($p < 0.001$). At all other times, including for Diastolic BP, there were no significant differences between the groups.

No statistically significant differences were found for oxygen saturation or end-tidal CO_2 at any time point.

The only notable difference was a higher systolic blood pressure in Group B at the 5-minute mark. For all other parameters and time points, the groups were statistically comparable. Please refer to Figure-1 for a graphical representation of these results.

All the data collected at different intervals was combined and analyzed. Detailed results are shown in the Table-II below.

TABLE-II

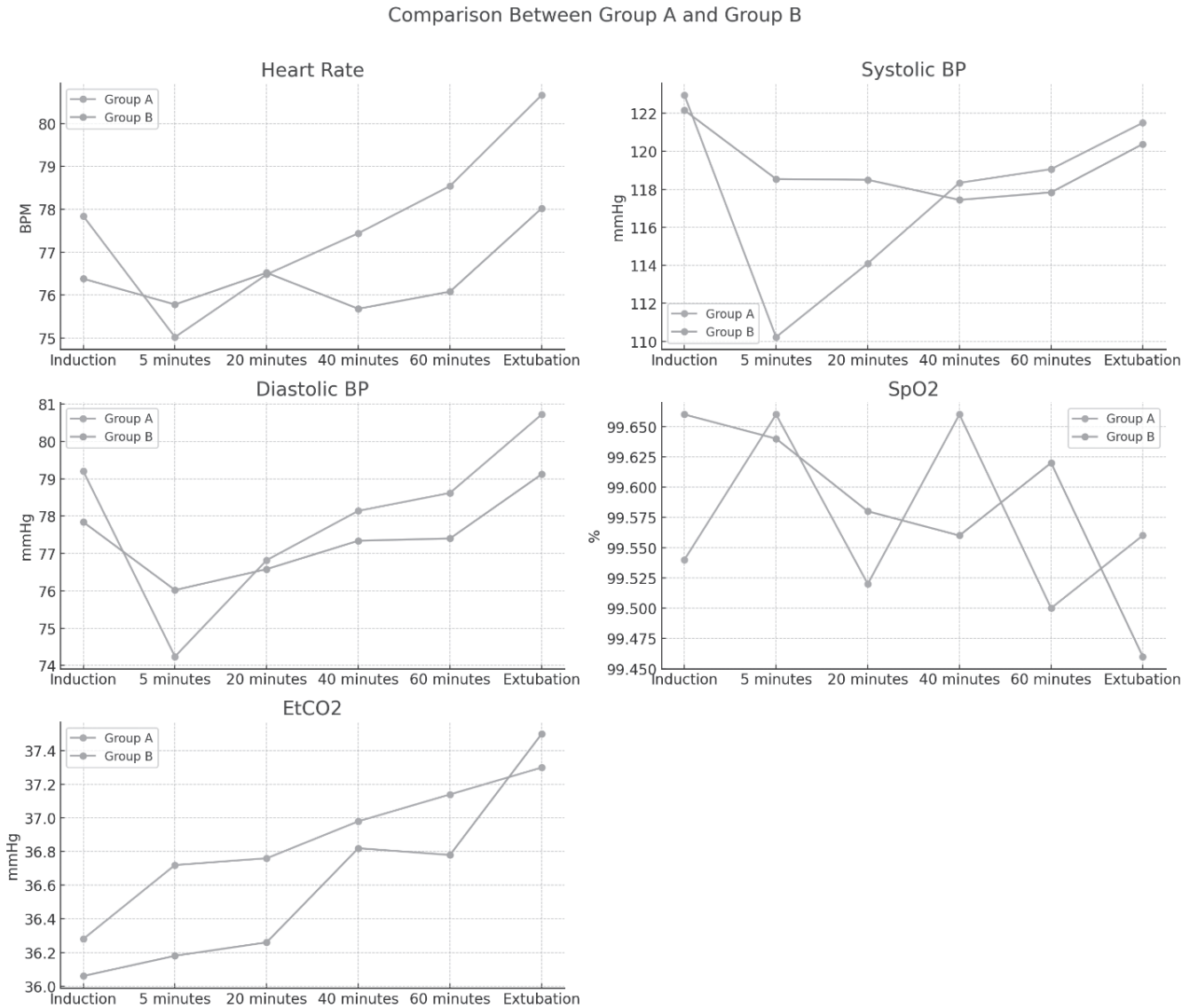
Comparison of hemodynamic and respiratory parameter with all intervals combined

Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	P-Value
Heart Rate (bpm)	77.66 ± 8.21	76.41 ± 7.47	0.051
Systolic BP (mmHg)	117.7 ± 12.13	119.14 ± 7.75	0.082
Diastolic BP (mmHg)	77.96 ± 6.45	77.38 ± 5.01	0.23
SpO_2 (%)	99.59 ± 0.53	99.6 ± 0.76	0.80
$EtCO_2$ (mmHg)	36.86 ± 2.38	36.6 ± 2.346	0.17

In group A, mean score for VAS was 2.34±0.72 while it was 2.06±0.24 for Group B. This difference was significant with p-value of 0.01. In Group A, 13 (26%) patients received injection pethidine due to pain while in Group B only 4 (8%) patients received pethidine, this difference was statistically significant. P-value was 0.017.

FIGURE-1

Comparison of hemodynamic and respiratory parameter at different intervals



DISCUSSION

Cholelithiasis is a significant global health problem affecting large portion of population. Cholelithiasis prevalence is 10-15% in western population and in KSA prevalence is approximately 11.7%.[15-16] This high number of cases lead to increased number of cholecystectomy procedures performed in the Kingdom.[17]

In our study, mean age of Group A was 44.10±9.17, and the mean age of Group B was 42.08±8.81. Mean age of all patients was 43.09±8.99 years. Difference between two Groups was insignificant as p-value was 0.123. These results correspond to studies conducted by Qassem MG et al.[18]

Female to male distribution was 2.4:1 which corresponds to studies conducted by Mirghani HO et al.[19]

In our study, heart rate values at various intraoperative intervals showed comparable trends between the two groups. At induction, both groups demonstrated similar baseline heart rates, and no significant differences were noted at 5, 20, or 40 minutes. Although a modest increase in heart rate

was observed in Group A compared with Group B at 60 minutes, this difference reached statistical significance (p = 0.048) but was not considered clinically meaningful. At extubation, heart rates again showed no significant difference between the groups. Overall, the hemodynamic response in both groups remained stable, and no persistent intergroup differences were observed. In A study conducted by Marimuthu et al. mean heart rate was significantly higher in high pressure pneumoperitoneum than low pressure pneumoperitoneum.[20] In their study this difference was due to reason that there was significant IAP difference between two methods but in our study this difference only at the start of the procedure as later there was no pressure difference.

In the present study, systolic blood pressure (SBP) differed significantly between the two groups at 5 minutes and 20 minutes following induction. Group A demonstrated a lower mean SBP compared with Group B at both intervals ($p < 0.001$ and $p = 0.030$, respectively). However, at subsequent time points no significant differences were observed, indicating that the early changes were transient. This initial reduction in SBP in Group A may be explained by the sudden increase in intra-abdominal pressure (IAP), whereas in Group B, the gradual elevation in IAP appeared to attenuate abrupt hemodynamic fluctuations. Similar to our findings, Ahila et al reported that patients in gradual pressure CO_2 pneumoperitoneum group patients had more stable systolic blood pressures during early intraoperative periods compared to the standard-pressure group, suggesting the rise in IAP dynamics plays a key role in BP fluctuations.[21]

Mean Diastolic Blood Pressure difference was insignificant at the start of the procedure. Mean Diastolic Blood Pressure at 60 minutes for Group A was 79.44±4.210 mmHg and Group B was 77.40±4.673 mmHg. P-value was0.012. Mean Diastolic Blood Pressure at the time of extubation for Group A was 80.72±5.099 mmHg and Group B was 79.12±4.835 mmHg. The results of our study were like study conducted by Küçüköztaş et al.[22]

SPO2 measurement showed insignificant differences at all intervals. Similar results were shown by study conducted by Oncu et al.[23]

$EtCO_2$ measurements in our study showed no significant differences between the two groups at any of the recorded intervals, indicating that both groups maintained comparable ventilatory status throughout the procedure. Similarly, in a study conducted by Marimuthu et al, no significant variation in $EtCO_2$ levels was observed between groups, further supporting the finding that pneumoperitoneum technique does not markedly affect end-tidal CO_2 when ventilation is adequately controlled.[24]

In our study, we found out that VAS score was significantly higher in group A (2.34±0.72) as compared to group A (2.06±0.24) with p-value of 0.01. Resultantly significantly lesser number of patients required the rescue analgesia in group B [4 (8%) vs 13 (26%)] with p-value of 0.017. This difference of pain and increased analgesia required in group A could be due to sudden stretch of the peritoneum. Similar results were observed in a study conducted by Rosenberg. On the other hand, Chang W et al in their study concluded that the pneumoperitoneum pressure does not significantly affect the post-operative pain.[25]

CONCLUSION

Gradual open pneumoperitoneum results in more stable physiological and hemodynamic parameters compared to standard rapid open insufflation, without compromising surgical conditions. This is particularly beneficial in patients with cardiovascular compromise.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Comparative study of Lichtenstein and darn repair surgery in obstructed hernia repair.

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ABSTRACT… Objective: To compare postoperative outcomes between Lichtenstein and Darns repairs in obstructed inguinal hernias. **Study Design:** Prospective quasi-experimental study. **Setting:** General Surgery Department, Arif Memorial Teaching Hospital. **Period:** September 2023 to February 2024. **Methods:** Sixty patients with obstructed inguinal hernia were recruited through non-probability purposive sampling and non-randomized into two groups of 30 each. Group 1 underwent Lichtenstein repair, while Group 2 underwent Darn repair. Postoperative pain, wound infection, seroma formation, and recurrence were assessed over a 6-month follow-up. Data were analyzed using SPSS version 25, applying independent t-tests and likelihood ratio tests, with $p \leq 0.05$ considered significant. **Results:** The mean age was 43.5 ± 11.6 years in the Lichtenstein group and 42.8 ± 10.4 years in the Darn group ($p = 0.797$). Seroma formation was noted in 13.3% of Lichtenstein versus 23.3% of Darn repairs, postoperative pain in 36.7% versus 46.7%, and wound infection in 10% versus 16.7%. No recurrences were observed during follow-up. None of the outcome differences were statistically significant ($p > 0.05$). **Conclusion:** Lichtenstein and Darn repairs demonstrated comparable short-term outcomes in obstructed inguinal hernia. Lichtenstein repair remains preferable where mesh is available, while Darn repair provides a suitable alternative in settings with limited resources.

Key words: Hernia, Inguinal, Postoperative Complications, Seroma, Treatment Outcome.

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INTRODUCTION

An organ or portion of an organ that protrudes or shifts through the wall that typically surrounds it is called a hernia. This protrusion originates via the inguinal canal when there is an inguinal hernia. The most frequent cause for which primary care physicians refer patients for surgery is a groin hernia.[1]

Inguinal hernias occur more frequently in men; while the diagnosis is usually straightforward on physical examination in male patients, ultrasonography is often required for accurate detection in women.[2] Approximately 75% of all abdominal wall hernias occur in the groin, making it the most frequent site for such defects.[3]

Mesh repair has been shown to reduce recurrence rates in incarcerated and strangulated groin hernias without significantly increasing postoperative complications, and it is recommended in clean cases. However, when bowel resection is required, the use of mesh may increase the risk of surgical site infection.[4]

Several perioperative factors, such as inadequate surgical technique, low surgical volume, limited operator experience, and the use of local anesthesia, have also been identified as risk factors for recurrence and should be taken into account when treating inguinal hernia patients. The Lichtenstein technique involves placement of a polypropylene mesh between the inguinal floor and the external oblique aponeurosis. This tension-free method avoids reliance on weakened tissues and eliminates the need for tension sutures. During straining, contraction of the external oblique muscle exerts counterpressure on the mesh, thereby utilizing intra-abdominal pressure to support the repair.[5,6]

Based on best practices, ten specific recommendations have been proposed for the

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Lichtenstein method: detailed neuroanatomical assessment, prevention of chronic pain, selective neurectomy, careful handling of spermatic cord structures, evaluation of the femoral canal, appropriate hernia sac management, optimal mesh selection, secure fixation, recurrence prevention strategies, and appropriate postoperative care.[7] Darn repair demonstrated benefits in resource-constrained settings, with fewer challenges, shorter hospital stays, and reduced expenses, making it a viable option where mesh is not easily accessible, even if both techniques produced comparable recurrence rates.[8]

Although both mesh-based and tissue-based techniques achieve comparable recurrence rates, Darn repair has certain advantages in resource-limited settings. It is associated with fewer complications, shorter hospital stays, and reduced overall costs, making it a viable alternative when mesh is unavailable.[8] Conversely, while the Lichtenstein repair is superior to Darn repair in terms of long-term recurrence prevention, it has been reported to require greater postoperative analgesic use, longer hospital stays, and slightly higher rates of superficial surgical site infections.[9]

The present study is designed to compare Lichtenstein mesh repair and Darn repair in patients with obstructed inguinal hernia, focusing on postoperative outcomes including pain, wound infection, seroma formation, and recurrence.

METHODS

This comparative, prospective, quasi-experimental study was conducted in the Department of General Surgery, Arif Memorial Teaching Hospital, Lahore, between September 2023 and February 2024, following approval from the hospital's Ethical Review Committee (Reference No. IRB/2023/192, dated September 10, 2023). Patients were recruited using a non-probability purposive sampling technique, and those fulfilling the eligibility criteria were enrolled after obtaining informed consent. The inclusion criteria consisted of adult patients aged 18–65 years with a diagnosis of primary inguinal hernia who were medically fit for elective surgery. Patients with recurrent or bilateral hernia, complicated hernias such as strangulated or obstructed types, significant systemic comorbidities including uncontrolled diabetes, coagulopathy, chronic liver or kidney disease, and those unwilling or unable to complete follow-up were excluded from the study. A total follow-up period of six months was maintained for each participant.

Eligible patients were divided into two equal groups. Group 1 underwent Lichtenstein tension-free mesh repair, in which a 6 × 11 cm polypropylene mesh was trimmed to size and sutured in place over the defect. Group 2 underwent Darn repair, in which the posterior wall of the inguinal canal was reconstructed using a continuous nylon 1 suture from the pubic tubercle to the internal ring and back. All patients were admitted postoperatively for 2–3 days and subsequently discharged once stable. Follow-up evaluations were scheduled at one week, two weeks, one month, three months, and six months to monitor outcomes, including seroma formation, wound infection, and postoperative pain.

Data were collected on a predesigned proforma and analyzed using SPSS version 25. Continuous variables such as age were compared between groups using the independent samples t-test. Categorical variables, including wound infection, seroma, and postoperative pain, were analyzed using the likelihood ratio test. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The study included 60 patients in total, allocated equally between the two surgery groups: 30 had Darn repair, and 30 had Lichtenstein repair. The average age of the patients in the Darn group was 42.8 ± 10.4 years, whereas the patients in the Lichtenstein group were 43.5 ± 11.6 years. Comparability at baseline was confirmed by the fact that the mean age difference was not statistically significant (p = 0.797).

TABLE-I

Surgical group distribution

Surgical Group	Frequency	Percent (%)
Lichtenstein repair	30	50.0
Darn repair	30	50.0

TABLE-II

Combined outcomes including seroma, pain, wound infection:

Outcome Type	Time Point	Lichten-stein (n=30)	Darn (n=30)	P-Value
Seroma	1 week	1 (3.3%)	1 (3.3%)	1.000
	2 weeks	2 (6.7%)	3 (10%)	0.640
	1 month	1 (3.3%)	3 (10%)	0.301
Pain	1 week	5 (16.7%)	7 (23.3%)	0.519
	2 weeks	2 (6.7%)	2 (6.7%)	1.000
	1 month	4 (13.3%)	5 (16.7%)	0.718
Wound Infection	1 week	2 (6.7%)	3 (10%)	0.640
	2 weeks	0 (0%)	1 (3.3%)	0.313
	1 month	1 (3.3%)	1 (3.3%)	1.000

DISCUSSION

In this prospective comparison of Lichtenstein mesh repair and Darn suture repair involving 60 patients, we found that short-term complication rates (seroma, postoperative pain and wound infection) were slightly higher in the Darn group than in the Lichtenstein group. Still, none of these differences reached statistical significance. Overall trends in our cohort consistently favored the Lichtenstein technique, with fewer early complications, although the absolute differences were small.

These results are broadly consistent with the recent body of evidence comparing mesh (Lichtenstein) and non-mesh (various tissue/darning) techniques. Systematic reviews and rapid reviews of mesh versus non-mesh groin hernia repair report that mesh repair achieves lower recurrence rates, while safety outcomes (early complications such as seroma, hematoma, infection and short-term pain) are similar between groups. This supports our observation that early complication profiles are comparable even when recurrence outcomes (which require longer follow-up) tend to favour mesh.[10]

Several randomized and prospective comparative studies have similarly reported that early postoperative outcomes—operative time, early pain, wound complications—can be comparable between selected non-mesh techniques (including modified Darn techniques) and Lichtenstein repair. For example, randomized trials and single-center prospective studies have reported no significant differences in early morbidity between Lichtenstein and modified Darn/other tissue techniques, though study sizes are often modest and follow-up durations are limited. Our findings of no statistically significant differences in 1-month complications align with these reports.[11]

That said, larger observational studies and recent comparative analyses emphasize important context for technique selection. Several recent retrospective cohorts and comparative series report that darn (or other non-mesh) repairs remain a reasonable option in resource-limited settings, offering lower immediate cost and acceptable short-term results; these reports caution that long-term recurrence and chronic pain data remain less complete and often underpowered. Our study's short follow-up (1 month) cannot address late recurrence or chronic groin pain, which are key outcomes when comparing mesh and non-mesh techniques.[12]

Mesh-based tension-free procedures (like Lichtenstein) are still recommended by bigger syntheses and guidelines bodies as the first-line open approach for primary inguinal hernia repair due to their consistent long-term follow-up recurrence reductions. The Hernia Surgery guidelines and updated reviews recommend mesh repair in most adult patients where resources and patient/surgeon factors permit, while recognizing that tissue repairs have a role when mesh is contraindicated or unavailable. Thus, while our short-term results show clinical equipoise for early complications, the wider literature and guidelines favor Lichtenstein when considering the full spectrum of outcomes, particularly recurrence.[13]

Chronic postoperative pain is another important outcome where the literature is mixed. Some analyses report no major difference in chronic pain between mesh and non-mesh repairs, whereas others note that technique, fixation method, and patient factors (age, nerve handling, fixation sutures) influence long-term pain. Because chronic pain typically manifests or persists beyond the early postoperative period, our study's 1-month window is insufficient to conclude chronic groin pain and

should be interpreted cautiously. Future surveillance of our cohort at 6–12 months (and beyond) would be essential to assess this outcome.[14]

Strengths of our study include prospective data collection and balanced allocation by surgical group, which reduced baseline confounding (age was similar between groups). The study limitations include the comparatively small sample size and shorter follow-up focused on early postoperative complications; consequently, the study is underpowered to detect small differences and cannot address recurrence or chronic pain. Finally, heterogeneity in non-mesh techniques reported in the literature (modified Darn, Moloney-type Darn, Desarda, Shouldice variants) complicates direct comparisons — many published non-mesh series use different technical modifications that may affect outcomes.[15]

CONCLUSION

Both Lichtenstein and Darn repairs for inguinal hernia demonstrated comparable short-term outcomes in terms of seroma formation, wound infection, and postoperative pain. Although complication rates were slightly higher in the Darn group, these differences were not statistically significant. Lichtenstein repair, being a tension-free mesh technique, remains the preferred option when mesh is available, as it provides stable outcomes and is associated with lower recurrence rates in long-term studies. However, Darn repair continues to be an acceptable alternative in resource-limited environments where mesh use may not be feasible. Further, studies with larger sample sizes and long-term follow-up are recommended to better assess recurrence rates and chronic pain outcomes between these two techniques.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Frequency of Hypoxia in patients handed over between operating room team and post anesthesia Care Unit team using PATH (Post-Anesthesia Team Handover) Checklist.

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ABSTRACT… Objective: To determine the frequency of hypoxia in patients handed over from Operating Room (OR) team to Post-Anaesthesia Care Unit (PACU) team using Post-Anesthesia Team Handover (PATH) checklist. **Study Design:** Observational Study. **Setting:** Department of Anesthesiology & Pain Medicine, Shifa International Hospital. **Period:** 6 months from 25th March 2025 to 25th September 2025. **Methods:** A total of 2016 patients were included. Data was collected for Pre and Post Implementation phase when patients were handed over using institutional practices and PATH Checklist respectively. Frequency of hypoxia was noted as primary outcome. Data was entered and analyzed using SPSS v27.0. **Results:** Mean SpO2 was 94.0±4.7% in Pre Implementation phase in contrast to 94.9±2.9% in Post Implementation phase. Frequency of Hypoxia was noted to be 11.2% during the whole study period. Before implementation of PATH Checklist, it was 16.2% while after implementation of PATH Checklist for handover in PACU, it was reduced to 6.9%. The decline in frequency of hypoxia was statistically significant. (p<0.001). **Conclusion:** Use of PATH checklist significantly reduces frequency of Hypoxia in PACU.

Key words: Handover, Hypoxia, PACU, PATH Checklist, Recovery.

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INTRODUCTION

Patient handovers between various departments in a hospital like Operation Room (OR), Intensive Care Unit (ICU) and Post Anesthesia Care Unit (PACU) is a routine matter.[1]

Effective communication between healthcare professionals during handover and transfer of complete relevant information ensures patient safety.[1] The consequences of mid-surgery handovers from one anesthesiologist to other have been attributed to increased risk of perioperative complications, morbidity and even mortality.[2]

Therefore, different techniques and checklists for effective handover from anesthesiologist to anesthesiologist during surgery, OR Team to PACU Team and OR Team to ICU Team have been proposed.[3] In fact, implementation of standard handovers improves caregiver involvement, reduce omission of critical information without affecting time commitment.[4]

Various Handover patterns like SBAR (Situation-Background-Assessment-Recommendation)[5], iSoBAR (Identify-Situation-Observations-Background-Agreed plan-Read back)[6], COLD (Connect-Observe-Listen-Delegate).[7] ABCDEFP (Airway-Breathing-Circulation-Disability-Exposure-Focus-Plan)[7] and PATH checklist (Post-Anesthesia-Team-Handover) have been proposed.[8] Standardization of handover like in PATH checklist, not only ensures effective communication but also improves nurse's satisfaction and patient outcomes like incidence of post-operative hypoxemic events. The frequency of hypoxia in PACU has been reported to be 4.1% in patients handed over with conventional techniques while 0.8% in patients handed over using PATH checklist.[8]

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While that study advocates effectiveness of PATH checklist in terms of hypoxia in PACU, yet it's the only study of its kind that has implemented the checklist in Pre and Post implementation study design.

Hence the role of PATH checklist in reduction of post-operative adverse events like hypoxemia is still understudied. Therefore, the objectives of this study were to determine the frequency of hypoxia in patients handed over from Operating Room (OR) team to Post Anaesthesia Care Unit (PACU) team using Post-Anaesthesia Team Handover (PATH) checklist at a tertiary care teaching hospital.

METHODS

This observational study was conducted in Department of Anesthesiology & Pain Medicine, Shifa International Hospital for a period of 6 months from 25th March 2025 to 25th September 2025 after ethical approval from Institutional Review Board of Shifa International Hospital (IRB# 494-24) and College of Physicians & Surgeons of Pakistan (CPSP/REU/ANS-2022-250-2861)

Frequency of hypoxia in patients handed over using PATH checklist has been reported to be 0.8%.[8] WHO sampling size calculator was used to calculate sample size using population proportion of 0.008 with Confidence level set at 95% and Precision required to be 0.004%. The sample size was calculated to be 1906.

However a total of 2016 patients were included using Non-probability consecutive sampling technique during the pre and post implementation study period. Patients of age 18-70, American Society of Anesthesiology (ASA) Status 1-4 undergoing surgeries in General Anesthesia, Regional Anesthesia and Monitored Anesthesia Care were included. However, based on history, physical examination and medical records, patients preoperatively diagnosed as cases of acute or chronic respiratory disease, patients either preoperatively or post operatively on ventilator as they were directly shifted from OR to ICU and not stationed in PACU and patients with excessive shivering as shivering interferes with breathing pattern were excluded. Data was collected for Pre-Implementation phase when patients were handed over using institutional practices. Hypoxia was noted as primary outcome. A series of educational sessions were conducted for attending anesthesiologists, operating room anesthesia practitioners, nursing team and PACU Team regarding implementation of PATH checklist. In post implementation phase, patients were handed over from Operating Room Team to PACU team using PATH[8] checklist which includes completion of urgent tasks before verbal handoff, determination of readiness of in-charge of team, general condition, patient identity, known allergies, relevant history, type of surgery, anesthesia, ASA score, positioning, airway management, vascular access, fluid management, intraoperative events, medications for analgesia, anti-emesis, paralysis, important laboratory values along with post-operative concerns, do's and don'ts. The verbal handover ended with closure of loop of communication.

Oxygen Saturation (SpO2) was measured using Pulse Oximeter placed on index finger of the arm other than the one with blood pressure monitoring cuff. It was ensured that the hand with pulse oximeter is under blanket with warmer on so as to minimize artifacts. Accurate finger plethysmograph was used to confirm correct placement and reliability of pulse oximeter. Incidence of Hypoxia i.e., SpO2<90% for more than 30 seconds during post-operative period was considered the primary outcome of this study.

Patient ASA score, type of surgery, minimum SpO2 recorded and Frequency of Hypoxia were noted. Independent observer monitored patient primary outcome i.e., hypoxia. The data was collected for post implementation phase as well.

When patients became hypoxemic, oxygen therapy was initiated along with optimization of patient position. Moreover, attending anesthesiologist assessed underlying cause of hypoxia and addressed accordingly.

Data was entered and analyzed using SPSS v27.0. Frequencies and Percentages were calculated for qualitative variables like ASA score, type of surgery and frequency of hypoxia. Mean and Standard Deviation was calculated for quantitative variables like minimum SpO2. Frequency of hypoxia was

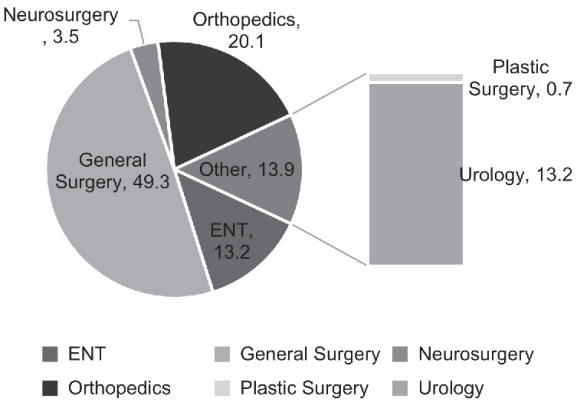
stratified for pre and post implementation phase and ASA Status. Post stratification chi-square test was applied, p-value ≤0.05 was considered statistically significant.

RESULTS

A total of 2016 patients were included in the study. 770 (38.2%) patients were ASA I, followed by 686 (34.0%) patients with ASA II and 560 (27.8%) patients with ASA III status. Majority of patients underwent General Surgical procedures followed by Orthopedics, Urology, ENT, Neurosurgery and Plastic Surgery. The distribution of patients as per surgical procedures performed is shown in Figure-1.

FIGURE-1

Percentage distribution of various procedures performed



Mean SpO2 was 94.0±4.7% in Pre Implementation phase in contrast to 94.9±2.9% in Post Implementation phase. Frequency of Hypoxia was noted to be 11.2% during the whole study period. Before implementation of PATH Checklist, it was 16.2% while after implementation of PATH Checklist for handover in PACU, it was reduced to 6.9%. The decline in frequency of hypoxia was statistically significant. (p<0.001)

Further stratification for ASA Status of was performed. Hypoxia was more commonly reported in patients with ASA III status as compared to ASA I and ASA II patients in pre-implementation phase. However, ASA Status was not associated with frequency of hypoxia in post-implementation phase. (P=0.012, p=0.905 respectively). Table-I

DISCUSSION

The role of a standardized checklist and handover tool in terms of improvements in patient outcomes, minimized information loss, reduction in morbidity and mortality has been well established with the global acceptance of WHO Safe Surgical Checklist that efficiently covers perioperative care.[9-11] Yet, the process of handover from operating room team to PACU team is overlooked by many esteemed patient safety and quality measures.

It's quite evident that there is a significant reduction in frequency of hypoxia noted in Post Anaesthesia Care Unit after implementation of PATH checklist for handover. The results of present study suggest that with PATH checklist hypoxia was noted in 6.9% of patients in comparison to 16.2% prior to its application. These results are in coherence with Jaulin et al who reported a decline from 4.1% to 0.8% with use of PATH checklist. The improvement in patient outcomes is prominent in both studies. However, the difference in pre and post implementation incidence of 16.2% and 6.9% in comparison to 4.1% and 0.8% (Jaulin et al.) could be attributed to differences in setting and types of surgical procedures performed.[8] The present study has highlighted various surgical interventions performed as well.

The role of PATH checklist in terms of hypoxia has also been investigated by Astilia et.al., A Quasi experimental study was conducted comparing PATH checklist with SBAR technique.

TABLE-I

Stratification of incidence of hypoxia in both phases in terms of ASA Status of patients

		Pre-Implementation			Post Implementation		
		ASA I	ASA II	ASA III	ASA I	ASA II	ASA III
Hypoxia	Absent	88.0%	81.8%	80.0%	93.3%	92.6%	93.3%
	Present	12.0%	18.2%	20.0%	6.7%	7.4%	6.7%

It's been reported that hypoxia was noted in 41.2% patients in intervention group (PATH) compared to 73.5% in control group. These outcomes are significantly higher than present study. However the significant improvement with utilization of PATH checklist is comparable. Moreover, we chose to conduct Pre and Post implementation study compared to experimental research on purpose as authors believed that it's practically not possible to segregate study groups as same staff and team members are working over the course of study duration. If parallel groups are carried out in same frame of time, the overlap of components of both tools was rendered unavoidable.[12]

The higher frequency of hypoxia in ASA III patients in pre implementation phase is consistent with findings of Tang et.al., who identified higher ASA status as a risk factor of hypoxia in PACU. With implementation of PATH checklist, it was noted in present study that patient's ASA status was not found to be associated with frequency of hypoxia which can be explained by the enhanced confidence and approach of attending nurse in PACU in terms of patient management owing to better transfer of information.[13]

Bang et.al., reports post-operative hypothermia and major abdominal surgeries as significant risk factors for hypoxia and failed weaning off oxygen in PACU. It should be highlighted that present study excluded patients with post-operative shivering but patients with all kinds of surgeries were included.[14]

Up to 14% of PACU related events have been attributed to communication errors.[15] Anesthesia Patient Safety Foundation (APSF) recommends standardized handovers during perioperative period.[16] With conventional handover techniques, loss of information regarding vital factors is well documented.[17] In fact, standardized handovers in pediatric population has been shown to effectively reduce communication errors in PACU.[18] Moreover, a standardized tool adds on to staff satisfaction as well.[19]

Authors believe that this study lacks details pertaining to nurse's satisfaction, quality of handover, improvement in loss of information and other patient related outcomes in PACU. Although it's a larger scale study in comparison to studies done before, yet, multi-centered studies need to be conducted to validate utilization of PATH checklist.

CONCLUSION

Utilization of PATH checklist for handover from Operating Room to PACU significantly reduces the frequency of hypoxia.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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3	**Muhammad Hussan Farooq:** Research methodology.
4	**Maria Yaqub:** Data collection.
5	**Zeeshan Asif Kayani:** Data analysis.
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ORIGINAL ARTICLE

Risk of deep venous thrombosis in abdomino pelvic surgeries.

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ABSTRACT… Objective: To determine the frequency and associated risk factors of deep venous thrombosis (DVT) among patients undergoing abdomino-pelvic surgeries and to evaluate their risk stratification according to the American College of Chest Physicians (ACCP) guidelines. **Study Design:** Descriptive Case Series. **Setting:** Surgical Unit, Hayatabad Medical Complex (HMC), Peshawar, Pakistan. **Period:** 1st July 2021 to 31st December 2021. **Methods:** A total of 174 hospitalized patients aged 15–70 years with duplex ultrasound–confirmed lower limb DVT were enrolled through consecutive convenience sampling. Patients with chronic or ambiguous DVT findings were excluded. Data on demographics, clinical characteristics, comorbidities, mobility, hospital stay, and surgical details were recorded. Risk stratification was performed as per ACCP guidelines into low, moderate, high, and very high-risk groups. Data were analyzed using SPSS version 22, applying chi-square tests for associations, with $p \leq 0.05$ considered statistically significant. **Results:** Among 174 patients, the majority were males (62.1%) with a predominant age group of 41–50 years. High and very high-risk categories accounted for 40.8% and 37.4% of patients, respectively. Obesity (33.3%), limited mobility (72.4%), and comorbidities (66.1%) were the most significant risk factors. Statistical analysis revealed strong associations between DVT risk level and age ($p < 0.001$), BMI ($p = 0.001$), comorbidities ($p < 0.001$), and mobility status ($p < 0.001$). Most patients (72.4%) had a hospital stay of ≤7 days, and 89.1% underwent surgeries lasting ≤1 hour. **Conclusion:** DVT risk in abdomino-pelvic surgical patients is strongly associated with age, obesity, immobility, comorbidities, and prolonged hospitalization. Regular risk assessment and adherence to thromboprophylactic guidelines are essential to reduce preventable morbidity and mortality.

Key words: Abdomino-pelvic Surgery, ACCP Guidelines, Deep Venous Thrombosis, Risk Stratification, Surgical Patients, Thromboprophylaxis.

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INTRODUCTION

Blood inside the vessels usually does not clot normally due to the body's natural defence system against clotting i.e. thrombomodulin, anti-thrombin III, protein C, protein S, smooth walls of the vessels and regular smooth flow of blood. Virchow in 1920s explained that blood clots inside the vessels leading to thrombus formation due to three factors which are known as the Virchow's Triad, i.e. changes in the blood vessel endothelium, changes in the blood flow, and changes in the composition of the blood chemistry. Any change in the defence mechanism leads to deep venous thrombosis (DVT).[1] The signs and symptoms of DVT include erythema of the limb or area at which the clot occludes the vessel, localised pain, oedematous swelling, prominent veins (non-varicose) and palpable veins etc.[2] Literature search on DVT risk factors highlights increasing age, immobilisation, active rheumatologic disease, acute myocardial infarction (AMI), arterial insufficiency, cancer, central catheters, hormone therapy, congestive heart failure, cerebrovascular accidents, infection, surgical procedures, inflammatory bowel disease, nephritic syndrome, obesity, paresis of legs, severe respiratory diseases, thrombophilias and varices/chronic venous insufficiency.[3] The number of people affected by DVT, according to the Centre of Disease Control (CDC) ranges from 60,000 to 100,000 each year in the United States alone.[4] The SMART study concluded that DVT prevalence and mortality rate is also not low in the Asian countries.[5] Less work has been done so far in Pakistan on conditions involving DVT or embolism.[6,7]

The study showed that these patients were at moderate risk of DVT according to accepted criteria a 15%incidence and these findings are now reflected in the American College of Chest Physicians and International Consensus Statements that recommend thromboprophylaxis.[8,9]

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The present study was conducted to determine the dominating risk factors to help in the prognosis of the disease. The current study is aimed to know the measures taken for prevention of this major preventable cause of death in a teaching hospital of Peshawar. Also to do the risk assessment and type of prophylaxis given to the hospitalized patients in a tertiary care hospital and compare with their requirements according to the American College of Chest Physicians (ACCP) guideline for DVT.

METHODS

This descriptive case series was conducted from 1st July 2021 to 31st December 2021 in the Surgical Unit at Hayatabad Medical Complex (HMC), Peshawar after taking approval from ethical board (REU: 44093). The primary objective was to determine the frequency of risk stratification among hospitalized patients diagnosed with Deep Venous Thrombosis (DVT).

The sample size was calculated using the WHO sample size calculator, assuming a 15% proportion of patients at moderate risk of DVT, with a 95% confidence interval and 5% margin of error [9]. A total of 174 patients were included using consecutive convenience sampling.

Inclusion Criteria

Hospitalized patients aged between 15 and 70 years with a diagnosis of DVT of the lower extremities confirmed via duplex ultrasound.

Exclusion Criteria

Patients with chronic DVT (duration >3 months), unclear duplex reports, or contradictory duplex findings were excluded.

Data collection was initiated after obtaining approval from the institutional ethical and research review board. Eligible patients who met the inclusion criteria were invited to participate after written informed consent was obtained. Data were recorded using a structured proforma, which captured demographic details (name, age, gender, height, weight), clinical characteristics (diagnosis, operative status, co-morbidities, duration of hospital stay and surgery, ambulatory status), and DVT risk factors. Risk stratification was conducted according to the American College of Chest Physicians (ACCP) guidelines, categorizing patients into low, moderate, high, and very high-risk groups.

The data were analyzed using SPSS version 22. Descriptive statistics were computed for all variables. Quantitative variables (age, height, weight, hospital stay, and surgery duration) were presented as mean ± standard deviation. Qualitative variables (gender, ambulatory status, procedure type, risk factors, and risk stratification) were expressed as frequencies and percentages. Stratification was performed for age, gender, height, weight, duration of hospital stay and surgery, and ambulatory status to assess effect modification. Post-stratification, the chi-square test was applied. A p-value ≤ 0.05 was considered statistically significant. Results were displayed in tabular and graphical formats.

RESULTS

The study population comprised 174 patients. The majority were between 41–50 years of age, accounting for 74 (42.5%) individuals. This was followed by those aged 51–60 years with 53 (30.5%), and 31–40 years with 29 (16.7%). Fewer patients belonged to the 61–70 years group, 12 (6.9%), and the 18–30 years group, 6 (3.4%). Regarding gender distribution, males predominated with 108 (62.1%), while females comprised 66 (37.9%). Risk stratification revealed that a considerable proportion of patients were in the high-risk category, 71 (40.8%), followed closely by the very high-risk group, 65 (37.4%). Moderate risk was noted in 21 (12.1%) patients, and a smaller proportion, 17 (9.8%), were classified as low risk. Most patients presented with a disease duration of ≤ 3 months, 122 (70.1%), while 52 (29.9%) had symptoms for more than 3 months. The distribution of BMI categories showed that 73 (42.0%) were overweight and 58 (33.3%) were obese. Normal BMI was observed in 38 (21.8%), and underweight individuals comprised only 5 (2.9%). Mobility status varied across the cohort, with 72 (41.4%) being minimally mobile and 54 (31.0%) bed bound. Additionally, 42 (24.1%) were partially mobile, while only 6 (3.4%) were fully mobile. A significant number of patients, 132 (75.9%), reported a past history of deep vein thrombosis (DVT), whereas 42 (24.1%) had no such history. In terms of hospital stay, the

majority of patients, 126 (72.4%), were admitted for ≤ 7 days, while 48 (27.6%) stayed beyond one week. Most procedures were completed within one hour, with 155 (89.1%) surgeries lasting ≤ 1 hour and only 19 (10.9%) exceeding this duration. Co-morbidities were present in 115 (66.1%) patients, while 59 (33.9%) had no known co-morbid conditions.

TABLE-I

Summary table of key variables (n = 174)

Variable	Categories	n (%)
Age Group	18–30 years	6 (3.4%)
	31–40 years	29 (16.7%)
	41–50 years	74 (42.5%)
	51–60 years	53 (30.5%)
	61–70 years	12 (6.9%)
Gender	Male	108 (62.1%)
	Female	66 (37.9%)
Risk Stratification	Low	17 (9.8%)
	Moderate	21 (12.1%)
	High	71 (40.8%)
	Very High	65 (37.4%)
Disease Duration	≤ 3 Months	122 (70.1%)
	> 3 Months	52 (29.9%)
BMI Classification	Underweight	5 (2.9%)
	Normal	38 (21.8%)
	Overweight	73 (42.0%)
	Obese	58 (33.3%)
Ambulatory Status	Fully Mobile	6 (3.4%)
	Partially Mobile	42 (24.1%)
	Minimally Mobile	72 (41.4%)
	Bed Bound	54 (31.0%)
Past History of DVT	Yes	132 (75.9%)
	No	42 (24.1%)
Hospital Stay	≤ 7 Days	126 (72.4%)
	> 7 Days	48 (27.6%)
Duration of Surgery	≤ 1 Hour	155 (89.1%)
	> 1 Hour	19 (10.9%)
Co-morbidities	Present	115 (66.1%)
	Absent	59 (33.9%)

When the cohort was stratified by risk levels, notable variations emerged across age groups. Among patients aged 51–60 years, 10 (58.8%) were in the low-risk group, while the majority of those aged 41–50 years were in the high-risk group, 48 (67.6%). Interestingly, the very high-risk category was most represented by patients aged 51–60 years, 30 (46.2%). Patients in the youngest age group (18–30 years) were sparsely distributed across all risk levels, making up only 1 (5.9%) in the low-risk and 4 (6.2%) in the very high-risk category. The association between age and risk level was statistically significant ($p < 0.001$). Gender distribution showed that males were more frequently categorised as low risk, 16 (94.1%), and high risk, 43 (60.6%), while females predominated in the moderate-risk group, 11 (52.4%). In the very high-risk category, males and females were nearly equally represented, 39 (60.0%) and 26 (40.0%) respectively ($p = 0.024$). The duration of disease did not significantly vary across risk groups ($p = 0.101$), although 16 (94.1%) of patients with low risk had disease duration of ≤ 3 months, compared to 41 (63.1%) in the very high-risk group. Among those with disease lasting more than 3 months, 24 (36.9%) were in the very high-risk group, reflecting a trend toward longer disease duration in higher-risk individuals.

Body Mass Index (BMI) showed a strong association with risk level ($p = 0.001$). Obese patients were notably concentrated in the low-risk group, 13 (76.5%), and the very high-risk group, 21 (32.3%). Overweight individuals accounted for the majority of high-risk patients, 50 (70.4%), while those with normal BMI were most common in the moderate-risk group, 8 (38.1%). Underweight status was rare and limited primarily to the very high-risk group, 4 (6.2%). Co-morbidities were significantly associated with risk stratification ($p < 0.001$). None of the patients in the low-risk group had co-morbidities, whereas the vast majority in the high-risk and very high-risk groups did, at 62 (87.3%) and 46 (70.8%) respectively. Conversely, patients without co-morbidities were primarily distributed in the low-risk group, 17 (100.0%), and to a lesser extent in the moderate-risk group, 14 (66.7%). Length of hospital stay also varied significantly with risk level ($p = 0.027$).

All low-risk patients, 17 (100.0%), were discharged within 7 days, whereas extended hospital stays (> 7 days) were more common in moderate-risk patients,

7 (33.3%), and high-risk patients, 25 (35.2%). While the duration of surgery did not show a statistically significant relationship with risk (p = 0.109), a greater proportion of short-duration procedures (≤ 1 hour) was seen across all groups, including 62 (95.4%) in the very high-risk group and 60 (84.5%) in the high-risk group.

Ambulatory status showed a clear association with risk level (p < 0.001). Bed-bound patients constituted the majority in the low-risk group, 10 (58.8%), while minimally mobile individuals were predominant in the high-risk group, 44 (62.0%). Among the very high-risk group, mobility was more evenly distributed: 24 (36.9%) were bed-bound and 17 (26.2%) were minimally mobile.

Fully mobile individuals were rare overall but most concentrated in the very high-risk group, 4 (6.2%). Lastly, although the past history of DVT did not reach statistical significance (p = 0.177), it was highly prevalent across all risk groups, especially in the very high-risk group, 51 (78.5%), and high-risk group, 51 (71.8%). Only 1 (5.9%) low-risk patient reported no prior DVT, reflecting the overall high burden of thrombotic history in this population.

TABLE-II

Comparison of DVT Risk levels with patients characteristics

Variable	Category	Low Risk n (%)	Moderate Risk n (%)	High Risk n (%)	Very High Risk n (%)	Total n (%)	P-Value
Age (years)	18–30	1 (5.9)	0 (0.0)	1 (1.4)	4 (6.2)	6 (3.4)	
	31–40	4 (23.5)	8 (38.1)	4 (5.6)	13 (20.0)	29 (16.7)	
	41–50	2 (11.8)	8 (38.1)	48 (67.6)	16 (24.6)	74 (42.5)	
	51–60	10 (58.8)	5 (23.8)	8 (11.3)	30 (46.2)	53 (30.5)	
	61–70	0 (0.0)	0 (0.0)	10 (14.1)	2 (3.1)	12 (6.9)	<0.001
Gender	Male	16 (94.1)	10 (47.6)	43 (60.6)	39 (60.0)	108 (62.1)	
	Female	1 (5.9)	11 (52.4)	28 (39.4)	26 (40.0)	66 (37.9)	0.024
Duration of Disease	≤ 3 Months	16 (94.1)	15 (71.4)	50 (70.4)	41 (63.1)	122 (70.1)	
	> 3 Months	1 (5.9)	6 (28.6)	21 (29.6)	24 (36.9)	52 (29.9)	0.101
BMI Classification	Underweight	0 (0.0)	0 (0.0)	1 (1.4)	4 (6.2)	5 (2.9)	
	Normal	2 (11.8)	8 (38.1)	5 (7.0)	23 (35.4)	38 (21.8)	
	Overweight	2 (11.8)	4 (19.0)	50 (70.4)	17 (26.2)	73 (42.0)	
	Obese	13 (76.5)	9 (42.9)	15 (21.1)	21 (32.3)	58 (33.3)	0.001
Co-morbidities	Present	0 (0.0)	7 (33.3)	62 (87.3)	46 (70.8)	115 (66.1)	
	Absent	17 (100.0)	14 (66.7)	9 (12.7)	19 (29.2)	59 (33.9)	<0.001
Hospital Stay	≤ 7 Days	17 (100.0)	14 (66.7)	46 (64.8)	49 (75.4)	126 (72.4)	
	> 7 Days	0 (0.0)	7 (33.3)	25 (35.2)	16 (24.6)	48 (27.6)	0.027
Duration of Surgery	≤ 1 Hour	16 (94.1)	17 (81.0)	60 (84.5)	62 (95.4)	155 (89.1)	
	> 1 Hour	1 (5.9)	4 (19.0)	11 (15.5)	3 (4.6)	19 (10.9)	0.109
Ambulatory Status	Fully Mobilized	1 (5.9)	0 (0.0)	1 (1.4)	4 (6.2)	6 (3.4)	
	Partially	4 (23.5)	4 (19.0)	14 (19.7)	20 (30.8)	42 (24.1)	
	Minimally	2 (11.8)	9 (42.9)	44 (62.0)	17 (26.2)	72 (41.4)	
	Bed Bound	10 (58.8)	8 (38.1)	12 (16.9)	24 (36.9)	54 (31.0)	<0.001
Past History of DVT	Yes	16 (94.1)	14 (66.7)	51 (71.8)	51 (78.5)	132 (75.9)	
	No	1 (5.9)	7 (33.3)	20 (28.2)	14 (21.5)	42 (24.1)	0.177

DISCUSSION

The present study analyzed the clinical and demographic determinants of venous thromboembolism (VTE) risk among surgical patients, revealing significant associations between age, gender, comorbidities, body mass index (BMI), ambulatory status, and DVT risk stratification. Most patients belonged to the 41–60-year age group, aligning with findings by bharti et al. [10], who reported a similar predominance of middle-aged individuals in thromboembolic cohorts. The observed male predominance (62.1%) also corresponds with the pattern noted by Zhao et al.[11], who attributed higher male risk to greater exposure to modifiable cardiovascular and metabolic factors. Conversely, Daves et al.[12] demonstrated a female preponderance in DVT cases, suggesting that hormonal influences, pregnancy, and oral contraceptive use may alter thrombotic risk profiles.

A significant correlation was observed between advancing age and elevated DVT risk, with individuals aged 41–60 years comprising the majority of high- and very high-risk categories. This relationship is consistent with the physiological decline in venous elasticity and increased platelet reactivity associated with aging, as described by Abudukadier et al.[13] However, the absence of a strong association in patients older than 60 years contrasts with the results of Li et al.[14], who reported progressive risk escalation beyond this age, possibly reflecting differing population characteristics or exclusion of severely ill elderly patients in the present cohort.

BMI demonstrated a strong and statistically significant association with thrombotic risk ($p = 0.001$). Overweight and obese patients accounted for nearly three-quarters of high- and very high-risk individuals. Obesity is known to promote venous stasis, systemic inflammation, and endothelial dysfunction—all key mechanisms underlying DVT pathogenesis. Similar trends have been observed by Hotoleanuet al.[15], who documented a threefold increase in DVT risk among obese surgical patients. Conversely, Sloan et al.[16] found no independent association after adjusting for immobility and comorbidities, suggesting that obesity may act as a surrogate for overall physical deconditioning rather than an isolated risk factor.

Mobility status also showed a pronounced effect, with minimally mobile and bed-bound patients constituting the majority of high-risk groups ($p < 0.001$). Prolonged immobility leads to venous stasis, decreased calf muscle pump activity, and hypercoagulability, consistent with Virchow's triad. These findings correspond with those of stone et al.[17], who highlighted immobility as a principal modifiable determinant of hospital-acquired thrombosis. Nonetheless, Lau et al.[18] observed that of early ambulation alone may not fully mitigate risk in patients with multiple comorbidities, emphasizing the need for comprehensive thromboprophylactic measures.

Co-morbid conditions were present in two-thirds of the cohort and were strongly associated with elevated DVT risk ($p < 0.001$). Patients with cardiovascular disease, diabetes mellitus, or malignancy are known to possess heightened thrombotic potential through endothelial injury and hypercoagulable states. This finding is supported by Aru et al.[19], who reported that the coexistence of systemic illness significantly increases postoperative DVT incidence. However, azeem et al.[20] found that aggressive prophylaxis and early mobilization can offset this risk, highlighting the importance of individualized preventive strategies.

The duration of hospital stay was also significantly associated with higher risk ($p = 0.027$). Prolonged hospitalization likely reflects either increased illness severity or delayed recovery, both of which contribute to extended immobilization. This is in agreement with Aggarwal et al.[21], who noted a direct correlation between inpatient duration and thrombotic events. Nevertheless, Tang et al.[22] reported that modern enhanced recovery protocols have substantially reduced inpatient DVT rates even with shorter stays, suggesting that hospitalization alone may not be the determining factor but rather the quality of perioperative care.

While most procedures in this study lasted less than one hour and the duration of surgery did not significantly affect risk levels, prior studies by Bui et al.[23] emphasized that operative time exceeding two hours markedly increases thrombotic risk due to venous stasis under anesthesia. The discrepancy may be attributed to the relatively shorter surgical

times in this study.

A past history of DVT was common, observed in 75.9% of patients, yet not statistically significant (p = 0.177). Recurrent thromboembolism is known to occur in up to one-third of cases as per Hwang et al. [24], but the high baseline prevalence of previous DVT in both groups may have obscured intergroup differences.

Overall, these findings underscore that DVT risk in surgical patients is multifactorial, influenced by age, gender, BMI, comorbidity burden, mobility, and hospitalization duration. The results reinforce the importance of systematic risk assessment and individualized prophylaxis. Future research should explore predictive models incorporating both clinical and biochemical markers to enhance precision in risk stratification.

This study has certain limitations. Being a single-center descriptive case series, its findings may not be generalizable to broader populations. The sample size, although statistically adequate, was relatively small and may not capture all potential confounding factors influencing deep venous thrombosis (DVT) risk. Furthermore, the absence of long-term postoperative follow-up precluded assessment of delayed thrombotic events or recurrence. Future multicenter studies with larger cohorts and longitudinal follow-up are recommended to validate and expand upon these findings.

CONCLUSION

An appropriate preventive strategy in general surgery should take into account the risk of VTE keeping in mind the safety of their use. In moderate-risk patients who are > 40 years of age or undergoing major operations, but who have no additional clinical risk factor.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Shahkar Ali Khan:** Conceptualization.
2	**Muhammad Abbas:** Methodology.
3	**Hamdullah:** Drafting.
4	**Sameer Khan:** Proof reading.
5	**Muhammad Danish Yasin:** Methodology.
6	**Wasif Khan:** Conceptualization.

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ORIGINAL ARTICLE

Preterm birth in women with asymptomatic bacteriuria.

Bhawna Mukesh[1], Falak Naz Baloch[2], Namia Nazir[3], Atrooba Ismail[4], Zakir Ali Punar[5], Laraib Unar[6]

ABSTRACT… Objective: To determine the frequency of preterm birth in women with asymptomatic bacteriuria. **Study Design:** Descriptive Cross-sectional study. **Setting:** Department of Obstetrics and Gynaecology Liaquat University Hospital Hyderabad. **Period:** Six Months from June 2020 to November 2020. **Methods:** A total of 151 women fulfilling the inclusion criteria was enrolled in the study. All the pregnant ladies with asymptomatic bacteriuria were recruited. The data was collected on pre-designed proforma, and all such manoeuvres were performed. **Results:** The average age of the patients with asymptomatic bacteriuria was 27.95±5.66 years. Frequency of preterm birth in women with asymptomatic bacteriuria was 17.88% (27/151). **Conclusion:** We conclude that asymptomatic bacteriuria during pregnancy has a significant impact on pregnancy outcome, mainly premature labour. By early screening and treatment of asymptomatic bacteriuria the unwanted sufferings of the pregnant mothers and their offspring could easily be reduced and even prevented. In light of our results, we recommend that, health education sessions about personal hygiene should be emphasized by the healthcare provider during antenatal care to all pregnant females, specifically those of low socio-economic level.

Key words: Asymptomatic Bacteriuria, Preterm Birth, Urinary Tract Infections.

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INTRODUCTION

Urinary tract infections (UTIs) are more common in women than in men, primarily due to anatomical factors such as a shorter urethra, the proximity of the vagina, and the increased risk of pathogen entry through sexual activity.[1] Pregnant women, in particular, are more vulnerable to asymptomatic UTIs because of physiological changes and elevated hormone levels during pregnancy.[2] If left untreated, a significant number of women with asymptomatic bacteriuria may develop pyelonephritis, which can lead to preterm labour.[3] Early screening for UTIs, particularly asymptomatic bacteriuria, during pregnancy is crucial in preventing significant complications. It serves as an effective method for identifying asymptomatic bacteriuria from urine specimens, which is essential for minimizing the risks.[4,5]

Preterm labour refers to the onset of labour before 37 weeks of gestation and is a major contributor to neonatal morbidity and mortality globally.[6,7] A urinary tract infection may signal an imbalance in vaginal flora, as the same pathogens present in the urine may also colonize the vagina.[8] Verma A et al. found that patients with bacteriuria had a significantly higher risk of low birth weight and were twice as likely to experience preterm delivery compared to those without bacteriuria. Furthermore, antibiotic treatment was shown to reduce the risk of preterm birth.[9] Identifying and treating genitourinary infections before they become clinically apparent can help decrease the incidence of preterm labour, ultimately reducing neonatal morbidity and mortality among theses infants.[10] Lockwood CJ reported that approximately 50% of preterm births are linked to asymptomatic bacteriuria,[11] while Chhabra S, et al reported 14% preterm birth are due to bacteriuria[12], whereas the reported prevalence for preterm birth in asymptomatic bacteriuria by Sheiner E, et al and Verma A, et al is 13.3% and 11.1% respectively.[13,14]

There is a limited local literature on the association between preterm birth and asymptomatic bacteriuria in our population, while international studies show varied results, influenced by the availability and accessibility of healthcare facilities in both developed and developing countries.

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This study will help generate local data for academic purposes and aassist healthcare providers in assessing the prevalence of asymptomatic bacteriuria. Early detection and management can prevent preterm births, and the findings will support the development of targeted health strategies based on the study's observations. Moreover, the results will also share and presented in various health orientation seminars at national as well as international forum as the approach may helpful and results in reducing the complications due to asymptomatic bacteriuria.

OBJECTIVES

To determine the frequency of preterm birth in women with asymptomatic bacteriuria.

OPERATIONAL DEFINITIONS

Asymptomatic Bacteriuria (ASB)
is characterized by the presence of a pure culture containing at least 10^5 organisms/ml of urine in two consecutive urine samples (or froma catheterized urine specimen), without any accompanying symptoms, as determined through clinical examination and laboratory testing.

Preterm Birth
was considered when there was birth of a baby between 25-36 gestational weeks of pregnancy (on inquiring about the history of last menstrual period LMP).

EFFECT MODIFIERS:

Booked Mother
as a part of antenatal care in which a woman who attends at least one antenatal clinic session by consultant gynaecologist.

Un-Booked Mother
Not attending the antenatal clinical sessions.

Anemia
was considered when haemoglobin concentration of less than 11 g/dL (laboratory manoeuvre).

Diabetes Mellitus
is defined as a history of at least 1 year with a blood glucose level of 200 mg/dl or higher at the time of presentation, with the individual already receiving treatment.

Fever
was labelled when the axillary temperature ≥100°F on thermometer (clinical examination).

Obesity
As defined by the National Heart, Lung, and Blood Institute (NHLBI), obesity is determined using the body mass index (BMI) tool for the Asian population, with a BMI of 27.5 kg/m2 of higher indicating obesity. BMI is calculated by dividing weight (in kilograms) by height squared (in meters), as measured on a weight-and-height scale.

Smoking
has ≥5 cigarette per day tobacco use for ≥ 01 years duration.

Hypertension
A history of at least 1 year with a blood pressure reading of 140/90 or higher at the time of presentation, with the individual already on treatment.

Low Birth Weight
Low birth weight refers to a newborn's body weight at birth, considered low if the baby weighs less then 2.5 kg, as determined through physical examination using a baby weighing scale.

METHODS

This descriptive cross sectional study was conducted at the Department of Obstetrics and Gynecology, Liaquat University Hospital, Hyderabad for Six months, from June 2020 to November 2020.

Based on the prevalence of 11.11% for preterm birth in women with asymptomatic bacteriuria[14], with a margin of error of 5%, the sample size was calculated to be 151 women with asymptomatic bacteriuria was taken.

Non-probability consecutive sampling technique was used.

SAMPLE SELECTION

Inclusion Criteria

Pregnant women aged 20-45 years, with a gestational age of ≤36 weeks (determined through clinical history and the last menstrual period L.M.P), either primiparous or multiparous, diagnosed with asymptomatic bacteriuria.

Exclusion Criteria

Pregnant women with congenital kidney disease (horseshoe kidney, unilateral renal agenesis and cystic kidneys), women already on oral or parenteral antibiotic, women with disseminated intravascular coagulation (DIC), bleeding disorder, or those using anticoagulants, as well as women experiencing postpartum hemorrhage (PPH) due to other causes, such as retained product of conceptions (RPOCs) or trauma to the birth canal were excluded from the study.

The above conditions were assessed based on the patient's previous health records or diagnosis slips provided by the relevant consultant gynaecologists and obstetricians.

Data Collection Procedure

All women who met the inclusion criteria were enrolled in the study after obtaining approval from the College of Physicians and Surgeons of Pakistan (CPSP) to conduct the research (CPSP/REU/OBG-2017-164-8073). Consent was sought from every relevant patient and all the pregnant ladies with asymptomatic bacteriuria as per operational definition was and enrolled in the study and was further evaluated for preterm birth according to the criteria mentioned in the operational definitions. Data was collected using a pre-designed proforma, and all procedures (history taking, clinical examinations, sampling and data collection) were carried out by the principal researcher under the supervision of senior obstetrician with at least 3 years of experience. The financial cost of the study were covered by the researcher. The variables which were explored are booked and un-booked mother, anaemia, diabetes mellitus, fever, smoking, obesity, parity, hypertension, residency (urban or rural) and low birth weight along with preterm birth as an outcome.

Data Analysis Procedure

The data for all patients were analysed using SPSS version 20.00. Frequency and percentage distributions were calculated for variables such as booked and un-booked status, anaemia, diabetes mellitus, fever, smoking, obesity, parity, hypertension, residency (urban or rural), low birth weight and preterm birth. The mean and standard deviation (SD) were calculated for weight, height, BMI, maternal age, gestational age and parity.

Stratification was performed based on booked or un-booked status, anaemia, diabetes mellitus, fever, smoking, obesity, parity, hypertension, residency (urban or rural) and low birth weight to assess their impact on the outcomes and control for potential effect modifiers. A post-stratification chi-square test was applied to categorical variables at a 95% confidence interval (CI), with a p-value of ≤0.05 considered statistically significant.

RESULTS

The average age of the 151 patients with asymptomatic bacteriuria was 27.95±5.66 years. Others demographic statistics of the women and their baby birth weight are also reported in Table-I. There were 92(60.93%) primigravida women and 59(39.09%) multigravida women (Figure-1). Most of the cases were un-booked and living in urban residency as shown in Figure-2 and 3. Regarding associated disease, 19.9% were anaemic, 27.8% were diabetic, 16.6% were hypertensive, 17.9% were obese, 14.6% had fever and only 6% were smokers (Table-II). Out of 151 women, low birth baby was observed in 19.87% as presented in Figure-4.

Frequency of preterm birth in women with asymptomatic bacteriuria was 17.88% (27/151) as shown in Figure-5. The rate of preterm birth was not statistically significant across age groups, parity, booking status, residency status, obese or smoker status as shown in Table-III. However, rate of preterm was high in women with anaemia, hypertension, fever and low birth weight as shown in Table-IV.

TABLE-I

Descriptive characteristics of patients

Variables	Mean	Std. Deviation	95% Confidence Interval for Mean	
			Lower Bound	Upper Bound
Age (Years)	27.95	5.66	27.04	28.86
Gestational Age (Weeks)	37.32	1.42	37.09	37.55
Weight (kg)	60.26	7.10	59.12	61.41
Height (cm)	155.56	6.52	154.51	156.60
BMI (kg/m^2)	24.99	3.34	24.45	25.53
Birth Weight (kg)	2.75	.41	2.68	2.81

FIGURE-1

Parity status of the patients (n=151)

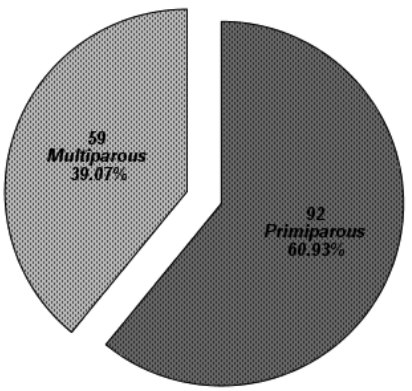


FIGURE-2

Booking status of the patients (n=151)

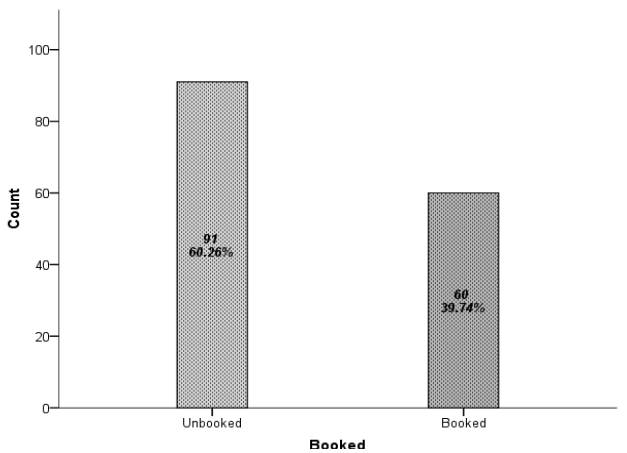


FIGURE-3

Residency status of the patients (n=151)

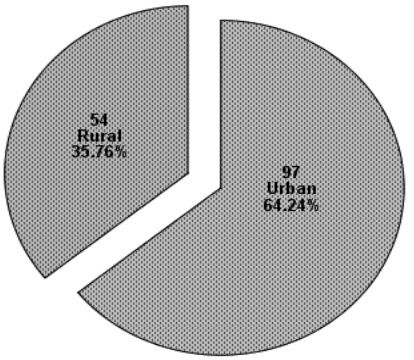


TABLE-II

Proportion of preterm birth by aetiology

Aetiology	Frequency (Percent)
Spontaneous preterm labor	30 to 50
PPROM	5 to 40
Multiple gestation	10 to 30
Preeclampsia/eclampsia	12
Antepartum bleeding	6 to 9
Fetal growth restriction	2 to 4
Other	8 to 9

PPROM: preterm premature rupture of membranes. Adapted from: Slattery MM, Morrison JJ. Lancet 2002; 360:1489.
Graphic 74561 Version 3.0

TABLE-III

Descriptive characteristics of patients

Variables	Mean	Std. Deviation	95% Confidence Interval for Mean	
			Lower Bound	Upper Bound
Age (Years)	27.95	5.66	27.04	28.86
Gestational Age (Weeks)	37.32	1.42	37.09	37.55
Weight (kg)	60.26	7.10	59.12	61.41
Height (cm)	155.56	6.52	154.51	156.60
BMI (kg/m^2)	24.99	3.34	24.45	25.53
Birth Weight (kg)	2.75	.41	2.68	2.81

TABLE-IV

Associated diseases with pregnant women

Variables	Frequency	Percentage
Anaemia	30	19.9%
Diabetes mellitus	42	27.8%
Hypertension	25	16.6%
Fever	22	14.6%
Smoking	9	6%
Obese	27	17.9%

FIGURE-4

Low birth weight (n=151)

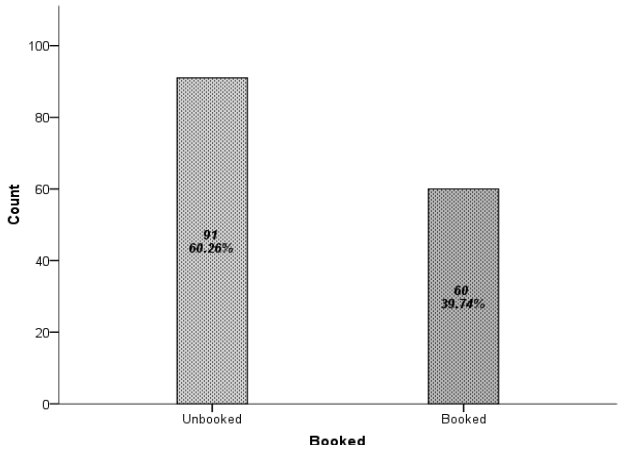
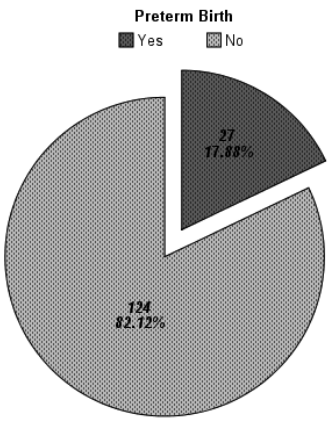


FIGURE-5

Frequency of preterm birth in women with asymptomatic bacteriuria (n=151)



DISCUSSION

Bacteriuria is the second most common bacterial infection seen during pregnancy.[15] Although the prevalence is the same in pregnant and non-pregnant female[16], changes in maternal physiology may alter the natural course of infection and make pregnant women, more susceptible to grave consequences of UTI.[17] The micro-organisms responsible for urinary tract infections (UTIs) during pregnancy are similar to those in non-pregnant individuals, with E. coli, Klebsiella and Enterobacteriaceae accounting for 90% of UTIs.[18,19] While first trimester screening and treatment for ASB during pregnancy are considered standard care in developed countries, and the role of specific antimicrobial therapy is well-established[20], there is insufficient data from developing countries to assess the impact of antimicrobial treatment for ASB during pregnancy. However, there is substantial evidence indicating that bacteriuria is prevalent in the developing regions of south Asia.[21,22] To determine the frequency of preterm birth in women with asymptomatic bacteriuria, 151 pregnant ladies of 20-45 years of age, either primipara or multiparous with asymptomatic bacteriuria were enrolled in this research study. The average age of the 151 patients with asymptomatic bacteriuria was 27.95±5.66 years, which is consistent with the study by Bachman[23], which reported a mean age of 28.2±4.5 years for pregnant women. Age and Gravidity are strongly correlated, as older women are generally more likely to have had multiple pregnancies compared to younger women. However, In our study out of 151women 92(60.93%) women were Primiparous and 59(39.09%) were multiparous. Savage et al.[24] observed that the prevalence of UTI increases by 1% to 1.5% per decade with age, and that the frequency of UTI is directly related to gravidity. In the study by Savage et al., 10% of the bacteriuric population were grand multigravidas and 20% were primigravida. In our study, 60.2% cases were un-booked. Multiple factors contributor to these pregnant women not accessing available resources, including familial taboos, lack of education, poverty, long distances to health care facility, lack of transportation and attitudes of healthcare providers toward delivering services. According to a demographic survey in Pakistan, 70% of births occurred at home without any antenatal care.[25] The incidence of hypertension (HYN) was 16.6, and diabetes was 27.8% in this study. Abayad et al[26] reported that asymptomatic bacteriuria is linked to both hypertension & diabetes.

Infection is a significant and common cause of

preterm births. Microbial studies indicate that infections are responsible for approximately 25–40% of all preterm births.[27] A strong association exists between asymptomatic bacteriuria (ASB) and preterm birth.[28] In our study, the prevalence of preterm birth among women with asymptomatic bacteriuria was 17.88% (27 out of 151). Some studies have reported an association between ASB and preterm labour, as well as fetal and maternal morbidities (p = 0.02).[15,16] However, the study by Verma et al. found no significant association between asymptomatic bacteriuria and preterm delivery (OR=3.231 CI: 1.108, 9.418, p>0.05).[29] Tahir et al. also reported no significant adverse perinatal outcomes, including premature delivery associated with ASB (p>0.05).[30] John and Michael[31], reported an odds ratio of 1.6 for the occurrence of premature labour among pregnant women with asymptomatic bacteriuria. Laura et al. (1994)[32], also documented that woman with antepartum asymptomatic bacteriuria were at a higher risk of experiencing premature labour (OR= 1.8). Several theories support the scientific plausibility of this association; far example, uterine contractions may be triggered by cytokines and prostaglandins released by microorganisms.[33] Urinary tract infections can directly influence preterm labor through the development of amnionitis.[32] Bacterial enzymes, such as collagenase, may compromise the integrity of fetal membranes.[34] It has also been suggested that bacterial products, such as phospholipase A and C or endotoxins, may stimulate prostaglandin biosynthesis in the foetal membranes, thereby initiating labour.[35]

CONCLUSION

We conclude that asymptomatic bacteriuria during pregnancy significantly affects pregnancy outcomes, particularly leading to premature labour. With effective early screening techniques and appropriate treatment of asymptomatic bacteriuria the unnecessary suffering of the pregnant women and their newborns could be effectively reduced and prevented. Based on our findings, we recommend that antenatal care providers emphasize health education on personal hygiene for all pregnant women, particularly those from low socio-economic level. During the first antenatal visit, urine cultures should be performed for high-risk patients, with follow-up cultures conducted as needed. Based on culture results, pregnant women should receive appropriate antibiotic therapy to prevent maternal-foetal complications.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Frequency of large for gestational age fetus in females presenting with increased maternal body mass index.

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ABSTRACT… Objective: To investigate the prevalence of large-for-gestational-age (LGA) fetuses among obese pregnant women and explore the relationship between LGA and maternal characteristics such as BMI, age, gestational age, and parity. **Study Design:** Cross-sectional study. **Setting:** Department of Gynecology and Obstetrics, HBS Medical & Dental College, Islamabad. **Period:** Six months October 1st, 2023 to March 30th, 2024. **Methods:** Ninety-five pregnant women with a gestational age of 30 weeks and above, and a BMI of 30 or higher, were recruited through non-probability consecutive sampling. Maternal demographic details, gestational age, BMI, and parity were recorded, and LGA diagnosis was made using ultrasound assessment. Data analysis was done using SPSS version 23. **Results:** Among 145 participants, 72 (49.66%) had LGA fetuses. However, no significant correlations were found between LGA and maternal age (p = 0.810), gestational age (p = 0.056), parity (p = 0.812), or BMI categories (p = 0.698). Maternal obesity emerged as a significant determinant of LGA. **Conclusion:** The high prevalence of LGA fetuses among obese pregnant women highlights the need for clinical consideration of maternal obesity's impact on pregnancy outcomes. This study emphasizes the importance of developing targeted intervention strategies to reduce maternal obesity and its effects on fetal weight.

Key words: BMI, Fetal Growth, Gestational Age, Large-for-gestational-age (LGA), Maternal Obesity, Neonatal Health, Pregnancy Outcomes, Parity, Risk Factors, Pakistan.

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INTRODUCTION

Obesity during pregnancy, especially in women with BMI greater or equal to 30 kg/m2, has become one of the most pressing health issues worldwide. Obesity has become a pandemic in the last few decades, and current estimates suggest that 38% of women are overweight or obese at the first antenatal clinic attendances.[1] Such an increasing trend has a significant impact on maternal and fetal health results. One of the many other adverse outcomes associated with maternal obesity, is the elevated chance of delivering an LGA baby; a condition that is described by birth weight more than the 90th percentile based on gestational age and sex.[2] This paper aims at establishing the rate of LGA among obese pregnant women, an issue of concern because of the short term and long term consequences on the welfare of the mother and her baby.[3]

LGA fetus is known to have increased prenatal growth rate and is on record to be causing some complications in the immediate perinatal period and in the future. The risks of short term include shoulder dystocia, fetal hypoxia, cesarean delivery and birth trauma while the long term complication include obesity during childhood, type 'k' diabetes and cardiovascular complications.[4,5] The risk of obesity to the mother is as well and other such complications like gestational diabetes, preeclampsia, or delivery complications hence, the Neonatal outcomes will be at higher risk for poor results.[6,7]

Multiple studies have established high concordance between maternal obesity and the risk of yielding LGA births.[8] For example, in the clinical study led by Michels[9], LGA birth rates were even higher and ranged from 32.3% to 40.2%; obesity and gestational diabetes were identified as independent risk factors positively associated with increased fetal size. In the same similar manner, the study conducted by Stuebe et al.[10] also established a

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positive correlation between maternal obesity and fetal hyperinsulinemia, a situation that arises from maternal high blood sugar level that causes the fetal tissues to double their size.[11,12] The metabolic interactions explain the importance of weight control in the period prior to conception and during gestation in the prevention of LGA.[13] Tutlam and his fellows[14] stated that the prevention of LGA births is possible if there is a slight decrease in maternal BMI before conception.[15]

Maternal obesity also has been shown to be associated with LGA, but ethnic and racial disparities exist. Published prevalence of LGA has been observed to differ in different population groups with African American and Hispanic women having the highest rates probably due to genetic markers as well as socio-environmental factors.[16,17] These findings conform with available epidemiological evidence indicating that maternal ethnicity along with other factors influences LGA by parity and gestational weight gain.[18,19,20]

According to past studies, efforts made towards controlling or preventing maternal obesity have been effective in preventing the occurrence of LGA births. In addition, it is equally important for the health care providers to enlighten pregnant women on consequences associated with weight gain and monitor pregnant women for compliance to the weight gain in pregnancy guidelines.[21,22]

The findings on the prevalence of LGA among obese pregnant women are not just an issue of clinical interest only, but a reflection of other social perinatal health risks. Higher rates of obesity in reproductive-aged women due to inadequate physical activity and energy consumption require attention to maternal and neonatal health consequences.[23] In this regard, the present study makes a valuable contribution to the existing literature on the effect of maternal obesity on pregnancy and birth outcomes in LAMI countries, where research is scarce.[24]

Specifically, in Pakistan, where maternal and child health end results are already unfavorable, the issue of maternal obesity, and its consequences, including LGA has not been well-addressed. Culturally and contextually focused interventions require such local research endeavors. Since the nutritional, genetic, and environmental antecedents of pregnancy outcomes differ across population, the conclusions of this study intend to fill this known gap by offering localized data on the frequency and factors associated with LGA in obese pregnant.[25,26,27]

Therefore, maternal obesity is an independent risk factor for LGA birth with implications to maternal and child health. Therefore, the findings of this study would contribute towards filling gaps identified in literature concerning frequency of LGA in obese pregnant women in a south Asian country –Pakistan.

METHODS

Cross sectional survey design was carried out in the HBS Medical & Dental College, Islamabad, Department of Gynecology and Obstetrics, which is a teaching hospital that specializes in maternal healthcare. The study took six months, from October 1st, 2023 to March 30th, 2024, and was undertaken after the institutional review board approved the research synopsis vide REF No.28/P23 dated 11.8.23.

The target population was isolated to pregnant women who were attending hospital on an outpatient basis. These criteria were used in identifying the sample; women 20–40 years of age with gestational weight gain of $\geq$ 30 kg/m2 after the 30th week of pregnancy, parity was controlled to be less than 5s. The participant's data was collected through non- probability consecutive sampling, whereby all eligible women attending the health facilities in the study period were recruited to the study, making a total of 145 women.

To rule out potential confounding factors, women with diseases affecting fetal size, including chronic or gestational hypertension (BP of 140/90 or above), gestational diabetes (blood sugar level above 186 mg/dL), anemia (hemoglobin level of 10 g/dL or below), and polyhydramnios (amniotic fluid index of 21 cm or higher), were omitted from the analysis. These exclusion criteria made it possible to associate the observed outcomes with maternal obesity only.

Operational Definitions

Maternal obesity was defined by a BMI of 30 kg/m^2 or greater recorded after 30 weeks of gestation based on the patient's LMP. LGA was defined as a birth weight more than the 90th percentile according to gestational age calculated based on ultrasound data obtained by the main researcher.

The participants were first asked for informed consent then information such as name, age, gestational age, and parity among others were obtained. The obstetric part of the case history was specifically completed in order to check the compliance of the patients in terms of the inclusion and exclusion criteria. In this study, all participants agreed to an abdominal ultrasonography conducted by the researcher herself following a consistent sequence of scanning protocol. The fetal weight has been assessed and it was compared to the gestational age – percentiles to define LGA. Data was documented systematically in a pre-developed format that has been prepared in advance.

The sample of 145 participants was estimated employing 95% confidence level with 8% error margin taking an estimated prevalence of LGA at 40.2% among women with increased BMI as described in prior studies.

Analysis of data was done using the statistical package of the social sciences (SPSS) version 23. Variables which are maternal age, gestational age, and BMI are being represented as continuous data therefore the mean and standard deviations were used for this study. The categorical variables including parity and LGA status were summarized using frequency and percentage. Original data were split post-hoc to assess the relationship between LGA and features under examination (maternal age, gestational age, BMI categories, parity). All tests included chi-square tests. In this case, tests were carried out and $p < 0.05$ was considered statistically significant.

RESULTS

Age distribution of the pregnant women involved in the study was determined by computing the ages of 145 participants with a mean maternal age of 31.03 years and standard deviation of 5.77 years. These observations were captured in Table-I which also shows the descriptive statistics of gestational age in this study. The participants were in their 34 to 38 weeks gestation, the mean gestational age of the participants being 36.15 ± 1.45 weeks. This range involves pregnancies that are almost complete, which creates a uniform time frame within which to assess fetal development.

All the participants had a BMI between 30.3 and 40.0 kg/m^2 with the mean of 35.09 and SD 2.89. These values support the orientation of an obese population, essential for estimating LGA risks. These results suggest that increases in BMI should be considered as a risk factor in case of LGA development, but there were no differences in the LGA proportions by BMI categories shown in this study.

TABLE-I

Descriptive statistics of maternal age, gestational age & BMI

	N	Mean	Standard Deviation	Minimum	Maximum
Age (years)	145	31.03	5.77	20	40
Gestational age (weeks)	145	36.15	1.45	34	38
BMI (Kg/m^2)	145	35.09	2.89	30.3	40.0

The parity of participants was also analyzed, and results showed that while there were 29 participants with zero parity, 30 participants had one parity, 35 participants had a parity of two, 23 had parity of three, and 28 participants had parity of four. This distribution is shown in the following Figure-1, representing the various parity experiences of the study participants. The results reveal that parity was not tainted with LGA results. Multiparity, which is associated with size of the fetal, was not an important factor as the rate of LGA was similar in both primary and multiples parity gravida.

Based on participants' self-identification of LGA, 145 of 145 participants were LGA with 72 cases (49.66%) being classified as LGA while 73 cases (50.34%) were classified as non-LGA. This almost parity accentuates the fact that a large proportion of pregnant women of obesity falls under the LGA category. Figure-2 also depicts this information showing the large percentage of pregnancies which

could be affected.

FIGURE-1

Frequency distribution of parity

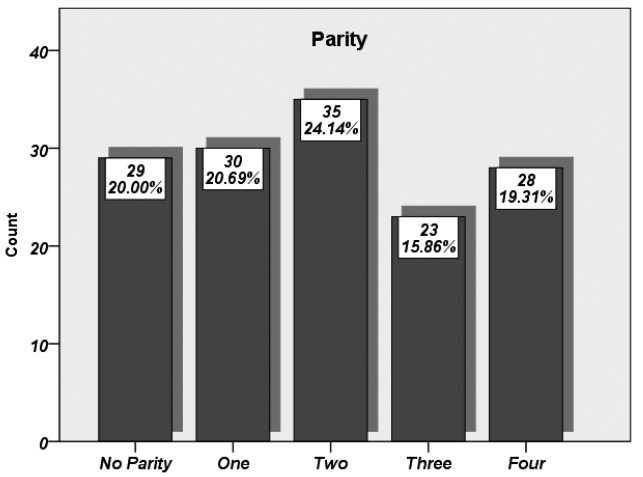

FIGURE-2

Frequency distribution of LGA

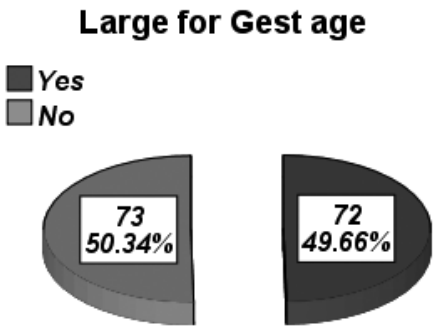

Table-II shows the relationship between the maternal age and the LGA outcomes. It also shows the relationship between LGA and gestational age

Table-III shows comparison of LGA with Parity and BMI

Thus, the present study contributes to the current literature focusing on the interaction of multiple factors that play a role in the development of LGA, especially in the case of maternal obesity, and underlines the need for the integrated approach to the enhancement of various aspects of maternal and fetal care.

DISCUSSION

The objective of this study was to identify the prevalence of LGA fetuses among obese pregnant women. It was possible to determine that 49.66% of the study population had LGA fetuses. While other antenatal factors like maternal obesity have been known to greatly increase the risk of LGA, none of the other examined maternal or fetal factors was shown to have any significant relationship with the development of LGA. These findings are in harmony with the trends marked internationally of the higher rates of maternal obesity and its potential consequences for the fetal macrosomia.

This LGA prevalence estimated in this study coincides with other studies conducted in the corresponding population.

TABLE-II

Comparison of LGA with Maternal Age & Gestational Age

		LGA		Total	%age	
		Yes	No			
Age (years)	≤ 30	32	31	63	43.4 %	Chi value=0.0510 p-value=0.810
	> 30	40	42	82	56.6 %	
Total		72	73	145		
LGA %				49.6%		
		Yes	No	Total		
GA (weeks)	34-36	43	32	75	57.3 %	Chi value=3.664 p-value=0.056
	37-38	29	41	70	41.4 %	
Total		72	73	145		
LGA %				49.6%		

TABLE-III

Comparison of LGA with Parity & BMI

		LGA		Total	%	
	Yes	No				
Parity	Primary	30	29	59	50.8 %	Chi value=0.057 p-value=0.812
	Multiple	42	44	86	48.8 %	
Total		72	73	145		
LGA %				49.6%		
		Yes	No	Total		
BMI	30-35	39	40	79	49.3 %	Chi value=2.06 p-value=0.698
	36-40	31	33	64	48.7 %	
	>40	2	0	2		
Total		72	73	145		
LGA %				49.6%		

For example, Kim et al.[25] acknowledged a 40.2 percent LGA prevalence among pregnant women who had elevated BMI. Another serious problem detected in obese women – LGA and its frequency according to Sneha et al.[26] constituted 35.5% – indicates the great impact of maternal obesity on excessive fetal growth. Overall these results supported the global trends observed for the current study population Prescribing for LGA Babies means that there is a necessity to employ appropriate strategies to deal with the problem of maternal obesity.

The impact of the mother's BMI on LGA is significant as the following studies have shown maternal obesity is one of the primary risk factors for a baby being classified as LGA.[27,28] The physiological elucidation of this association includes factors such as maternal diabetes that contributes to hyperglycemia that in turns fosters fetal insulin secretion leading to fetal growth.[29] These mechanisms are supported by this study as 46% of the obese women gave birth to LGA pregnancies. On the other hand, the non-perfect correlation between BMI categories and LGA in the current study, indicates that other factors may exist that influence the effects of maternal obesity on LGA birth, such as genetic factors and lifestyles.[30,31]

Despite the contributions that this study offers, the following limitations are worth mentioning. Cross-sectional design decreases possibilities to make causal conclusions, and the origin from only one centre may decrease the transferability of results. To build on these findings, subsequent research should use studies of a longer duration, enabling investigators to trace the mechanisms through which maternal obesity is connected to LGA. Furthermore, recruitment of various populations and the assessment of other possible covariates, for example, gestational weight gain, and maternal metabolism would be useful.

CONCLUSION

Therefore, the present study results affirm a similarly increased proportion of LGA among obese pregnant women compared to the global literature. In the present study, there was no materially significant relationship between fetal growth and maternal age, gestational age, parity, or BMI categories; however, these concordant data suggest that thinking about the factors controlling fetal growth should take into account the consideration of maternal obesity. These findings stress the importance of an integrated approach towards understanding and combating maternal obesity with specific focus on its effects on neonates. Future studies should expand on these associations in order to contribute to the litigation of rational clinical practices and health policies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Determinants of high cesarean section rates in resource-constrained healthcare system, Peshawar, Pakistan.

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ABSTRACT… Objective: To investigate the key determinants of high CS rates in Peshawar's resource-constrained healthcare system, exploring both demand-side (patient-related) and supply-side (healthcare provider and facility-related) factors. **Study Design:** Mixed-method approach. **Setting:** Three Major Hospitals from Peshawar Including Lady Reading Hospital, Hayatabad Medical Complex and Rehman Medical General Hospital. **Period:** January 2023 to December 2023. **Methods:** A hospital-based mixed-methods study was conducted across three major public and private facilities (N=221 CS cases). Quantitative data from medical records were analysed using multivariate logistic regression to identify independent predictors. Complementary in-depth interviews with providers (n=15) and mothers (n=15) explored decision-making processes. **Results:** The CS rate among study facilities was 48.6%, far exceeding WHO recommendations. Key independent predictors included: private hospital delivery (aOR=3.24, 95% CI:1.87-5.61), previous CS (aOR=4.83, 95% CI:2.42-9.65), low-income status (aOR=2.67, 95% CI:1.51-4.72), and primiparity (aOR=2.15, 95% CI:1.25-3.71). Qualitative data revealed three major themes: (1) defensive medical practices in private sectors, (2) inadequate labour monitoring leading to "failure to progress" diagnoses, and (3) socioeconomic perceptions of CS as superior care. Paradoxically, low-income women had higher CS rates despite typically facing access barriers. **Conclusion:** Multiple modifiable factors drive unnecessary CS in Pakistan's resource-constrained setting, particularly in private facilities and among disadvantaged populations. Targeted interventions should include: VBAC protocol implementation, provider training on labour management, and policy reforms addressing perverse financial incentives. The inverse socioeconomic gradient warrants particular attention in future research and programming.

Key words: Cesarean Section, Developing Countries, Healthcare Disparities, Health Services Misuse, Maternal Health Services, Obstetric Labour Complications, Pakistan.

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INTRODUCTION

Cesarean section (CS) rates have risen globally, with significant increases observed in both high- and low-resource settings.[1] While CS can be a life-saving intervention when medically indicated, unnecessary procedures pose risks for maternal and neonatal health, including surgical complications, prolonged recovery, and higher healthcare costs.[2] The World Health Organization (WHO) recommends an optimal CS rate of 10–15%, yet many countries, including Pakistan, exceed this threshold.[3] In resource-constrained settings such as Peshawar, Pakistan, where healthcare infrastructure is often overburdened, the determinants of high CS rates remain understudied despite their implications for maternal and child health outcomes.[4]

Existing literature on CS rates in low- and middle-income countries (LMICs) has primarily focused on urban tertiary care facilities or national-level data, leaving a critical gap in understanding the drivers of high CS rates in resource-limited settings like Peshawar.[5,6] Factors such as socioeconomic status, healthcare provider preferences, lack of access to skilled vaginal delivery care, and financial incentives may contribute to rising CS rates, but localized evidence is scarce.[7] Without a clear understanding of these determinants, effective policy interventions to promote evidence-based obstetric care remain challenging.[8]

This study aims to investigate the key determinants of high CS rates in Peshawar's resource-constrained healthcare system, exploring both demand-side (patient-related) and supply-side (healthcare provider and facility-related) factors.

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Findings from this study will inform policymakers, healthcare providers, and public health practitioners on targeted strategies to optimize CS use in Peshawar and similar settings. By identifying modifiable factors contributing to unnecessary CS deliveries, this research can guide interventions to improve maternal and neonatal health outcomes while ensuring efficient use of limited healthcare resources.

METHODS

This study employed a mixed-methods approach, combining a quantitative cross-sectional analysis of hospital records with qualitative interviews involving healthcare providers and mothers who underwent cesarean delivery. The research was conducted in Peshawar, Pakistan, a region characterized by a resource-constrained healthcare system with significant maternal health challenges. Data were collected from three major hospitals, including both public and private facilities, selected based on their high delivery volumes and varying levels of obstetric care provision. These hospitals were chosen to ensure representation of different healthcare delivery models and socioeconomic patient profiles.

Study Population and Sampling

For the quantitative component, we systematically reviewed electronic and paper-based medical records of 221 women who delivered via cesarean section over a defined study period (January 2023 to December 2023). This sample size was determined based on the average monthly cesarean delivery rate in the participating hospitals, ensuring adequate statistical power for the analysis. A stratified random sampling strategy was employed to ensure proportional representation across different hospital types, including public, private, and semi-private facilities. The qualitative component involved in-depth interviews with key stakeholders, including obstetricians, midwives, and mothers who had undergone cesarean delivery. A purposive sampling technique was used to select participants, ensuring diversity in professional experience, clinical settings, and patient backgrounds to capture a wide range of perspectives.

Data Collection

Quantitative data were extracted from hospital delivery registers and patient medical records of all 221 cases. Key variables included maternal demographic characteristics such as age, parity, education level, and socioeconomic status, as well as obstetric history, including previous cesarean deliveries, pregnancy complications, and gestational age. Healthcare-related factors, such as the type of facility, provider recommendations, and whether the cesarean was performed as an emergency or elective procedure, were also recorded. Indications for cesarean delivery, such as fetal distress, obstructed labor, or maternal request, were documented to assess clinical justifications.

For the qualitative component, semi-structured interviews were conducted with healthcare providers and a subset of mothers from the 221 cases to explore their experiences and decision-making processes. Interviews with providers focused on institutional policies, perceived barriers to vaginal delivery, and potential influences on cesarean rates. Mothers were interviewed about their birth experiences and factors influencing their delivery choices. All interviews were audio-recorded, transcribed verbatim, and translated into English for analysis while ensuring accuracy and confidentiality.

Variables and Measurements

The primary outcome of this study was the cesarean section rate among the 221 cases, analyzed in relation to total births within the study period. Key independent variables included demographic factors such as maternal age, education, and household income, as well as clinical factors like previous cesarean history, pregnancy complications, and multiple gestations. Health system-related variables encompassed the type of hospital, provider experience, and availability of emergency obstetric care services. These variables were selected based on existing literature and their relevance to the study context in Peshawar.

Data Analysis

Quantitative data from the 221 cases were analyzed using descriptive statistics to summarize cesarean section rates and maternal characteristics. Bivariate analyses were conducted to examine associations between independent variables and cesarean delivery outcomes. Multivariate logistic regression

models were employed to identify significant determinants of cesarean section while adjusting for potential confounders. Adjusted odds ratios with 95% confidence intervals were reported, with statistical significance set at $p < 0.05$. All quantitative analyses were performed using SPSS version 26.

Qualitative data were analyzed using thematic analysis to identify recurring patterns in cesarean section decision-making. Interview transcripts were coded inductively using NVivo 12 software, with codes grouped into broader categories such as fear of labor and systemic barriers to vaginal delivery. Emerging themes were compared across different participant groups, and qualitative findings were triangulated with quantitative results from the 221 cases to provide a comprehensive understanding of the factors driving high cesarean rates.

Ethical Considerations

Ethical approval (Ref No: INU/AHS/017-23, Dated: 3-01-2023) for this study was obtained from the relevant institutional review board. All participants provided written informed consent prior to their involvement in the study. For the quantitative component, patient identifiers were removed from medical records to ensure confidentiality. Interview participants were assured of anonymity, and all research materials were stored securely with access restricted to the research team. These measures were implemented to uphold ethical standards while studying the 221 cases and their associated healthcare providers.

RESULTS

Table-I presents the sociodemographic and clinical characteristics of the 221 women who underwent cesarean delivery in this study. The cohort had a mean maternal age of 21.0 years (±3.2 SD), reflecting a relatively young population. Educational attainment was limited, with 67% of women having ≤10 years of formal schooling. The majority (71%) belonged to low-income households (≤$100/month), highlighting the socioeconomic context of the study population. Nearly 60% of cases were multiparous women, while 24% had a previous cesarean delivery. The sample was evenly distributed between public (50.7%) and private (49.3%) healthcare facilities. The most common indications for cesarean delivery were fetal distress (28.1%) and obstructed labor (22.2%), with maternal request accounting for 14.9% of cases. These baseline characteristics establish the profile of women experiencing cesarean deliveries in this resource-constrained setting and provide context for subsequent analyses of determinants.

TABLE-I

Sociodemographic and clinical characteristics of women undergoing cesarean delivery (N=221)

Characteristic	Measure	Frequency (%) / Mean ± SD
Maternal Age	Mean ± SD	21.0 ± 3.2 years
Education Level	≤10 years of schooling	148 (67.0%)
	>10 years of schooling	73 (33.0%)
Parity	Primiparous	89 (40.3%)
	Multiparous	132 (59.7%)
Socioeconomic Status	Low income (≤$100/month)	157 (71.0%)
	Middle/High income (>$100/month)	64 (29.0%)
Previous CS	Yes	53 (24.0%)
	No	168 (76.0%)
Hospital Type	Public	112 (50.7%)
	Private	109 (49.3%)
Gestational Age	Mean ± SD	38.2 ± 1.8 weeks
CS Indication	Fetal distress	62 (28.1%)
	Obstructed labor	49 (22.2%)
	Maternal request	33 (14.9%)
	Other indications*	77 (34.8%)

Table-II displays the bivariate associations between cesarean delivery and key maternal/healthcare factors. The analysis revealed several significant predictors of cesarean section. Women delivering in private facilities had substantially higher CS rates (73.4%) compared to public hospitals (36.6%), with an unadjusted odds ratio of 3.88 (95% CI: 2.30-6.54, $p<0.001$). Socioeconomic disparities were evident, as low-income women showed 3.25 times higher odds of CS than their higher-income counterparts ($p<0.001$). Obstetric history emerged as a strong predictor, with women having a previous CS demonstrating 5.12-fold increased odds ($p<0.001$). Primiparous women had significantly

higher CS rates than multiparous women (68.5% vs 39.4%, OR=2.90, p<0.001). While lower educational attainment (≤10 years) was associated with higher CS rates (62.2% vs 45.2%, p=0.027), maternal age showed only borderline significance (p=0.089). These unadjusted associations highlight important relationships that were further examined in the multivariate analysis.

Table-III presents the results of the multivariate logistic regression analysis identifying independent predictors of cesarean delivery after controlling for potential confounders. The adjusted model confirmed private hospital delivery as a strong independent predictor (aOR=3.24, 95% CI:1.87-5.61, p<0.001), persisting after accounting for other factors. A history of previous cesarean section remained the strongest predictor (aOR=4.83, 95% CI:2.42-9.65, p<0.001). Socioeconomic disparities were maintained in the adjusted analysis, with low-income women having 2.67 times higher odds (95% CI:1.51-4.72, p=0.001). Primiparity remained significantly associated with cesarean delivery (aOR=2.15, 95% CI:1.25-3.71, p=0.006). Notably, maternal age and education level, which showed significance in bivariate analysis, were no longer significant after adjustment, suggesting their effects were mediated by other variables. The model demonstrated good fit (Hosmer-Lemeshow test: p=0.612), supporting the robustness of these findings. These results highlight how both non-modifiable (obstetric history) and modifiable (healthcare setting, socioeconomic status) factors independently contribute to cesarean delivery risk in this resource-constrained setting.

DISCUSSION

This study identified several key determinants of high cesarean section rates in Peshawar's resource-constrained healthcare system through robust mixed-methods analysis. Our findings reveal a complex interplay of medical, socioeconomic, and health system factors that contribute to the escalating CS rates in this setting.

The strongest predictor of CS was a history of previous cesarean delivery (aOR=4.83), aligning with global evidence about the "once a cesarean, always a cesarean" phenomenon.[6] This practice persists despite WHO recommendations promoting trial of labor after cesarean (TOLAC) in resource-appropriate settings.[3] Our qualitative data revealed provider fears about uterine rupture and limited emergency obstetric capabilities as key drivers of this trend.

Private hospital delivery emerged as another significant independent predictor (aOR=3.24), consistent with studies from other LMICs.[9]

TABLE-II

Bivariate associations between cesarean delivery and maternal/healthcare factors (N=221)

Predictor Variable	Category	CS Rate (%)	χ^2/t-value	P-Value	Unadjusted OR (95% CI)
Maternal Age	<20 years	58.3	1.72	0.089	1.45 (0.82–2.56)
	≥20 years	48.1			Ref.
Education	≤10 years	62.2	4.91	0.027*	1.82 (1.07–3.10)
	>10 years	45.2			Ref.
Parity	Primiparous	68.5	12.4	<0.001*	2.90 (1.72–4.89)
	Multiparous	39.4			Ref.
Socioeconomic Status	Low income	71.3	18.2	<0.001*	3.25 (1.92–5.51)
	Middle/High income	34.4			Ref.
Previous CS	Yes	83.0	25.6	<0.001*	5.12 (2.64–9.93)
	No	42.9			Ref.
Hospital Type	Private	73.4	22.1	<0.001*	3.88 (2.30–6.54)
	Public	36.6			Ref.

*Statistical significance at p<0.05. OR = Odds Ratio; CI = Confidence Interval; Ref. = Reference category.

TABLE-III

Multivariate logistic regression of factors associated with cesarean delivery (N=221)

Predictor Variable	Category	Adjusted OR (95% CI)	P-Value
Maternal Age	≥20 years (Ref)	1.00	-
	<20 years	1.32 (0.71–2.45)	0.378
Education	>10 years (Ref)	1.00	-
	≤10 years	1.45 (0.82–2.56)	0.201
Parity	Multiparous (Ref)	1.00	-
	Primiparous	2.15 (1.25–3.71)	0.006*
Socioeconomic Status	Middle/High (Ref)	1.00	-
	Low income	2.67 (1.51–4.72)	0.001*
Previous CS	No (Ref)	1.00	-
	Yes	4.83 (2.42–9.65)	<0.001*
Hospital Type	Public (Ref)	1.00	-
	Private	3.24 (1.87–5.61)	<0.001*

Adjusted for: maternal age, education, parity, socioeconomic status, previous CS, and hospital type. Hosmer-Lemeshow goodness-of-fit test: χ^2=6.32, p=0.612 (model fit adequate). *Statistically significant at p<0.05.

Financial incentives, perceived convenience, and defensive medicine practices emerged as contributing factors during provider interviews. One obstetrician noted: "In private practice, there's pressure to schedule deliveries during working hours and avoid complications." This finding raises important questions about equitable maternity care in mixed health systems.

Socioeconomic disparities were striking, with low-income women having 2.67 times higher adjusted odds of CS. Contrary to global patterns where wealthier women typically have higher CS rates[10], our inverse association may reflect several local factors: limited access to skilled vaginal birth attendants in public facilities, perception of CS as "premium care," and perverse insurance incentives that paradoxically make CS more accessible than vaginal delivery for some low-income women.

Notably, primiparity remained significant in adjusted analysis (aOR=2.15), suggesting first-time mothers represent a high-risk group for potentially unnecessary interventions. Qualitative data revealed frequent diagnoses of "failure to progress" based on outdated labor curves, compounded by limited availability of continuous labor support.

Strengths and Limitations

Our mixed-methods design strengthened findings through triangulation, while hospital-based sampling provided detailed clinical data. However, the study was limited by its cross-sectional nature and potential selection bias at participating facilities. Generalizability may be affected by Peshawar's unique healthcare ecosystem.

Policy Implications

These findings suggest several urgent interventions:

1. Implement VBAC protocols in public hospitals with adequate emergency coverage
2. Develop CS reduction guidelines tailored for private facilities
3. Address socioeconomic disparities through insurance reform
4. Train providers on modern labor management techniques

Future research should evaluate cost-effective strategies like midwife-led units and doula programs in this setting. The paradoxical socioeconomic gradient particularly warrants investigation into demand-side factors influencing delivery choices.

CONCLUSION

This study highlights critical determinants of high cesarean section rates in Peshawar's resource-constrained setting, including private hospital

delivery, previous CS, low-income status, and primiparity. The paradoxical socioeconomic gradient and provider-driven factors underscore systemic challenges in maternal healthcare. Urgent interventions—such as VBAC protocols, provider training, and policy reforms—are needed to curb unnecessary CS while ensuring equitable, safe delivery options. Addressing these issues requires a multifaceted approach targeting both healthcare practices and socioeconomic disparities.

Conflict of Interest

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Afshan Jehan Zeb:** Conceptualization.
2	**Nabeela Wazir:** Writing.
3	**Khaliq Jan:** Data collection.
4	**Noor Zada:** Statitistical analysis.
5	**Waqif Shehzad:** Literature review.
6	**Shallozan:** Data collection.
7	**Arsalan Waqas Ahmad Shah:** Review & Editing.

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ORIGINAL ARTICLE

Frequency of pre-analytical errors in chemical pathology section of tertiary care hospital.

Kainaat Mahzaib John[1], Maliha Simran[2], Rehma Dar[3]

ABSTRACT… Objective: To determine the frequency of Pre-Analytical Errors in the Chemical Pathology Section of Tertiary Care Hospital. **Study Design:** Descriptive study. **Setting:** Central Diagnostic Laboratory (CDL), KEMU/, Mayo Hospital, Lahore. **Period:** May 2022 to May 2024. **Methods:** The pre-analytical errors were noted out of 135,000 samples sent to Chemical pathology section both from indoor and outdoor. All the collected data was analysed by SPSS version 23. The frequency and percentage of errors were calculated. **Results:** A total of 12,852 (9.52%) laboratory errors including pre-analytical, analytical and post-analytical errors were observed. Out of the total errors, 8919 (69.4%), 1607 (12.5%), 2326 (18.1%) were pre-analytical errors, analytical and post-analytical errors, respectively. Haemolysis, unlabelled vial, quality not sufficient (QNS), EDTA, IV contamination, wrong vial, illegible hand writing, empty vial, spillage was 69, 20.4, 4.1, 2.6, 2.3 1.1, 0.3, 0.2, 0.1% respectively. **Conclusion:** The pre-analytical errors were the most common followed by post-analytical and analytical errors. The pre-analytical errors were more common in IPD samples than samples received from OPD and haemolysis was the most common pre-analytical error.

Key words: Laboratory Errors, Pre-analytical Errors, Post-analytical Errors and Analytical Errors.

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INTRODUCTION

Clinical laboratories are an essential component of the hospital setting, as almost 70% of clinical decisions are based on the laboratory results. Laboratory testing contributes tot the right and timely diagnosis, thus consequently impacting the correct treatment, term of hospital stay, prognosis, and the overall well-being of patient.[1-3]

Laboratory work is generally divided into three phases, i.e., pre-analytical, analytical and post-analytical phase. The pre-analytical phase includes all steps from requesting a test by clinician to processing of the sample, these steps involves collection of the specimen, transportation, entry at laboratory's reception and preparation of sample for processing. The analytical phase includes analysis of sample and validation of results. The post-analytical phase involves incorporation of data in the laboratory information system (LIS), endorsement from the lab manager, posting the reports and interpretation of laboratory reports by the clinician.[1,3-5]

All three of these testing phases are vulnerable to errors. According to International Organization for Standardization (ISO), a laboratory error is stated as "any flaw from ordering tests to reporting results and appropriate interpretation."[6,7] These errors can compromise the entire quality management system of the laboratory leading to increased utilization for resources, inappropriate clinical decisions, delayed diagnoses or extended hospital stays. Among three phases of laboratory testing, the pre-analytical phase is the most error-prone stage of the total testing process. The errors in analytical phase are greatly reduced due to induction of internal and external quality control programs and automation of the analytical work. The errors in post-analytical phase are also reduced due to direct integration of analytical results to laboratory information system (LIS), reducing transcriptional mistakes.[1-4,7,8]

Around 70% of the total laboratory errors occur in the pre-analytical phase.[3,6] This high frequency is largely due to the involvement of many non-laboratory professionals in this phase and lack of

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their proper training. The pre-analytical errors include two types of variables: patient-related and sample-related. Patient-related variables include improper patient preparation, misidentification, workout, stress, age, sex, postural effects, drug intake and menstruation. Sample related variables include poor sample collection technique, mishandling, transport and storage issues, haemolysis, clotting, lipemia, icterus, insufficient quantity, inappropriate vial/ preservative.[4,9,10]

The poor understanding of these potential errors, inadequate training of phlebotomy and poor sample transportation practices are responsible for these problems. The regular monitoring of pre-analytical errors in laboratory is essential to improve overall quality and reliability of the laboratory.[6,11]

In this context, this study was conducted to evaluate frequency of pre-analytical errors in the chemical pathology section of a tertiary heath care hospital.

METHODS

This descriptive study, approved by the Institutional Review Board (IRB), KEMU was conducted in Central Diagnostic Laboratory (CDL), KEMU/, Mayo Hospital, Lahore. A random selection of 135000 samples sent to the Chemical pathology section from May 2022 to May 2024 was made to include in this study. The pre-analytical errors such as quantity not sufficient (QNS), samples in wrong vial, unlabelled samples, haemolysis, EDTA contamination and IV contamination were noted at various levels of sample handling. Immediately, after receiving the sample in laboratory, the sample vial was matched with the requisition number and department from where it was requested. The samples from indoor patient department were marked as IPD while those from the outdoor patient department were marked as OPD.

The samples were then assessed for the adequacy, after matching patient details. Vials having sample volume inadequate for requested tests were marked as quantity not sufficient (QNS). Mislabelled and unlabelled vials were also detected during checking samples against test requirements. If the corresponding details did not match the request form it was marked as mislabelled and those samples having no label on them or missing request form were considered unlabelled vials. Similarly, empty vials were identified using the same way. The samples were centrifuged at 3000 rpm for 3 to 5 minutes to separate serum and were checked qualitatively by visual inspection method. The degree of discoloration helped us in marking degree of haemolysis such as 1+ (light pink serum, mild haemolysis), 2+ (red tinge serum, moderate haemolysis), 3+ (dark red serum, marked haemolysis), and 4+ (deep red serum, gross haemolysis). The samples were run on Beckman Coulter Chemistry auto-analyzer for analysis. Samples showing spuriously high potassium and low calcium were considered for EDTA contamination. IV contamination was considered if the serum was clear or diluted and after running it on the analyser, their biochemical profile was unexpectedly disturbed. Samples suspected of EDTA or IV contamination were redrawn with special care and reanalysed for obtaining accurate results. Those samples which then showed the change in results after redrawing the sample were labelled as EDTA or IV contaminated.

Mislabelled and unlabelled samples were rejected for the analysis while sample marked as QNS were run for tests from STAT test panel and remaining tests were requested with a repeat sample.

+1 haemolysed sample was considered for analysis but a cautionary note was mentioned for the haemolysis sensitive electrolytes such as potassium, iron, CK, LDH and AST. +2 haemolysis was considered as rejection for haemolysis sensitive analytes while samples were still analysed for relatively stable parameters such as cholesterol, urea and glucose. +3 and +4 haemolysed samples were rejected for all type of analysis and were requested again with repeat sample request. All the collected data was transferred on data file lists and analysed by SPSS 23. The frequency and percentage of all pre analytical errors were calculated.

RESULTS

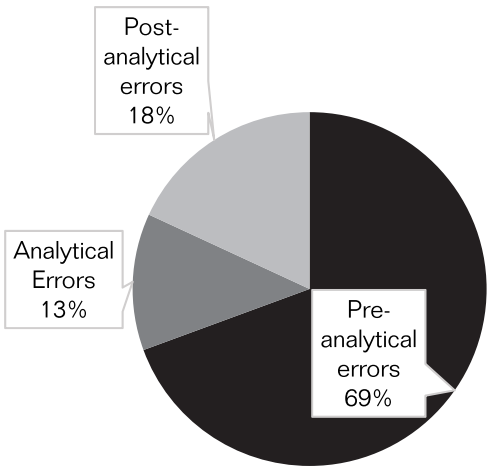
A random selection of a total of 135,000 samples was made in Chemical pathology section from 1st May 2022 to 31st May 2024. Out of these 135000, 92500 samples were from indoor patient department (IPD) while 42500 samples were from the outdoor

patient department (OPD).

A total of 12,852 (9.52%) laboratory errors including pre- analytical, analytical and post-analytical errors were observed. Out of these total errors, 8919(69.4%), 1607(12.5%), 2326(18.1%) were pre-analytical errors, analytical and post-analytical errors respectively.

FIGURE-1

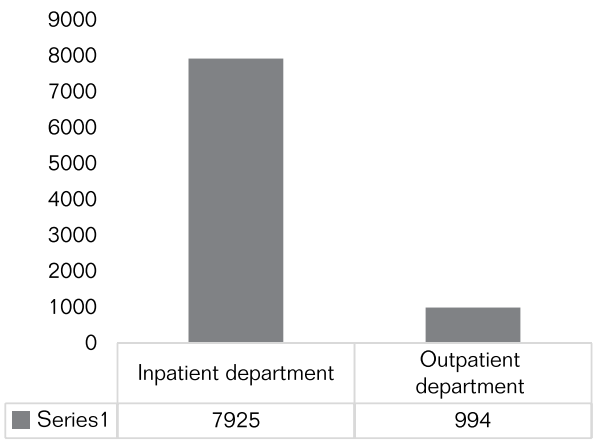
Frequency of various laboratory Errors



Of the total 8919 pre-analytical errors, 7925(88.9%) were detected in the IPD samples while 994(11.1%) were detected in the OPD samples as depicted in Figure-2.

FIGURE-2

Comparison of frequency of pre-analytical errors between IPD and OPD



The commonly encountered pre-analytical errors in are shown in Table-I.

TABLE-I

Frequency of pre-analytical errors.

Sr. No.	Types of Pre -Analytical errors	IPD (n= 7925)	OPD (n= 994)	Frequency	Percentage
1	Heamolyzed sample	5706	437	6143	68.9
2	Unlabelled vial	1425	394	1819	20.4
3	Quantity not sufficient (QNS)	271	97	368	4.1
4	EDTA contamination	180	53	233	2.6
5	IV Contamination	202	-	202	2.3
6	Wrong vial	96	-	69	1.1
7	Illegible hand writing	16	10	26	0.3
8	Empty vial	20	-	20	0.2
9	Spillage	9	3	12	0.1

DISCUSSION

Laboratory diagnostics have been transformed from manual to complex testing methods, to fully automated systems, but all the three phases i.e. pre-analytical, analytical and post-analytical of laboratory are still vulnerable to errors. Developing a strategy to understand the errors, note them down, evaluate methods to identify and prevent them is considered as the first step to the patient safety.[1]

In this background this study was carried out in Clinical chemistry section of the KEMU / Mayo Hospital. A total of 135,000 samples were collectively added in our study from the IPD and OPD of the hospital, in a six month period. Out of these, 12,852(9.52%) total errors including pre-analytical, analytical and post-analytical errors were detected. There has been varied information on error rate within whole laboratory testing procedure (0.1%-9.3%).[12] Comparing our study with other studies done in tertiary hospital laboratories gave varied results, with 1.48% errors in a study by Alavi et al., while 15.3% in other study by Teshome et al.,[5,13]

The pre-analytical, analytical and post-analytical

errors in our study were 8919 (69.4%), 1607 (12.5%) and 2326 (18.1%) respectively. The findings of our study are comparable to other studies that showed that majority of laboratory errors occur in the pre-analytical phase (61.9 - 68.2%), followed post-analytical (18.5 - 23.1%) and analytical (13.3 - 15%) phase of the total testing process (TTP).[14-16]

The errors were mostly encountered in pre-analytical phase followed by post-analytical and analytical phase. The findings of our study are in accordance with the study by Sadiq et al.[7], The results are also comparable to previous studies showing most of the errors in the pre-analytical phase.[2,3,6]

The commonly encountered pre-analytical errors in our study were haemolysis, unlabelled vial, quality not sufficient (QNS), EDTA contamination, IV contamination, wrong vial, illegible handwriting, empty vial and spillage. Hemolysis was the most common pre-analytical error followed by unlabelled vials and quantity not sufficient (QNS).[7,13,17,18] In vitro haemolysis remains the leading cause of unsuitable specimens for both outpatient and inpatient samples. The possible causes of haemolysis are improper phlebotomy technique, including the clenching of fists by patients during sampling, forcing blood through a fine needle, vigorous shaking of tubes after collection and during transportation, high speed centrifuge and freezing and thawing of the samples. Haemolysis leads to falsely elevated potassium, aspartate amino transferase (AST), lactate dehydrogenase (LDH).[16,19-21]

Unlabelled vial (20.4%) was the second common error found in our study. The findings are comparable to study by Alavi et al.,.[5] Different studies concluded varied results for this error. The results of our study are contrary to study by Bhutani et al., and Dikmen et al., in which unlabelled vial was not a common error.[18,22] According to the Centres for Disease Control and Prevention (CDC) guidelines, a specimen should be labelled with patient name, patient ID number etc. in the presence of the patient, before or after phlebotomy.[16]

QNS (4.1%) was the third common error found in our study. The findings are relatively closer to study by Alavi et al., in which 8.8% of the total pre-analytical errors were found to be of insufficient volume. The findings are not in accordance with the studies by Bhutani et al., Zaini et al., and Dikmen et al., in which QNS was the frequent.[5,18,22,23] The main reason for this error is the ignorance of phlebotomist, difficult sampling in paediatric, debilitated and chemotherapy patients and those with difficult veins localization.[19]

EDTA contamination was found to be 2.3% of pre-analytical errors. EDTA contamination happened when order of draw is not obeyed, i.e., Lavender top tube is filled before golden top vial. The findings are in agreement with the study by Sharratt, and Gilbert's. This study didn't reproduce the findings of White et al., due to far smaller sample size of the study. EDTA contaminated were determined according to the following criteria: hyperkalaemia (> 6.0 mmol/L), hypocalcaemia (ionized calcium < 0.70 mmol/L), normal renal functions and LDH.[24,25] Although sequence of sample draw is recommended, still it remains one of the commonest mistake.[16,26] This error can be reduced by training and awareness as was seen in another study.[27]

Another commonly found pre-analytical error in the IPD samples was the sample contamination by IV line (2.2%). The results are similar to study by Dikmen et al. According to a study done by Plebani and Carro in 1997 and then 2007, 20.6% errors were due to direct sample collection from IV lines in 1997 and 1.9% in 2007 that shows that error rate can be grossly decreased by great focus on the phlebotomy techniques.[14,15,22] This error was detected as diluted sample after centrifugation or during result verification, when all results are extremely low except electrolytes.

The sample in wrong vacutainer was relatively less frequent error (1.1%) in our study. The results are similar to the study by Bhutani et al.[18] The training on use and interference of different vacutainers additives on different analytes can help to reduce this error.[16]

Illegible handwriting was found to be 0.3% on the test request forms. According to a research by Chhillar et al., it was found to be the major error making 89.29% found in all of the requisition forms. The major reason is the casual attitude of

the phlebotomist. It results in waste of time and resources. This can be reduced by computerised requisition of tests.[17,28]

The empty vials were found to be 0.2% of the total pre-analytical errors in our study. The findings are comparable to study by Goswami et al., but not in agreement with studies by. Plebani et al., The empty vials were mainly received from In Patient Department. The main reason of this error may be due to inattentiveness of the nurses/ young doctors. It may also occur when during transportation, the sample is lost by the ward boys and instead of going through the proper channels of informing the staff, they replace it with an empty vial.[15,17]

The spillage of sample due to test tubes breakage during centrifugation or the samples spilled while transportation were found to be 0.1% of the total pre-analytical errors. This result was similar to the study by Teshome et al., (13). Kale et al., found 0.4% tube breakage errors in centrifuge, while Goswami et al., found 0.6% breakage errors out of the total errors seen in laboratory which was different than our study.[17,29]

The pre-analytical errors in our study were more in the indoor samples (89%) as compared to the outdoor samples (11%). The findings are similar to studies by Ian et al., and Sadiq et al., The reason underlying this trend is that in OPDs the sample is drawn by trained phlebotomists with SOPs. On the other hand, the sampling in IPD is performed by nursing students or the trainee doctors who are not directly under laboratory's control. Moreover, the phlebotomy of OPD patients is relatively easy than admitted patients.[7,11]

CONCLUSION

On the basis of findings of our study, we concluded that pre-analytical errors were the most common followed by post analytical and analytical errors. Pre-analytical errors were 69.4 percent of all the errors The pre-analytical errors were more common in IPD samples than samples received from OPD. Haemolysis was the most common pre-analytical error followed by unlabelled vials and QNS constituting 68.9%, 20.4% and 4.1% respectively. High pre-analytical are attributed due to involvement on many non-laboratory professionals in this phase. The very high percentage of pre-analytical errors in a tertiary care hospital demands training of phlebotomy staff particularly the staff in IPD section.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Kainaat Mahzaib John:** Conceptualization of study, write up.
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ORIGINAL ARTICLE

Association of mobile usage with Depression Disorder.

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ABSTRACT… Objective: To evaluate the association of mobile usage with depression disorder. **Study Design:** Case Control study. **Setting:** Private medical university and schools of Karachi. **Period:** Jan 2022 to June 2022. **Methods:** Mobile phone user depression level was assess with the help of Patient Health Questionnaire (PHQ-9) Score. Statistical analysis was done by version 25 SPSS and all data was expressed using mean and standard deviation. **Results:** Out of 258 participants, 172(66.7%) were male and 86(33.33%) female with male to female ratio of 2:1 with mean 32.85±10.85 years. Most of the participants were single 231(89.5%) cases and followed by married 27(10.5%) cases. The participants were student 159(61.6%) cases and followed by house hold 26(10.1%) cases, jobless 7(2.7%) cases and shop keeper 6(2.3%) cases. According to language majority participants were sindhi 159(61.6%) cases and followed by balochi 60(23.3%) cases, pashto 13(5%) cases, panjabi 7 (2.7%) and Urdu 6(2.3%) cases. Majority of the participants 150(58.1%) were used more than 3 hours, followed by 1 to hours 46(17.8%) and 2 to 3 hours 42(16.3%) and 20(7.8%) used were less than one hour (Table-I and II). Majority of the participants suffering the mild depression observed in 168(65.1%) due to mobile used, followed by moderate depression in 20(7.8%). **Conclusion:** Our study concludes that excessive mobile phone usage is associated with increased anxiety, stress, and mild depression symptoms.

Key words Depression Disorder, Mobile Usage, Smartphones.

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INTRODUCTION

In recent years, the use of mobile phones has spread widely across the world.[1] Although smartphones offer benefits like improved social connections and increased productivity, research increasingly shows that many people use them excessively, which disrupts their daily routines.[2-4] Overusing mobile phones has been linked to serious health risks, such as accidents caused by texting while driving, as well as mental health issues like anxiety and depression[5-7] According to Karthikeyan Selvaganapathy, heavy smartphone usage is connected to problems such as anxiety, headaches, insomnia, depression, poor sleep quality, fatigue, reduced concentration, and dependency on mobile phones.[8]

The idea of the mobile phone originated during the Second World War and was later developed by American scientist Dr. Martin Cooper in April 1973 in New York. The invention aimed to enable faster communication across various locations.[9] Previous research has also indicated a high prevalence of mental health issues, particularly depression, anxiety, and stress, among university students worldwide[10,11], who are going through a unique phase filled with significant challenges and risks. In today's world, there is ongoing concern that the growing use of mobile phones may negatively impact certain aspects of health. However, mobile phones, especially smartphones, also provide many valuable benefits in areas such as medicine, education, and other fields.[12,13] An international study by Zahra Babadi-Akashe[14] in 2014 found that cell phone addiction can lead to social and psychological issues. The results revealed notable rates of depression (17.30%), obsessive-compulsive disorder (OCD) (14.20%), and interpersonal sensitivity (13.80%).

The purpose of this study is to investigate the patterns and extent of mobile phone usage and to assess its impact, particularly the long-term effects on specific mental health aspects, by evaluating depression levels among university students in Karachi.

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METHODS

The case control study was carried out at Private medical university and schools of Karachi from January to June 2022, after ethical permission taken for the current study by the Institutional Review Committee of College of Physician and Surgeon Pakistan Karachi (Ref No. App-1516R-014, Dated: November 07, 2015). Data was collected on questionnaire through interview from public health tertiary care hospital and school employee. Taking detailed history regarding socio-demographic and symptoms of depressive disorder. The depression levels among mobile phone users were assessed using the Patient Health Questionnaire (PHQ-9) score. The study included both male and female participants over the age of 18, specifically those between 18 to 30 years, including employees and students who provided consent, were present during the study period, and could read and write in English. The exclusion criteria involved employees and students who were unwilling to participate or were not available at the time of the study.

Frequencies and percentages were calculated for qualitative variables such as gender, marital status, employment status, educational level, and Patient Health Questionnaire (PHQ-9) scores. The mean and standard deviation were determined for the quantitative variable, which is age. Age, considered as an effect modifier, was controlled through stratification. The chi-square test was used to assess the impact of these factors on the PHQ-9 score outcome. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among the 258 participants, 172 (66.7%) were male and 86 (33.3%) were female, resulting in a male-to-female ratio of 2:1. The participants' ages varied widely, ranging from 18 to 60 years, with a mean age of 32.85 ± 10.85 years. In our study, most of the participants were primary graduate 159(61.6%) cases, followed graduate in 53(20.5%) cases, Matriculate in 19(7.4%) cases and undergraduate 7(2.7%) cases. In our study, most of the participants were single 231(89.5%) cases and followed by married 27(10.5%) cases. In our study, most of the participants were student 159(61.6%) cases and followed by house hold 26(10.1%) cases, job less 7(2.7%) cases and shop keeper 6(2.3%) cases. In our study, most of the participants were sindhi 159(61.6%) cases and followed by balochi 60(23.3%) cases, pashto 13(5%) cases, panjabi 7 (2.7%) and Urdu 6(2.3%) cases. Majority of the participants 150(58.1%) were used more than 3 hours, followed by 1 to hours 46(17.8%) and 2 to 3 hours 42(16.3%) and 20(7.8%) used were less than one hour (Table-I and II).

Majority of the participants suffering the mild depression observed in 168(65.1%) due to mobile used, followed by moderate depression in 20(7.8%) (Table-I and II).

TABLE-I

Demographic variables (n=258)

Variables	Frequency	Percentage
Age		
18-25 years	82	31.8%
26-30 years	52	20.2%
31-35 years	21	8.1%
36-40 years	31	12%
41-45 years	40	15.5%
46-50 years	21	8.1%
>50 years	11	4.3%
Gender		
Male	86	33.33%
Female	172	66.7%
Educational Status		
Primary	82	31.8%
Matriculate	52	20.2%
Under Graduate	21	8.1%
Graduate	31	12%
Others	40	15.5%
Marital Status		
Married	27	10.5%
Unmarried	231	89.5%
Occupation Status		
Student	152	61.6%
House hold	26	10.1%
Shop keeper	6	2.3%
Job less	7	2.7%
Other	60	23.25%
Duration of mobile phone used per day		
≤ 1 hr	159	61.6%
1 to 2 hrs	60	23.3%
2 to 3 hrs	7	2.7%
≥3 hrs	6	2.3%
Health Questionnaire (PHQ-9) Score		
0-4 none	69	26.7%
5-9 Mild Depression	168	65.1%
10-14 Moderate Depression	20	7.8%
15-19 Moderately severe	0	0%
Depression	1	0.4%
20-27 severe Depression		

TABLE-II

Chi-square relationship of PHQ-9 with socio-demographic details (n=258)

Variables	PHQ-9					P-Value
	0-4 None	5-9 Mild Depression	10-14 Moderate Depression	15-19 Moderately Severe Depression	20-27 Severe Depression	
Gender						
Male	21(8.13%)	60(23.25%)	5(1.9%)	0	0	0.001
Female	48(18.6%)	108(41.86%)	15(5.8%)	0	1(0.38%)	
Age						
18-25 years	20(7.75%)	53(20.54%)	8(3.1%)	0	1(3.8%)	0.012
26-30 years	13(5.03%)	36(13.95%)	3(1.16%)	0	0	
31-35 years	6(2.32%)	13(5.03%)	2(0.77%)	0	0	
36-40 years	6(2.32%)	22(8.52%)	3(1.16%)	0	0	
41-45 years	15(5.8%)	24(9.3%)	1(3.8%)	0	0	
46-50 years	7(2.71%)	12(4.65%)	2(0.77%)	0	0	
>50 years	2(0.77%)	8(3.1%)	1(3.8%)	0	0	

DISCUSSION

Mobile usage has become an integral part of our daily lives, and it has been observed that people with depression disorder tend to use their mobile phones more frequently than others.[14] Mobile phones offer a sense of connection and distraction from negative thoughts, which can be beneficial for those struggling with depression.[15] However, excessive mobile usage can also have negative effects on mental health. It was observed in the current study out of 258 patients, 172(66.7%) were male and 86(33.33%) female with male to female ratio of 2:1. Shima Hashemi[16] reported that out of 1100 cases, 153 (72.2%) were females and 59 (27.8%) males with female to male ratio 2.5:1."

In the present study, participants ranged in age from 18 to 60 years, with a mean age of 32.85 ± 10.85 years. Among the 134 cases, the majority were distributed in the third and fourth decades of life. Age-related differences were observed in the association between mobile phone usage and depression disorder. Younger individuals, particularly college students, exhibited a stronger link between excessive mobile usage and depressive symptoms. This group appeared more susceptible to emotional disturbances caused by social media exposure, online comparisons, and mobile addiction, which can contribute to social isolation, poor academic performance, and sleep disturbances—all factors that increase the risk of depression. In the study conducted by Andrea K. Graham[17] reported mean ages of participants were 42.3±13.8 years.

In contrast, employees, mostly from the older age group, showed a different pattern. The association in this group was more related to work-related mobile stress, such as after-hours communication, digital overload, and difficulty maintaining work-life balance. Although social media had a less significant emotional impact on employees compared to college students, prolonged exposure to mobile devices for work and continuous connectivity contributed to mental fatigue, stress, and depressive tendencies. These findings highlight that both college students and employees are affected by mobile usage, but the underlying causes and psychological impacts vary according to age.[18,19]

The majority of participants, 150 (58.1%), reported using mobile phones for more than three hours per day. This was followed by 46 participants (17.8%) who used mobile phones for one to two hours, and 42 participants (16.3%) who used them for two to three hours daily. Only 20 participants (7.8%) reported using mobile phones for less than one hour per day. In the study conducted by Lukasz[20] Tomczyk and reported in August 2023, screen time was measured using data directly retrieved from participants' smartphones. On average, adolescents used their devices for about 3 hours and 49 minutes per day. Of this time, approximately

37 minutes were spent browsing the internet, while around 2 hours and 22 minutes were dedicated to social media platforms. More than half of the adolescents surveyed reported daily phone usage exceeding 2 hours and 20 minutes. Additionally, the top 25% of users (above the 75th percentile) spent over 5.5 hours per day on their smartphones, with at least 2 hours and 15 minutes devoted to social networking. The highest recorded usage in the study was nearly 13 hours per day on a smartphone, including more than 14 hours specifically on social media platforms.[21]

The findings indicate that prolonged mobile phone use is a common behavior, particularly among the younger age group and college students. The study further showed a significant association between mobile usage duration and depression severity, as assessed by the PHQ-9 scores. Mild depression was the most frequently observed condition, affecting 168 participants (65.1%), followed by moderate depression in 20 participants (7.8%). A very small number of cases, only one participant (0.4%), showed severe depression. The data suggest that excessive mobile phone usage is strongly linked to higher levels of mild depression, especially among younger participants aged 18 to 30 years. Additionally, the results highlighted a statistically significant relationship between gender and depression levels, with female participants experiencing higher rates of depression compared to males. Overall, the study emphasizes that both mobile usage patterns and demographic factors such as age and gender play an important role in influencing the risk of depression.

In the study of Baoan Feng[22] reported in 2024 presents the distribution of smartphone usage per day and its association with different levels of depression. The majority of participants, 1374 (49.7%), reported using their smartphones for more than six hours per day, followed by 1148 participants (41.5%) who used their phones between three to six hours daily. A smaller proportion, 226 participants (8.2%), used their phones for one to three hours per day, while only 16 participants (0.6%) reported using their phones for less than one hour daily. Regarding depression levels, most of the participants, 1859 (67.3%), were classified as normal with no significant depressive symptoms. However, mild depression was observed in 450 participants (16.3%), moderate depression in 330 participants (11.9%), and severe depression in 125 participants (4.5%). These findings suggest that prolonged smartphone usage, particularly usage exceeding three hours per day, is common among participants and may contribute to varying levels of depression, with a notable portion of the sample experiencing mild to severe depressive symptoms. The data indicates a potential link between excessive smartphone use and increased risk of developing depressive symptoms.[23]

CONCLUSION

In conclusion, overuse of mobile phones is linked to higher levels of anxiety, stress, and mild symptoms of depression. Continuous alerts and frequent social media updates can create a sense of overload and pressure to stay connected. Moreover, exposure to blue light from screens can interfere with sleep cycles, further worsening depressive symptoms.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Syed Alamdar Raza:** Conception, Statistical analysis.
2	**Shabnam Khan:** Critical revision.
3	**Rozina Khan:** Data collection.
4	**Ubedullah Shaikh:** Revision.
5	**Nida Lathiya:** Drafting.

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ORIGINAL ARTICLE

An audit of pre-analytical errors and specimen rejection in the haematology laboratory of a tertiary care transplant center: Clinical and financial impact: Root cause analysis of specimen rejection in haematology laboratory.

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ABSTRACT… Objective: To identify specific problems regarding pre-analytic processes susceptible to errors and their impact on sample rejection in a haematology laboratory. **Study Design:** A retrospective audit. **Setting:** The study was conducted at the Haematology laboratory of the Pakistan Kidney and Liver Institute and Research Center (PKLI&RC). **Period:** The audit covered a four-year period from 2019 to 2022. **Methods:** A retrospective audit of all samples rejected in the Haematology laboratory was performed. The reasons for rejection and the potential clinical impact of these rejections were investigated. The study was approved by the Institutional Review Board (IRB) of PKLI&RC (Ref No.: PKLI-IRB/AP/110, Approval date: 28 March 2023). **Results:** Out of 250,000 samples received, 568 specimens were rejected, yielding a rejection rate of 0.22%. The most common reasons for rejection were clotted samples (n=274, 48%), results not matching the patient's given history (n=142, 25%), hemolyzed samples (n=40, 7%), insufficient quantity (QNS) (n=34, 5.9%), vial defects (n=15, 2.6%), patient identification errors (n=6, 1%), and sample switches (n=4, 0.7%). **Conclusion:** The implementation of a barcoding system and positive patient ID can help prevent mislabelling and patient ID issues. Proper training and continuing education for all healthcare professionals involved in collecting, handling, and transporting patient samples is crucial to the mitigation of pre-analytical errors. Standardization of processes and procedures can efficiently prevent pre-analytical errors.

Key words: Audit, Financial Impact, Haematology Laboratory, Patient Care, Pre-analytical Errors, Rejection Rate, Turnaround Time.

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INTRODUCTION

Specimen rejection is not only a laboratory problem but it has direct negative affects on patient care jeopardizing patient safety. Not only that it is an inconvenience and discomfort for the patient but the accompanying delay can compromise the safety window we have for ideal patient care.[1] Q- probe analysis by CAP found out that there is an average lag of 65 minutes in availability of test results, implying that the safe time period of conveying the critical value and the golden hour in our septic patients or other life threatening conditions can potentially lead to increase in mortality.[2] A study by Green Et al suggested that financial consequences rise up to around 1 lac PKR per patient and this comprises 1.2% of total hospital operating cost. Based on above dire consequences it was imperative that we as a resource constrained institute, in otherwise constrained country, need to save such hefty amounts. These resources can have a much better utilization and also saving time and energy can be effectively availed for better opportunities. We conducted an audit to serve the following purposes:

1. Identify and subsequently prevent the common causes of specimen rejection.
2. The depreciation cost threshold to be brought to minimum.
3. Capacity building of our staff to work with more precision.
4. Re-evaluation our practices to reject or accept the sample.

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In haematology laboratory the sample stability is the matter of huge concern as we are dealing with cellular elements and long storage by freezing is not possible therefore, samples do get rejected due to following reasons[3,4,5,6,7,8,10]:

1. Clotting
2. Hemolysis
3. Insufficient quantity
4. Mislabeling
5. Broken vials
6. Wrong vials

METHODS

This audit was conducted at our PKLI, which is a 450 bedded medical center which serves as tertiary care transplant center. Samples are also accepted from the community by walk-in patients. The following departments are mainly function Nephrology and Kidney transplant, Hepatology and Liver transplant, Pulmonology, ICU and Pediatric unit. Although specimens are collected by Phlebotomist and Nurses. The study was approved by the Institutional Review Board (IRB) of PKLI&RC (Ref No.: PKLI-IRB/AP/110, Approval date: 28 March 2023). This retrospective research to identify all phlebotomy specimens were received in our Haematology laboratory during last 3.5 years i.e. June 2019 till December 2022. These samples included Haematology, coagulation, and hemoglobin study tests. The total number of specimens collected as well as rejected were tabulated as Type of Sample Rejected (Table-I), Reason of rejection (Table-II), Location of patient or from where the sample was taken (Table-III), Rejection rate per year (Table-IV).

Most test require minimum volume of 1ml and have to be received in appropriate tube. After taking samples, the hematology samples specially CBC are placed on rotator to prevent clotting and adequate mixing of anticoagulant until the sample is transported to the laboratory. The samples are transported in a transportation box forming all biosafety principles and ensured that temperature does not fluctuate. The ideal time for sample transportation which is also a Key Performance Indicator of Lab administration is 30 minutes. An evaluation was performed for comparing specimen rejection rate with every passing year. Data assessment and statistical analysis were performed using Microsoft excel.

TABLE-I

Types of specimens rejected

Type of Samples Rejected	Number of Samples Rejected (Total 568)	Percentage of Samples Rejected
Complete Blood Count	238	42%
Coagulation Profile	330	58%

TABLE-II

Reasons and proportions of specimen rejected

Reasons of Rejection	Rejected Specimen (N) (Total 568)	Percentage (%) of rejected Specimen
Clotting	274	48.2%
Results mismatched with the History of Pt	194	34.1%
Hemolysis	40	7%
Insufficient Quantity	34	5.9%
Vial Defects	15	2.6%
Mislabeling	6	1%
Sample switch	4	0.7%

TABLE-III

Location of the specimen collection

Site of Service	Number of Samples Rejected (total 568)	Percentage of Samples Rejected
Inpatient Department	255	44.8%
Outpatient Department	104	18.3%
ICU	99	17.4%
SICU	6	1.05%
MICU	24	4.2%
PICU	4	0.7%
Emergency Department	30	5.28%
Dialysis Unit	5	0.8%
Blood Bank	11	1.9%
HPTC	30	5.28%

ICU: Intensive Care Unit; SICU: Surgical Intensive Care Unit; MICU: Medical Intensive Care Unit; PICU: Paediatric Intensive Care Unit; HPTC: High Point Treatment Center.

TABLE-IV	
Per year specimen rejection rate	
Year	**Number of Samples Rejected per year**
2019 (June-Dec)	36
2020	42
2021	206
2022	284

DISCUSSION

This quality improvement audit highlights the impacts of specimen rejection on patient's clinical care and financial burden on our institute. As of now we are an on-site laboratory where distance is not an issue and identifying the pre analytical factors leading to sample rejection need to be corrected sooner than later. This will help us to predict problems when we expand our services to outside collection centers in the future. The studies mentioned here include centers with outsource services and therefore the rate of rejection is expected to be higher than our on-site laboratory, though the sample size is pretty comparable. Every laboratory might have their own specimen rejection pattern. Few studies have reported that clotting is the predominant cause of specimen rejection 10. At PKLI&RC Clotted sample comprise (48.2%) of rejected samples (Table-II). Our study indicates that pre-analytical errors including mislabeling and insufficient volume are also one of the major causes this is a preventable issue and educational counselling can be provide adequate support mitigating these reasons (Table-II). A very important aspect shows that specimen acceptability can be variable within the hospital and amongst the technologists. Our usual method to determine the clotting of sample is a stick method and for hemolysis its naked eye interpretation. Difficult sampling in pediatric patient accounted for (0.7%) of sample rejection due to insufficient volume. These methods need to be standardized among laboratories. Currently no standard is being followed by most of the laboratories and there is an element of biasedness. The college of American Pathologist[1] consider specimen acceptability as one of laboratory quality measure whereas most of preanalytical variables including sample quantity and labeling occur outside the laboratory therefore, this measure should be viewed as a multidisciplinary measure for healthcare institution right from patients bedside physician to the person uploading patient report on HMIS. A collaboration between laboratory and nursing staff and other hospital patient care provider group is essential. The chain from sample taking to sample analysis involves multiple hands and frequent links and mismanagement at any single point can spoil the entire chain.[9] Continuous monitoring and tracking on performance improvement can be helpful.

In reference to Table-I, the types of samples studied were Complete Blood counts, Coagulation Profile, Thrombophilia work up and Hemoglobin studies. Out of which only CBC and Coagulation Profile Samples were rejected comprising of more weightage to the Coagulation profile i.e. 58% while 42% samples of CBC were rejected. most of the samples rejected were collected from the inpatient departments i.e. 44.8% (Table-III) where staff nurses draw the samples, while the sample rejection proportion is less in OPDs in which samples are taken by Phlebotomists. So in reference to this study, problem lies mostly at the end of nursing staff for which we can arrange educational sessions for the proper sampling techniques.

Our Rejection Rate per year is being consistent (Table-IV). As there was Pandemic going on in 2020, less samples were received so is the rejection rate.

Our 568 samples were rejected that cost us 0.38 million PKR. Our rejection rate is way below than even the most renowned centers. It is attributed to because most of our samples are inpatient and no remote sampling, our phlebotomy staff is experienced, however deviation from normal rejection parameters to reject a sample need to be looked at.

Although we are already doing much better than most of the centers however with the expansion of services and opening of collection centers this rate is expected to rise exponentially. To improve our ongoing services and preempt the expected problems with outsourcing of services we suggest the following mechanisms:

1. Design a customized educational plan for each role.
2. Standardize the acceptance and rejection

criteria.
3. Design effective workflow practices and devising methods for effective phlebotomy with vessel scan in difficult patients.

CONCLUSION

This audit shows that even small pre-analytical errors like clotted or mislabelled samples can delay care, increase costs, and cause unnecessary discomfort for patients. Although our rejection rate is low, most issues came from inpatient areas, highlighting where better training and support are needed. By improving sampling techniques, strengthening identification systems, and standardizing our processes, we can make testing safer, faster, and more reliable for our patients. As our services grow, these improvements will be essential to maintaining high-quality care.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Mussawair Hussain:** Manuscript writing.
2	**Hira Hassan:** Data analysis.
3	**Unaiza Qamar:** Formatting.
4	**Fayyaz Hussain:** Data collection.
5	**Asif Ali Shah:** Referencing.
6	**Murad Ali:** Writing, methodology.
7	**Shukrya Khan:** Reviewing.

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ORIGINAL ARTICLE

Prevalence of adult ADHD: A cross-sectional analysis using the self-report scale (ASRS) among undergraduate and post-graduate medical students in Peshawar, Pakistan.

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ABSTRACT… Objective: To determine the prevalence of adult ADHD among undergraduate and postgraduate medical students in Pakistan, explore gender and academic-level differences, and assess the relationship between symptom severity and ADHD medication use. **Study Design:** Descriptive Cross-sectional study. **Setting:** Northwest School of Medicine, Peshawar. **Period:** May 2023 to September 2023. **Methods:** Was conducted among 394 medical students (227 undergraduates, 167 postgraduates) in Peshawar, Pakistan. Participants completed the Adult ADHD Self-Report Scale (ASRS). Using stratified random sampling from medical colleges and teaching hospitals in Peshawar. The ASRS (Urdu-translated and pre-validated version; Cronbach's α = 0.84) was employed. Data were analyzed using SPSS 27, with chi-square tests used to evaluate associations among ADHD severity, gender, academic status, and medication use. **Results:** Overall, 53.3% of students screened positive for mild ADHD and 18.8% for severe ADHD. Females reported higher symptom severity than males (p = 0.039 (Cramér's V = 0.13, 95% CI 0.04–0.23)"), and undergraduates more than postgraduates (p = 0.003 (Cramér's V = 0.17, 95% CI 0.07–0.27)). Common symptoms included procrastination (78.2%), organizational difficulties (73.4%), and restlessness (77.9%). Students using ADHD medication (primarily modafinil) had a significantly lower prevalence of severe ADHD (37.83%) compared to those unmedicated (62.17%; p < 0.001), though side effects such as insomnia (62%) and anxiety (38%) were frequent. **Conclusion:** ADHD is prevalent among Pakistani medical students, especially females and undergraduates. While medication appears to reduce symptom severity, adverse effects may limit adherence. Early identification and targeted academic support are critical for improving outcomes in this population.

Key words: Attention Deficit Disorder with Hyperactivity Disorder, Medical, Prevalence, Pakistan, Students, Screening Tools.

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INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental condition characterized by persistent patterns of inattention, hyperactivity, and impulsivity that are developmentally inappropriate and cause functional impairment.[1] While historically conceptualized as a disorder of childhood, longitudinal studies demonstrate that symptoms frequently persist into adulthood, often manifesting differently across the lifespan.[8] The global prevalence estimates range from 5% to 13% in children and adolescents[2], with community studies traditionally reporting a 2-3:1 male-to-female ratio.[3] However, emerging evidence suggests this gender disparity may reflect diagnostic biases rather than true incidence, as females often present with less overt hyperactive symptoms that may be overlooked.[1,4]

The clinical presentation of ADHD is frequently complicated by comorbid conditions, with approximately 60% of affected individuals meeting criteria for additional mental, behavioral, or developmental disorders - a clinical scenario termed "complex ADHD" (4). The disorder carries significant health consequences across the lifespan, including elevated risks for metabolic conditions like obesity, increased prevalence of chronic illnesses, higher rates of accidental injuries, and greater healthcare utilization compared to neurotypical peers.[4] Adolescents and adults with ADHD demonstrate particular vulnerability to health-risk behaviors, including substance abuse, dangerous driving practices (associated with 50% more traffic violations and three times as many severe accidents), and risky sexual behavior.[5]

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The societal burden is substantial, with ADHD imposing serious financial costs on families and healthcare systems[6], while also contributing to lost productivity - factors that collectively establish ADHD as a major public health concern.[6]

Within educational environments, ADHD symptoms create specific challenges that may be particularly pronounced in demanding academic programs. The core features of inattention, impulsivity, and executive dysfunction directly conflict with the cognitive demands of higher education.[7] Medical training, with its rigorous curriculum, need for sustained concentration, and high-stress environment, may disproportionately affect students with ADHD. Existing research indicates that individuals with ADHD are more likely to experience academic difficulties, lower graduation rates, and impaired professional functioning.[1,4,8] However, most available data comes from the West, high-income countries, with limited research examining ADHD prevalence and characteristics among medical students in low- and middle-income nations like Pakistan.[6]

This study aims to investigate the prevalence and clinical characteristics of ADHD among medical students in Pakistan using the validated Adult ADHD Self-Report Scale (ASRS). Specifically, we examine: (1) the point prevalence of ADHD symptoms in undergraduate and postgraduate medical students; (2) gender differences in symptom presentation and severity; (3) variations between academic levels; and (4) patterns of symptom severity. The findings will enhance understanding of ADHD in high-achieving populations within resource-limited settings and inform the development of targeted support strategies for medical trainees with neurodevelopmental challenges.[7,8]

METHODS

The study employed a descriptive, cross-sectional design to examine ADHD prevalence among medical students in Peshawar, Khyber Pakhtunkhwa, Pakistan. Data collection occurred across multiple medical colleges for undergraduate students and tertiary care hospitals for postgraduate trainees, ensuring representation from different stages of medical education. Using OpenEpi software with a 95% confidence level and 5% margin of error, we calculated a required sample size of 394 participants, comprising 227 undergraduates and 167 postgraduates. This sample size determination considered the estimated prevalence of ADHD in similar populations while maintaining statistical power for subgroup analyses by gender and academic level. Participants were selected through probability sampling techniques to enhance generalizability, with inclusion criteria specifying medical students aged 18 years or older who were physically present during data collection, capable of understanding the questionnaire, and willing to provide informed consent. Exclusion criteria systematically removed non-medical students, healthcare professionals, individuals with confounding psychiatric diagnoses (e.g., bipolar disorder, schizophrenia), and those submitting incomplete responses or withdrawing consent, ensuring sample homogeneity for accurate ADHD assessment.

The sampling frame consisted of enrolled medical students listed in the official registers of four medical colleges and two tertiary hospitals. Stratified random sampling was used within each institution. Of 432 invited participants, 394 returned complete questionnaires (response rate = 91%). Missing or incomplete items (< 2% of all responses) were handled by listwise deletion. Ethical approval was obtained from the Institutional Review Board of Northwest School of Medicine (152/RC/NWSM/2024.). All procedures adhered to the Declaration of Helsinki and STROBE reporting guidelines

The research utilized the standardized Adult ADHD Self-Report Scale (ASRS) as the primary data collection instrument, demonstrating reliability and validity across diverse cultural contexts. The ASRS captures both inattentive and hyperactive-impulsive symptom domains through its 18-item questionnaire, with Part A focusing on core symptoms and Part B assessing associated features and functional impairments. Trained research assistants administered the survey following a standardized protocol to maintain consistency, while also being available to clarify any participant questions without influencing responses. The data collection process emphasized confidentiality and voluntary participation, with all participants providing written

informed consent after receiving detailed information about the study's purpose and procedures. To minimize selection bias, researchers approached potential participants during designated times when classes and clinical duties permitted maximum availability, while avoiding examination periods that might artificially elevate stress-related symptoms. The ASRS-v1.1 was administered in Urdu following forward–backward translation and pilot testing. Scores were categorized as: 0–3 = no ADHD, 4–8 = mild ADHD, ≥ 9 = severe ADHD, based on validated thresholds for population screening (Kessler et al., 2005). Internal consistency for the Urdu version in this study was Cronbach's $\alpha = 0.86$.

For data analysis, we employed IBM SPSS Statistics version 27, applying both descriptive and inferential statistical techniques. Initial analysis computed frequencies and percentages for sociodemographic variables (gender, academic level) and ASRS item responses, providing a comprehensive profile of the sample characteristics. Chi-square tests of independence examined relationships between categorical variables, particularly focusing on associations between gender and ADHD severity categories (no ADHD, mild ADHD, severe ADHD), as well as between educational status (undergraduate vs. postgraduate) and symptom severity. The analysis treated ASRS responses as ordinal data (Never/Sometimes/Very Often) to capture the spectrum of symptom frequency. All statistical tests used a significance threshold of $p < 0.05$, with effect sizes calculated using chi-square tests to assess the strength of observed associations.

RESULTS

Prevalence and Demographic Associations

The study revealed significant demographic variations in ADHD prevalence among medical students. A chi-square analysis demonstrated a statistically significant relationship between gender and ADHD severity ($\chi^2 = 6.53$, df = 2, *p* = 0.039). While the distribution of individuals without ADHD was balanced across genders (55 males and 55 females), females exhibited a higher prevalence of both mild and severe ADHD. Specifically, 122 females reported mild ADHD compared to 88 males, and 51 females reported severe ADHD compared to 23 males. This suggests that ADHD may present more prominently in females within this population, possibly due to differences in symptom manifestation, diagnostic biases, or hormonal influences (Table-I).

The distribution of ADHD severity (No ADHD, Mild ADHD, and Severe ADHD) across gender among a total of 394 study participants. A chi-square test was conducted to evaluate the association between gender and ADHD severity. The total number of male and female participants was 166 and 228, respectively. A statistically significant association was found between gender and ADHD severity ($p = 0.039$).

Similarly, academic level was significantly associated with ADHD severity ($\chi^2 = 11.42$, df = 2, *p* = 0.003). Postgraduates were more likely to report no ADHD (61 vs. 49 undergraduates), whereas undergraduates showed higher rates of both mild and severe ADHD (50 vs. 24 postgraduates. This pattern may reflect the academic attrition of students with severe ADHD symptoms, as well as the increased coping mechanisms and adaptations developed by postgraduates over time (Table-II).

The distribution of ADHD severity levels (No ADHD, Mild ADHD, and Severe ADHD) between undergraduate and postgraduate students among a total of 394 participants. A chi-square test was applied to assess the association between academic level and ADHD severity. The number of undergraduates and postgraduates was 227 and 167, respectively. A statistically significant association was observed between academic level and ADHD severity ($p = 0.003$).

Symptom Profile and Behavioral Manifestations

The ASRS Part A results highlighted key ADHD symptoms among participants. A substantial proportion reported difficulties in task completion (67.7%), organizational challenges (73.4%), and memory lapses (62.7%). Notably, task avoidance was prevalent, with 78.2% of participants admitting to procrastination. Motor restlessness and hyperactivity were reported by 77.9% and 78.4% of participants, respectively. These findings align with established ADHD symptomatology, particularly inattention and impulsivity, which may be exacerbated

by the demanding academic environment of medical education (Table-III).

Medication Use

Among 394 participants, 78 (19.8%) reported current or prior use of stimulant or non-stimulant ADHD medication, primarily modafinil. Given the self-selected nature of this subgroup, findings should be interpreted cautiously as confounding by indication may exist.

The prevalence of severe ADHD was significantly higher in the unmedicated group (62.17%, n=46) compared to the medicated group (37.83%, n=28), with the difference being statistically significant (p = 0.000). In contrast, the prevalence of moderate ADHD was markedly lower in the medicated group (2.84%, n=6) compared to the unmedicated group (97.16%, n=204), also showing a statistically significant difference (p = 0.000) (Table-V).

The prevalence of severe and moderate ADHD among individuals who were either receiving medication (n=78) or were unmedicated (n=316). Statistical significance was assessed for differences in ADHD severity prevalence between the two groups, with p-values indicating highly significant differences (p = 0.000) (Table 5).

DISCUSSION

The findings of this cross-sectional screening study contribute to the limited literature on adult ADHD symptoms, particularly among high-achieving student populations in low- and middle-income nations. The gender disparities in prevalence reported in this study contradict the traditional perspective of ADHD as a condition that is most prevalent among males, and lead to shifting patterns of diagnosis during adulthood. This finding is supported by a review article by Quin Po. et al, that females with ADHD learn to suppress symptomatology in childhood and then develop worse problems later in life when executive function demands are higher.[9] The higher prevalence among female medical students in our sample is a manifestation of this effect, plus the high cognitive and organizational requirements of medical school. Sabir et al. also reported a higher prevalence in females at 69.7% of the sample size.[10] One Saudi study also reported relatively higher rates of symptoms of ADHD among female students compared to males (26.1% vs 25.7%), but this did not reach significance.

TABLE-I

Association between Gender and ADHD Severity among Medical Students (N = 394).

ADHD Severity	Gender of participants		Total	P-Value (chi-square test)
	Male	Female		
No ADHD	55	55	110	0.039
Mild ADHD	88	122	210	
Severe ADHD	23	51	74	
Total	166	228	394	

Severity categories defined per ASRS thresholds (0–3 = none, 4–8 = mild, ≥ 9 = severe). Chi-square test used; Cramér's V reported as effect size." Replace "p = 0.000" with "p < 0.001

TABLE-II

Association between Academic Level and ADHD Severity among Medical Students (N = 394).

ADHD Severity	Undergraduates	Postgraduates	Total	P-Value (Chi-square test)
No ADHD	49	61	110	0.003
Mild ADHD	128	82	210	
Severe ADHD	50	24	74	
Total	227	167	394	

Severity categories defined per ASRS thresholds (0–3 = none, 4–8 = mild, ≥ 9 = severe). Chi-square test used; Cramér's V reported as effect size." Replace "p = 0.000" with "p < 0.001

TABLE-III

Frequency distribution of responses to Part A of the adult ADHD self-report scale (ASRS)

Part A of ASRS	Never n (%)	Sometimes n (%)	Very often n(%)	Total
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?	127(32.2)	218(55.3)	49(12.4)	394
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?	105(26.6)	207(52.5)	82(20.8)	394
3. How often do you have problems remembering appointments or obligations?	147(37.3)	161(40.9)	86(21.8)	394
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?	86(21.8)	182(46.2)	126(32.0)	394
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?	87(188)	188(47.7)	119(30.2)	394
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?	85(21.6)	215(54.6)	94(23.9)	394

TABLE-IV

Part B of ASRS	Never n(%)	Sometimes n(%)	Very often n(%)	Total
1. How often do you make careless mistakes when you have to work on a boring or difficult project?	94(23.9)	230(58.4)	70(17.8)	394
2. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?	53(13.5)	195(49.5)	146(37.1)	394
3. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?	131(33.2)	195(49.5)	68(17.3)	394
4. How often do you misplace or have difficulty finding things at home or at work?	70(17.8)	215(54.6)	109(27.7)	394
5. How often are you distracted by activity or noise around you?	63(16.0)	174(44.2)	157(39.8)	394
6. How often do you leave your seat in meetings or other situations in which you are expected to remain seated?	204(51.8)	134(34.0)	56(14.2)	394
7. How often do you feel restless or fidgety?	63(16.0)	238(60.4)	93(23.6)	394
8. How often do you have difficulty unwinding and relaxing when you have time to yourself?	119(30.2)	199(50.5)	76(19.3)	394
9. How often do you find yourself talking too much when you are in social situations?	136(34.5)	164(41.6)	94(23.9)	394
10. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to before they can finish them themselves?	125(31.7)	198(50.3)	71(18.0)	394
11. How often do you have difficulty waiting your turn in situations when turn taking is required?	109(27.7)	204(51.8)	81(20.6)	394
12. How often do you interrupt others when they are busy?	196(49.7)	151(38.3)	47(11.9)	394

TABLE-V

Comparison of severe and moderate ADHD prevalence between medicated and unmedicated groups

Variable	Medicated Group (n=78)	Unmedicated Group (n=316)	Statistical Significance
Severe ADHD Prevalence	37.83% (n=28)	62.17% (n=46)	*p* = 0.000
Moderate ADHD Prevalence	2.84% (n=6)	97.16% (n=204)	*p* = 0.000

This suggests that many high-achieving female medical students have ADHD, perhaps evidence of underdiagnosis of girls in childhood.[11] The undergraduate-postgraduate differences at the academic level that we identified between the two groups are informative about the longitudinal development of ADHD within difficult educational environments. The lower rate in postgraduates is because of several potential explanations: a survivorship effect in which only individuals with milder sickness or better coping skills survive through to advanced education; greater development of more efficient self-regulation abilities over the course of time; or perhaps greater availability of diagnosis and treatment among advanced students. This outcome is of particular interest to medical education systems, suggesting that recognition and adjustments for students with ADHD symptoms in their early years may improve retention and academic success.

Symptom profiles revealed in this study reveal remarkable congruence with present conceptualizations of adult ADHD, particularly the element of executive dysfunction. The frequency of procrastination and task avoidance is elevated in accordance with current neuropsychological studies that have identified deficits in motivation regulation as core to ADHD.[12] The elevated frequencies of distractibility and attentional failures in our sample emphasize the challenge that medical students with ADHD face in learning environments that require sustained attention, e.g., lectures or clinical rotations. These findings take on further significance when considered against the possible effect on the care of patients, since attentional difficulties may theoretically be extended to clinical competence and patient safety. The behavioral manifestation of impulsivity, including interrupting and turn-taking issues, also has implications for professional communication skill development during medical training.[13]

Our examination of medication effects contributes to the controversy regarding the use of pharmacological treatment in adult samples with ADHD. The identification of fewer severe symptoms in medicated adults aligns with current treatment practice guidelines that indicate medication can be applied as a first-line treatment in adults with significant impairment.[14]

The rate of prevalence we observed overall is very similar to rates in other nations' research, and this provides good cross-cultural validity to ADHD as a neurodevelopmental disorder."[15,16] However, the medical education environment of culture and schooling must influence both the symptom presentation and the availability of support services. The emphasis on competition in medical education, along with possibly limited mental health services, could exacerbate challenges for ADHD students. This aligns with new international public health perspectives emphasizing how the structural health environment within a nation affects the experience and course of neurodevelopmental disorders.[17,18] This study adds to the growing perception that ADHD looks the same in every culture, but is heavily influenced by the schooling system in place locally, healthcare infrastructure, and mental illness attitudes within a culture.

Medication use analysis showed inferred ADHD treatment issues in this sample. Implications of the findings of medication use are that medication is effective for controlling basic symptoms, but must be combined with diagnosis and counseling to put the majority of patients on medical treatment to achieve symptom relief across most individuals. The response heterogeneity we observed requires individualized treatment plans by symptom profiles, comorbidities, and academic needs.

Because the ASRS is a screening rather than a diagnostic instrument, the reported rates represent probable ADHD symptomatology rather than confirmed diagnoses. The reliance on self-report may introduce recall or social-desirability bias. Additionally, the cross-sectional design limits causal inference, and inclusion of medical students only may restrict external validity.

Its methodological advantages of a comparatively large sample size and administration of standardized evaluation instruments provide a solid foundation for these findings. There are, however, some drawbacks to be considered while interpreting the results. The cross-sectional design precludes making causal inferences about the correlation between ADHD symptoms and academic performance. The reliance on self-report measures, though useful for

population screening, is prone to response bias or variation in self-knowledge. The selection of medical students as subjects, as informative as it proves in evaluating ADHD among high-achievers, limits the applicability to other student groups or the entire adult population. These limitations provide promising areas for future research, including longitudinal examinations tracking ADHD symptoms through medical training, best support practices studies among students with ADHD in low-resource contexts, and trials of how ADHD symptoms overlap with specific medical education competencies. Such a study would inform the development of focused interventions that treat both the cognitive and emotional challenges of medical students with ADHD, ultimately benefiting their academic performance and professional development.

CONCLUSION

This study identifies a high screening prevalence of ADHD-related symptoms among medical students, particularly in females and undergraduates. Medical colleges should consider implementing structured screening, counseling, and academic-support programs for students exhibiting ADHD symptoms. Future multi-institutional and longitudinal studies are warranted to validate these findings

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Usaram:** Conception of idea, write up.
2	**Komail Hussain:** Critical review.
3	**Aqsa Sehrai:** Methodology.
4	**Muhammad Anas Khan:** Writing.
5	**Emad Khan:** Data analysis.
6	**Amir Zaman Khan:** Critical review.
7	**Sarwat Jahan:** Proof reading.

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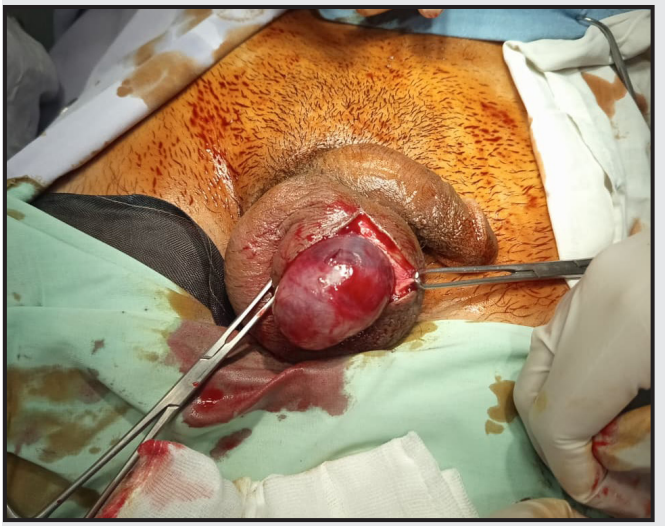

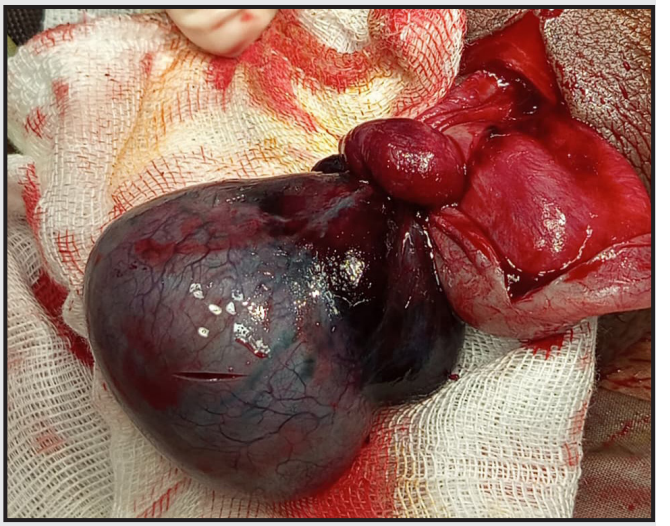

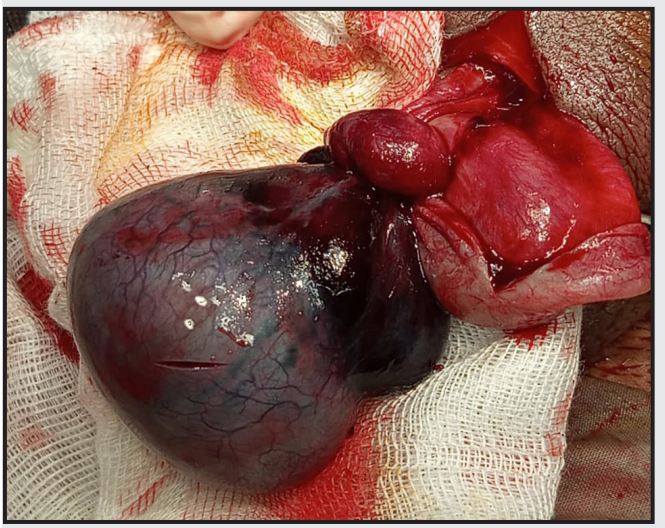

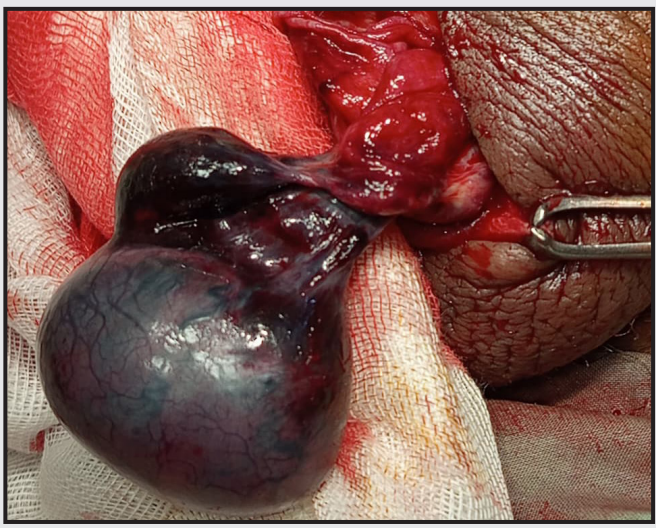

A 24 year old male presented with left scrotal swelling and pain. On further evaluation he was diagnosed as acute torsion of testis. On exploration the non-viable was removed and contralateral was fixed at three points.

Post-operative recovery was uneventful.

Courtesy:
Prof. Awais Shuja FRCS, FCPS, MCPS-HPE
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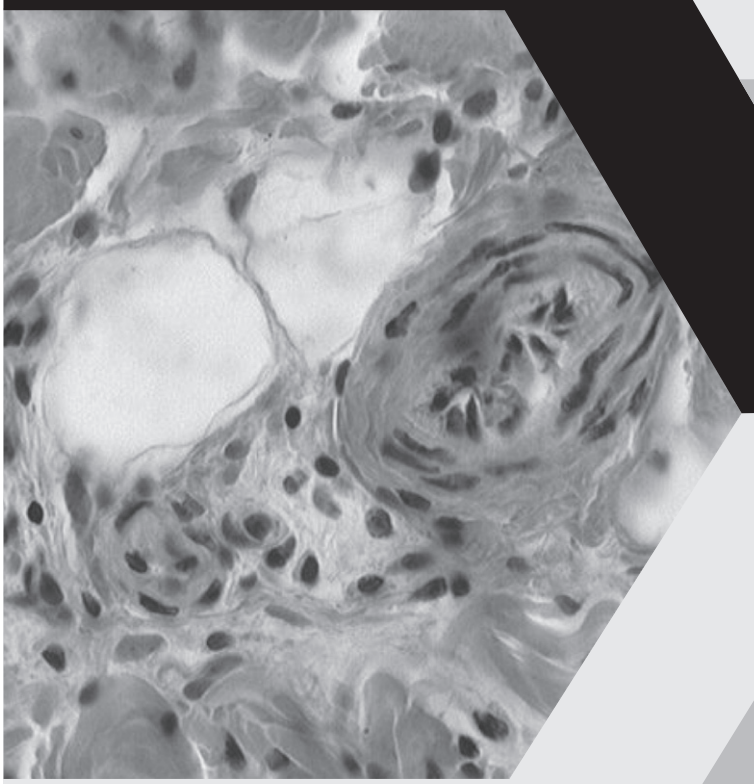

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