ISSN 2411-5096

JSMDC

Journal of Sharif Medical & Dental College

SHARIF
Medical & Dental College

02/ Vol. 11
December
2025

JSMDC

Journal of Sharif Medical & Dental College

Volume 11 | Number 02 | December 2025

JSMDC is recognized by:

- Higher Education Commission (HEC), Pakistan
- Pakistan Medical & Dental Council (PMDC)

JSMDC is indexed in:

- Directory of Open Access Journals (DOAJ)
- Asian Science Citation Index (ASCI)
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Editorial

Rising Rates of Antimicrobial Resistance: A Slow Crisis Demanding Urgent Action

Maria Aslam

Antimicrobial resistance (AMR) is no longer a distant threat; it is a crisis that is encountered in our hospitals and communities. Across the world, patients present with infections that no longer respond to previously effective antibiotics. This silent but relentless threat is undermining decades of medical progress and putting even routine procedures at risk. According to the World Health Organization (WHO), resistance to commonly used antibiotics has become widespread, with alarming levels seen in bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*.[1] The WHO warns that the situation is deteriorating faster than expected, particularly in low- and middle-income countries where antibiotic misuse and poor infection control practices are common. The Global Burden of Disease (GBD) 2021 and Antimicrobial Resistance Collaborators, led by Naghavi and colleagues, analyzed data from 204 countries and concluded that antimicrobial resistance was directly responsible for 1.27 million deaths and associated with nearly 5 million deaths in 2019. The study projected a continued rise by 2050 if urgent global action is not taken.[2]

Antimicrobial resistance is not just a medical problem, it is a social and economic challenge. Antimicrobial resistance ranks as the third most common cause of mortality in Pakistan. Around 59,200 deaths are directly and an additional 221,300 deaths are indirectly caused by AMR in Pakistan. In Pakistan, drug resistance is most commonly seen in *Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Salmonella enterica, Enterobacterales, and non-Enterobacterales*.[3]

The etiology of this escalating issue is multifactorial. The major factor is the over-the-counter availability and inappropriate prescription of antibiotics. Patients often demand antibiotics for viral infections, while physicians may prescribe them empirically without diagnostic evidence of bacterial etiology. In the agricultural sector, antibiotics are still used for growth promotion and prophylaxis in livestock, which contributes to resistant bacterial strains entering the human food chain. Environmental contamination from pharmaceutical manufacturing and poor sanitation further amplifies resistance.[4] Bertagnolio and colleagues emphasized the need for global research priorities to address gaps in diagnostics, surveillance, and the discovery of new antimicrobials. They stressed that effective AMR control requires a coordinated "One Health" approach, integrating human, animal, and environmental health.[5]

The clinical consequences of AMR are already evident. Patients with antimicrobial-resistant infections experience higher treatment failure rates, longer hospital stays, and increased mortality. A meta-analysis revealed that multidrug-resistant infections significantly increase mortality risk compared with susceptible infections.[6] Methicillin-resistant *Staphylococcus aureus*, Carbapenem-resistant *Klebsiella pneumoniae*, Extended-spectrum beta-lactamase (ESBL)-producing organisms are particularly concerning, as they are often resistant to multiple drug classes, with limited available treatment options. The economic burden of AMR is immense. Increased hospitalization, expensive second-line therapies, and the need for infection isolation facilities contribute significantly to healthcare costs. A study reported that if current trends persist, the global cost of AMR could exceed USD 100 trillion by 2050.[7]

Antimicrobial resistance has continued to rise silently across the world despite repeated warnings and stewardship programs for antimicrobial resistance. Many countries have developed and implemented their national action plans on antimicrobial resistance in alignment with the WHO Global Action Plan on AMR. In many low-resource settings, access to reliable diagnostic tools, effective infection control measures, and antimicrobial stewardship programs remains far from adequate.

To tackle this escalating crisis, the global community must act on several urgent priorities. Strengthening laboratory-based surveillance is fundamental; accurate and timely data are essential

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Received: October 15, 2025; Accepted: October 25, 2025

to guide local treatment policies and track emerging resistance patterns. Increased access to rapid diagnostic testing can ensure that antibiotics are used only when truly necessary, preserving their effectiveness for the future. Rigorous infection control measures are vital and should be integrated into every healthcare system's strategy. Governments and health organizations must also provide both financial and regulatory incentives that encourage responsible antibiotic innovation. Without such support, the antibiotic pipeline will continue to decline, leaving clinicians with fewer options to combat increasingly resistant infections.[3]

Combating it requires a united effort across all sectors: clinicians, pharmacists, policymakers, and the general public. Awareness campaigns should reshape public perception of antibiotics, viewing them not as quick remedies for all illnesses, but as valuable and limited resources that require careful and responsible use. If the world continues on its current trajectory, the consequences will be catastrophic with common infections once again becoming deadly. Strong antibiotic stewardship programs with collective global commitment can still change the course of this crisis. Now it's the time to act decisively together.[8]

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Original Article

Association of HbA1c Levels with Complexity of Coronary Artery Disease in Diabetic Patients Presenting with Acute Coronary Syndrome

Umer Shafiq, Ismail Ahmed Khan, Sohail Aziz, Kashif ur Rehman, Tayyeb Muhammad, Farman Ullah

ABSTRACT

Objective: To determine the association of Hemoglobin A1c (HbA1c) levels with the complexity of coronary artery disease (CAD) in diabetic patients presenting with acute coronary syndrome (ACS), in terms of higher synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score measured during coronary angiography.

Methodology: This cross-sectional comparative study was conducted at Fauji Foundation Hospital, Rawalpindi from July to September 2025 after approval from the ethical committee of the institution. Patients were divided into two groups. Those with HbA1c ≤7% were labeled as group 1 and group 2 had patients with HbA1c >7%. After informed written consent, 122 confirmed diabetic patients who presented with ACS and underwent coronary angiography were included using non-probability convenience sampling. The SYNTAX score was estimated to determine angiographic disease complexity. The patients with scores of 0-22 were labeled as low risk, 23-32 as intermediate, and >32 as high-risk CAD. The blood samples of patients were taken and sent for HbA1c levels and fasting lipid profile. Data analysis was carried out with the Statistical Package for the Social Sciences (SPSS) version 26.

Results: When CAD risk categories were compared with HbA1c groups, the majority of the patients in group 1 (34.4%) and group 2 (24.6%) had low risk and intermediate risk CAD, respectively. There was a significant and moderate positive correlation (r=0.528) between HbA1c and SYNTAX scores (p-value=0.001). Only the lipid profile showed a significant relationship with CAD risk categories.

Conclusion: The majority of patients with HbA1c ≤7% had low-risk CAD, while patients with HbA1c >7% had intermediate-risk CAD. The SYNTAX score significantly increased with increasing HbA1c levels. In addition, the patients with intermediate and high-risk CAD also had dyslipidemia.

Keywords: *Glycated hemoglobin. Coronary artery disease. Acute coronary syndrome.*

INTRODUCTION

Cardiovascular diseases (CVDs) are a major contributor to deaths and disability, leading to 21 million deaths worldwide. Around three quarter of these deaths take place in low- and middle-income countries.[1] In South Asian countries, the burden of CVDs will double in the coming 20 years.[2] Similarly, diabetes mellitus (DM) is also rising globally, being most common in low- and middle-income countries. The reported prevalence of DM is 537 million across the world. In addition, these diseases are leading to a significant financial burden of healthcare costs. The United Nations Sustainable Development Goal is to decrease the deaths attributed to non-communicable diseases by one-third in these countries.[1,3]

Acute coronary syndrome (ACS) includes three fatal conditions: ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina. There are various predisposing factors of ACS, such as hypertension, obesity, diabetes mellitus, and smoking.[4] In diabetic patients, coronary artery disease causes a significant proportion of mortality and morbidity.[5] It has been documented that not only the prevalence of CAD is higher in diabetic patients but DM is also linked with complicated CAD and bad prognosis. This link between DM and CAD is attributed to persistent hyperglycemia in diabetic patients. Hyperglycemia impairs the function of endothelial cells and causes inflammation, and accelerates atherosclerosis.[6]

Hemoglobin A1c (HbA1c) is the standard for monitoring and diagnosis of diabetes mellitus. Some studies have reported the positive relation of HbA1c with the severity of CAD. But others have not found any such association.[5] Diabetes mellitus is prevalent in Pakistan, reaching a frequency of 17.1%.[7] Understanding the relation between the two diseases has a great effect on global health owing to the higher prevalence of both diseases. This study was done to determine the association of HbA1c levels with the complexity of CAD indicated by the SYNTAX score in patients presenting with ACS who underwent coronary angiography. This study would provide insight into the possible relation between the two diseases and help in risk stratification for identifying patients at high risk.

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Received: September 30, 2025; Accepted: October 28, 2025

METHODOLOGY

This cross-sectional comparative study was conducted at Fauji Foundation Hospital, Rawalpindi after ethical approval (Letter No. 981/RC/FFH/RWP, 30-06-2025) from July to September 2025. Patients were divided into two groups. Those with HbA1c ≤7% were labeled as group 1 and group 2 had patients with HbA1c >7%. The sample size of 61 for each group was calculated using 80% power, 5% margin of error, and the mean SYNTAX scores of 24.33±5.00 & 27.19±6.17 in diabetic patients with HbA1c ≤7% & HbA1c >7%, respectively.[8] After written informed consent, diabetic patients who presented with ACS and underwent coronary angiography were included using non-probability convenience sampling technique. The exclusion criteria were non-diabetic patients, patients who had previous percutaneous coronary intervention or coronary artery bypass grafting, severe renal or liver diseases, malignancy, and autoimmune disorders.

The medical history & previous laboratory reports of patients were used to confirm diabetes mellitus. The age, body mass index (BMI), and co-morbidities such as hypertension, smoking, dyslipidemia & family history of CAD were noted on a proforma. The blood samples of patients were taken and sent for HbA1c levels and fasting lipid profile. The lipid profile, which includes total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, very low-density lipoprotein (VLDL) cholesterol, and triglycerides, is considered normal when total cholesterol is less than 200 mg/dL, LDL cholesterol is less than 130 mg/dL, HDL cholesterol is greater than 40 mg/dL in men and greater than 50 mg/dL in women, triglycerides are less than 150 mg/dL, and VLDL cholesterol is between 5-30 mg/dL.[9]

The HbA1c levels of ≤7% showed good glycemic control and >7% was considered suboptimal and often categorized as poor glycemic control.[10] The patients with ACS were diagnosed on suggestive clinical history, raised troponin levels, and electrocardiogram changes.[11]

The patients then underwent coronary angiography and SYNTAX score was estimated to determine angiographic disease complexity. It was calculated by summing up the score given to individual lesions in the 16 segments of the coronary tree. Patients with >50% stenosis in coronary arteries of >1.5 mm diameter had significant CAD.[12] The range of SYNTAX score was from 0 to >60 and the higher scores meant more complex CAD. The patients with scores of 0-22 were labeled as low risk, 23-32 as intermediate and >32 as high-risk CAD.[13]

STATISTICAL ANALYSIS

Data analysis was carried out using the Statistical Package for the Social Sciences (SPSS) version 26. Numerical and categorical variables were expressed using mean±standard deviation and frequency (percentage), respectively. The association between categorical variables like CAD risk categories indicating disease complexity and HbA1c groups was determined using Pearson's Chi-square test. Similar test was used to compare demographic variables and other risk factors with HbA1c groups and CAD risk categories. Pearson's correlation was used to evaluate the correlation between HbA1c levels and SYNTAX scores of the participants. The p-value <0.05 was considered significant for both tests.

RESULTS

The average age of participants in our study was 54.3±9.35 years. Most of the patients (32.8%) were 51-60 years of age, followed by 41-50 years (28.7%) and >60 years (27.9%). Most of the patients (77.1%) were females. The mean BMI of the patients was 28.18±4.09 kg/m^2. Most of the patients (44.3%) were overweight, while 36.8% were obese. Out of 122 patients, 30.3% had hypertension, 41% had a deranged lipid profile, 14.8% were smokers, and 37.7% had a positive family history of CAD. There was no significant difference in demographic variables and co-morbidities between the two groups, showing no significant association of these variables with HbA1c (Table 1).

The statistically significant results of the association of CAD risk categories with HbA1c groups showed that the majority (34.4%) of the patients in group 1 had low risk CAD. However, most (24.6%) of the participants in group 2 had intermediate risk CAD indicating increasing complexity of CAD with increasing HbA1c levels (Table 2).

The mean HbA1c level of the patients was 7.8±1.10 and the mean SYNTAX score was 21.68±6.93. The Pearson's correlation coefficient was 0.528, indicating a moderate positive correlation between HbA1c & SYNTAX scores (p-value=0.001). This showed that as the HbA1c levels of participants increase, the SYNTAX score, indicating the complexity of CAD, also tends to increase (Figure 1).

When the CAD risk categories were compared with demographic variables and risk factors, only significant association was observed with lipid

profile. The majority (38.5%) of patients with normal lipid profile had low risk CAD indicating lesser complexity of the disease. Most of the patients with intermediate (20.5%) and high risk (9%) CAD had deranged lipid profiles (Table 3). The other factors, like age groups, gender, BMI, hypertension, smoking, and family history of CAD showed no statistically significant results.

Table 1: Association of Demographic Variables and Risk Factors with HbA1c Groups

Variables		Group 1 (HbA1c ≤7%) (n=61)	Group 2 (HbA1c >7%) (n=61)	Total	p-value
Age Groups (Years)	**≤40**	8(6.5%)	5(4.1%)	13(10.6%)	0.516
	41-50	20(16.4%)	15(12.3%)	35(28.7%)	
	51-60	18(14.8%)	22(18%)	40(32.8%)	
	>60	15(12.3%)	19(15.6%)	34(27.9%)	
	Total	61(50%)	61(50%)	122(100%)	
Gender	**Male**	12(9.8%)	16(13.1%)	28(22.9%)	0.389
	Female	49(40.2%)	45(36.9%)	94(77.1%)	
	Total	61(50%)	61(50%)	122(100%)	
BMI (kg/m^2)	**Normal (18.5-24.9)**	15(12.3%)	8(6.6%)	23(18.9%)	0.077
	Overweight (25-29.9)	29(23.8%)	25(20.5%)	54(44.3%)	
	Obese (≥30)	17(13.9%)	28(22.9%)	45(36.8%)	
	Total	61(50%)	61(50%)	122(100%)	
Clinical Presentation	**NSTEMI**	34(27.9%)	40(32.8%)	74(60.7%)	0.266
	STEMI	27(22.1%)	21(17.2%)	48(39.3%)	
	Total	61(50%)	61(50%)	122(100%)	
Hypertension	**Hypertensive**	17(13.9%)	20(16.4%)	37(30.3%)	0.554
	Non-Hypertensive	44(36.1%)	41(33.6%)	85(69.7%)	
	Total	61(50%)	61(50%)	122(100%)	
Lipid Profile	**Deranged**	24(19.7%)	26(21.3%)	50(41%)	0.712
	Normal	37(30.3%)	35(28.7%)	72(59%)	
	Total	61(50%)	61(50%)	122(100%)	
Smoking	**Smoker**	10(8.2%)	8(6.6%)	18(14.8%)	0.609
	Non-Smoker	51(41.8%)	53(43.4%)	104(85.2%)	
	Total	61(50%)	61(50%)	122(100%)	
Family History of CAD	**Positive**	21(17.2%)	25(20.5%)	46(37.7%)	0.454
	Negative	40(32.8%)	36(29.5%)	76(62.3%)	
	Total	61(50%)	61(50%)	122(100%)	

Table 2: Association of CAD Risk Categories with HbA1c Groups

CAD Risk Categories (SYNTAX Score)	HbA1c Groups		Total	p-value
	Group 1 (HbA1c ≤7%)	Group 2 (HbA1c >7%)		
Low Risk (0-22)	42(34.4%)	19(15.6%)	61(50%)	0.001*
Intermediate Risk (23-32)	14(11.5%)	30(24.6%)	44(36.1%)	
High Risk (>32)	5(4.1%)	12(9.8%)	17(13.9%)	
Total	61(50%)	61(50%)	122(100%)	

**Significant p-value*

Table 3: Association of CAD Risk Categories with Lipid Profile

Lipid Profile	CAD Risk Categories (SYNTAX Score)			Total	p-value
	Low Risk (0-22) n=61	Intermediate Risk (23-32) n=44	High Risk (>32) n=17		
Deranged	14(11.5%)	25(20.5%)	11(9%)	50(41%)	0.0002*
Normal	47(38.5%)	19(15.6%)	6(4.9%)	72(59%)	
Total	61(50%)	44(36.1%)	17(13.9%)	122(100%)	

**Significant p-value*

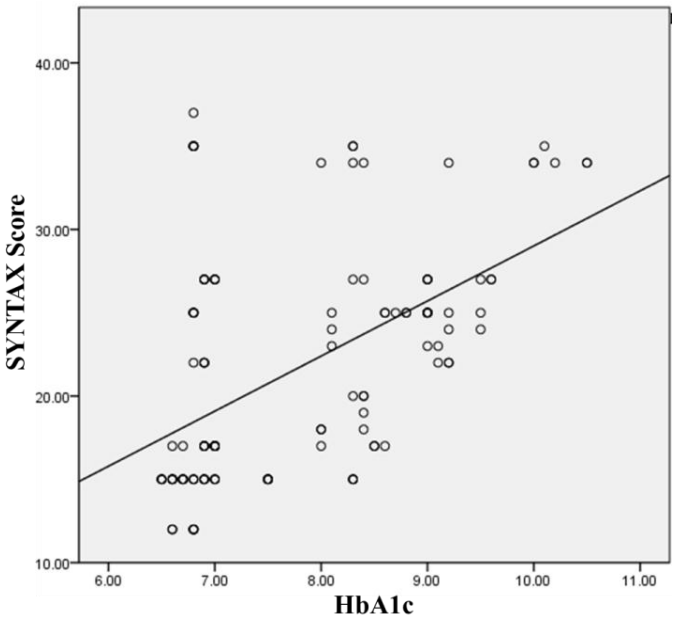

Figure 1: Scatter Plot showing a Positive Association between HbA1c and SYNTAX Score

DISCUSSION

The variation in blood glucose levels strongly influences the development of CAD. Hemoglobin A1c is a prognostic indicator of glycemic control in diabetic patients and can predict the complexity of CAD. Therefore, it is mandatory to monitor HbA1c levels continuously for risk assessment of patients.[14,15]

The average age of patients in our study was 54.3±9.35 years, with the majority (77.1%) of females. However, the age groups and gender did not differ significantly when compared with HbA1c groups and CAD risk categories. In a study done by Rashid et al., the mean age was 58.77±18.24 years with 60% males. In contrast to our results, the mean age of their participants had a statistically significant association (p=0.06) with CAD severity where increased severity was shown by older ages. The gender didn't show any such association.[16] Qadir et al. observed that 56.6% of their patients were males and the average age was 57.54±3.47 years.[17] A study from China showed that the average age of their participants was 65 years with 64.3% females. The age and gender didn't differ significantly when compared with adverse cardiac events indicating the complexity and severity of CAD in diabetic patients.[18] The average age was 57.6±9.5 years in another study with 65% males.[19] Patients had an average age of 54±10.2 years with 79.8% males in another study conducted in Karachi, Pakistan. But neither age nor gender had any statistically significant association with the prediction of CAD severity.[20]

Our results revealed that the mean BMI of the patients was 28.18±4.09 kg/m^2. Most of the patients (44.3%) were overweight, while 36.8% were obese. There was no significant association between BMI and HbA1c groups and CAD risk categories. Jiao et al. showed that the mean BMI of participants was 24.9±2.4 kg/m^2 and BMI and disease severity/complexity in diabetic patients had no significant association (p>0.05).[17] Another study reported that BMI had no statistically significant role in the prediction of CAD severity.[20] The risk factors profile of the current study showed that 30.3% of the patients were hypertensive, 14.8% were smokers, 41% had a deranged lipid profile, and 37.7% had a family history of CAD. None of these risk factors showed a statistically significant association when compared with HbA1c groups or CAD risk categories except lipid profile. The majority (38.5%) of patients with normal lipid profile had low risk CAD indicating lesser complexity, while most of the patients with intermediate (20.5%) and high risk (9%) CAD had deranged lipid profiles. Rashid et al. observed in their study that there were 73.77% hypertensive, 44.89% smokers, and 56.88% patients with dyslipidemia. These risk factors showed no significant relationship with the severity of CAD.[16] Similar to our results, Garg et al. observed that a deranged lipid profile was significantly related to CAD severity.[19] The most common risk factor in a

study was smoking (44.5%), followed by hypertension (42%), family history of CAD (37%), and dyslipidemia (10%). These risk factors didn't serve as significant predictors of CAD severity.[20]

Our results revealed that most of the ACS patients (60.7%) presented with NSTEMI. More than half of the patients presented with NSTEMI (52.1%), followed by STEMI (25.2%) and unstable angina (22.7%) in another study done by Habib et al. Similar to our results, clinical presentation wasn't related to CAD complexity.[20] However, a previous study observed that patients with STEMI presentation had more complex disease indicated by higher SYNTAX scores ($p<0.05$).[21]

The current study reported statistically significant results of the association of CAD risk categories with HbA1c groups. The majority (34.4%) of the patients in group 1 had low risk CAD. However, most (24.6%) of the participants in group 2 had intermediate risk CAD indicating increasing complexity of CAD with higher HbA1c levels. Another study showed that the patients with higher HbA1c levels had significantly increased complexity/severity of CAD indicated by higher Gensini scores.[16] Similar results were shown by another study, which revealed that HbA1c was a significant predictor of the severity of coronary artery disease and major adverse cardiac events.[18] Garg et al. revealed a significant association between HbA1c in diabetic patients and severity of CAD, where 41.7% of the patients with HbA1c >10.5% had triple vessel CAD.[19] Our study showed a significant and moderate positive correlation of HbA1c and SYNTAX scores. Similar results were reported in a study by Xu et al., where HbA1c and SYNTAX scores were significantly & positively correlated in diabetic patients.[8] The study by Dar et al. also found a significant correlation between HbA1c and Gensini scores showing increasing complexity of CAD with higher HbA1c levels.[22] Habib et al. conducted a study on non-diabetic patients with ACS and did not find any significant correlation between HbA1c and SYNTAX scores.[20]

CONCLUSION

The majority of patients with HbA1c ≤7% had low-risk CAD, while patients with HbA1c >7% had intermediate-risk CAD. Our study also found a significant, moderate positive correlation between HbA1c and the complexity of coronary artery disease (indicated by SYNTAX score) in diabetic patients presenting with ACS. The SYNTAX score significantly increased with increasing HbA1c levels. In addition, the patients with intermediate and high-risk CAD indicated by higher SYNTAX scores also had dyslipidemia.

LIMITATIONS & RECOMMENDATIONS

This study had a few limitations: cross-sectional design, non-probability convenience sampling technique, and single-institution research. The study did not evaluate the association of higher HbA1c in diabetic patients with complications of CAD, such as cardiac mortality and major adverse cardiovascular events. In the future, multi-centered studies should be conducted with follow-up of the patients to assess long-term complications.

Diabetic patients with higher HbA1c levels should be considered at higher cardiovascular risk as higher HbA1c is linked with higher SYNTAX scores, indicating complex CAD. The need for strict glycemic control in diabetic patients should be emphasized to reduce cardiovascular risk.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
U.S: Assisted in patient recruitment and data acquisition, analyzed data, and drafted the manuscript.
I.A.K: Contributed to study design, data interpretation, and critical revision.
S.A: Conceived and designed the study.
K.R: Performed statistical analysis and literature review.
T.M: Assisted in data collection and manuscript formatting.
F.U: Supervised the study, validated results, and approved the final manuscript.

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Original Article

Efficacy of Lacosamide in Patients with Diabetic Neuropathy

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ABSTRACT

Objective: To compare the efficacy of lacosamide versus placebo in patients with diabetic neuropathy in terms of reduction of the mean pain score.

Methodology: This randomized controlled trial (RCT) was conducted at the Department of Medicine, Nishtar Hospital, Multan from April to August 2025. After informed written consent, 60 patients with diabetic neuropathy were included and their baseline pain levels at recruitment were assessed using the visual analogue scale (VAS). The patients were enrolled using non-probability convenience sampling technique and subsequently randomized equally through a lottery method. Randomization was used to assign patients to either group A (lacosamide) or group B (placebo). Participants were administered either lacosamide (LCM; brand name atcomid) or a placebo that contained microcrystalline cellulose, which was commercially available and widely used in clinical trials involving diabetics. Both placebo & lacosamide were started at 100 mg daily and escalated to 400 mg/day over four weeks. Both were maintained at 400 mg for 12 weeks. The VAS was used to measure baseline and post-treatment pain scores. The variables of age, gender, duration of diabetes, obesity (body mass index ≥30 kg/m^2), and diabetes control were documented. Statistical Package for the Social Sciences (SPSS) version 26 was used for the analysis of the data.

Results: The age distribution of the study population was statistically similar in the two groups (46.67±9.66 years vs. 49.30±8.38 years; p=0.264). Majority of the participants were males in both groups (66.7% vs. 56.7%). The baseline VAS values were almost similar across the groups (group A: 7.40±1.96 vs. group B: 6.87±2.01; p=0.31). The lacosamide group showed a notable decrease in post-treatment pain scores as compared to placebo (3.90±1.92 vs. 6.73±1.72; p <0.001).

Conclusion: Lacosamide provided a statistically and clinically significant reduction in pain intensity among patients with diabetic neuropathy compared to placebo. The marked decrease in post-treatment VAS scores highlighted its potential as an effective adjunctive option for managing neuropathic pain in this population.

Keywords: *Diabetic neuropathy. Diabetes mellitus. Small fiber neuropathy. Visual analog scale. Lacosamide.*

INTRODUCTION

A significant public health challenge of this century is Diabetes mellitus. Its extended duration leads to a multitude of macro and microvascular complications that impact nearly all organ systems.[1] One in five individuals diagnosed with diabetes experiences chronic diabetic painful neuropathy (DPN). Distal symmetric polyneuropathy, which represents 80-90% of diabetic neuropathies, involves both small and large fiber damage. It is typically characterized by sensory disturbances that begin in the feet, progress upward to the calves, and, in advanced stages, extend to the upper limbs.[2] Damage to large nerve fibers leads to paresthesia, sensory loss, and muscle weakness, whereas small fiber damage is linked to pain, anesthesia, foot ulcers, and autonomic dysfunction.[3] Painful diabetic peripheral neuropathy significantly reduces quality of life in individuals with diabetes and, if left unrecognized and untreated, increases morbidity and mortality through non-traumatic amputations. Neuropathic symptoms, however, may be minimized with proper blood glucose control, lifestyle modifications, dietary management, and regular follow-up.[4]

Pharmacological approaches to managing DPN encompass a range of options, including antiepileptics like pregabalin & gabapentin, opioids, selective serotonin reuptake inhibitors, norepinephrine reuptake inhibitors, and tricyclic antidepressants (TCA). However, it is essential to note that these treatments may not yield optimal results for all individuals.[5] Furthermore, certain medications may exhibit significant negative consequences when used over prolonged periods.[3]

Lacosamide (LCM) is a newly recognized antiepileptic drug that demonstrated analgesic and neuroprotective properties across various studies. It works by blocking voltage-gated sodium channels in a slow inactivating manner and is linked to side effects like nausea and dizziness. Research conducted within Western populations has shown that LCM effectively alleviates neuropathic pain and is generally well tolerated in cases of DPN.[6]

Many foreign studies have examined lacosamide in diabetic neuropathy. Due to variations in glycemic

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Received: September 25, 2025; Accepted: October 27, 2025

management patterns, comorbidity burden, and medication metabolism, the effectiveness and tolerance of lacosamide may differ among local and international populations. There is a paucity of local evidence on the effect of lacosamide in painful diabetic neuropathy, where diabetes is among the most common diseases, and neuropathic consequences cause significant morbidity. Thus, this study fills a significant gap by comparing lacosamide to a placebo in Pakistani patients to enhance local guidelines and improve patient outcomes.

METHODOLOGY

This randomized controlled trial was conducted at the Department of Medicine, Nishtar Hospital, Multan from April to August 2025. The study was approved by the institutional ethical board (Letter No. 3607/NMU, 10-03-2025) and registered with the Iranian Trial Registry (IRCT20250211064704N1; 21-05-2025). The sample size was calculated via OpenEpi software with 80% power, 95% confidence level, and based on mean post-treatment pain scores of 3.39±1.94 in the lacosamide group and 6.35±1.52 in the placebo group.[7] After informed written consent, 60 patients were included in the study and they were divided into two groups (30 in each). Male and female patients, aged between 20 to 60 years who had been diagnosed with diabetes mellitus for a minimum of five years and developed diabetic neuropathy were included. Patients were excluded if they had cardiovascular disease, renal impairment, elevated liver enzymes that were twice the normal range. Additionally, those receiving treatment with any painkiller like non-steroidal anti-inflammatory drugs, tramadol, TCA, mexiletine hydrochloride, lidocaine patch, or opioids were also excluded. Pregnant and breastfeeding mothers were also not included. The patients were enrolled using non-probability convenience sampling technique and subsequently randomized equally through a lottery method. A lottery employing sealed, opaque envelopes assigned patients to either group A (lacosamide) or group B (placebo).

Diabetic neuropathy was assessed clinically with history and physical examination for small and large fiber neuropathy. Age, gender, duration of diabetes, obesity (body mass index ≥30 kg/m^2), and diabetes control were documented. Diabetes control was evaluated by HbA1c results. HbA1c levels of all the patients were tested from the same laboratory. Patients exhibiting HbA1c values of 7% or lower had controlled diabetes, while those with values of more than 7% were classified as having uncontrolled diabetes. Participants were administered either lacosamide (LCM; brand name atcomid) or a placebo that contained microcrystalline cellulose, which was commercially available and widely used in clinical trials involving diabetics. Both placebo & lacosamide were given as oral tablets, starting from 100 mg/day during the first week and escalated to a maximum of 400 mg per day at the end of four weeks, with a weekly increase of 100 mg each week. After achieving the maximum dose of 400 mg/day as 200 mg BD (twice a day), the patients were maintained on this dosage for twelve weeks. Pain levels were assessed using the VAS at baseline and after a three-month treatment period with 400 mg/day dose. Pain scores ranged from 0 to 10 (0 as no pain, and 10 as extreme pain). In accordance with the established protocol, an evaluator, unaware of the treatment allocation, assessed the patients' pain levels at baseline and after the therapeutic intervention.

STATISTICAL ANALYSIS

The data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 26. The mean±standard deviations were presented for age, duration of diabetes, HbA1c level, and pain scores. The frequencies & percentages of gender, obesity, and both controlled & uncontrolled diabetes were documented. Categorical data were analyzed using the Chi-square test and an independent t-test was used to compare means of quantitative variables between two groups. Paired t-test was applied to compare mean pain scores at baseline and post-treatment (3 months) within the groups. A p-value of <0.05 was considered significant.

RESULTS

The mean age of patients was 46.67±9.66 years in group A and 49.30±8.38 years in group B, and most of the patients in both groups were more than 40 years old. The male demographic was more prevalent in both groups. The mean duration of diabetes mellitus in groups A and B was 22.90±13.08 years and 23.50±13.94 years, respectively. Less than half in both groups were obese (40% vs. 43.3%). However, both of the groups showed no statistically significant difference in terms of distributions of age, gender, obesity, and duration of diabetes mellitus. The two groups also showed no significant difference in terms of mean HbA1c levels (5.97±2.01% vs. 6.71±1.77%) (Table 1).

The baseline VAS values for pain were similar across the groups, with group A scoring 7.40±1.96

and group B scoring 6.87±2.01 (p=0.31). Group A experienced a significant decrease in pain score to 3.90±1.92, whereas group B exhibited no significant difference after treatment (p=0.736). A statistically significant difference in post-treatment scores was found between the study groups (p <0.001) (Table 2).

Regarding age, gender, obesity, and diabetes control, mean VAS score was significantly lower in Lacosamide group (p <0.001). The duration of diabetes did not significantly influence treatment response in terms of VAS improvement (p >0.05) (Table 3).

Table 1: Demographic and Baseline Characteristics of the Study Groups

Characteristics		Group A (Lacosamide) Frequency & Percentage	Group B (Placebo) Frequency & Percentage	p-value
Age Groups (Years)	**20-40**	9(30%)	5(16.7%)	0.22
	41-60	21(70%)	25(83.3%)	
Gender	**Male**	20(66.7%)	17(56.7%)	0.43
	Female	10(33.3%)	13(43.3%)	
Duration of Diabetes Mellitus (Years)	**≤10**	8(26.7%)	9(30%)	0.77
	>10	22(73.3%)	21(70%)	
Obesity	**Yes**	12(40%)	13(43.3%)	0.79
	No	18(60%)	17(56.7%)	
Diabetes Control	**Controlled**	20(66.7%)	14(46.7%)	0.12
	Un-Controlled	10(33.3%)	16(53.3%)	

Table 2: Baseline and Post-Treatment Pain Score of the Study Groups

VAS score	Group A (Lacosamide)	Group B (Placebo)	p-value
Baseline Pain Score (Mean±SD)	7.40±1.96	6.87±2.01	0.31
Post-Treatment Pain Score (Mean±SD)	3.90±1.92	6.73±1.72	<0.001*
p-value	0.001*	0.736	

**Significant p-value*

Table 3: Post-Stratification Analysis of Post-Treatment VAS Scores in Groups A & B

Variables		Group A (Lacosamide) Mean±SD	Group B (Placebo) Mean±SD	p-value
Age Groups (Years)	**20-40**	4.44±2.06	7.00±2.12	<0.001*
	41-60	3.67±1.85	6.68±1.68	<0.001*
Gender	**Male**	3.90±1.84	6.47±1.88	<0.001*
	Female	3.90±2.18	7.08±1.49	<0.001*
Duration of Diabetes Mellitus (Years)	**≤10**	4.00±1.69	3.86±2.03	0.77
	>10	6.44±1.81	6.86±1.71	0.36
Obesity	**Yes**	3.25±1.54	7.23±1.42	<0.001*
	No	4.33±2.05	6.35±1.86	0.0002*
Diabetes Control	**Controlled**	3.95±1.72	7.29±1.68	<0.001*
	Un-controlled	3.80±2.25	6.25±1.65	<0.001*

**Significant p-value*

DISCUSSION

In Pakistan, diabetes stands as the leading cause of peripheral neuropathy. The occurrence of peripheral neuropathy in individuals with diabetes in Pakistan exhibits considerable variation, with rates spanning from 16.30% to 79.50%.[8]

In our study, the mean age of the patients was 46.67±9.66 years in group A and 49.30±8.38 years in group B with a majority of males. A study reported that most of the patients with diabetic neuropathy were males (61.8%) and above 60 years old (85.6%).[9] Hussain et al. observed that age above 50 years was significantly associated with DNP.[8] A study conducted at Sheikh Zayed Hospital, Lahore, reported a 20% prevalence of DNP in patients aged ≥60 years, compared to 8.9% in those aged ≤35 years.[10] The majority of patients presenting with diabetic neuropathy had more than 10 years of duration since diagnosis, and the mean duration of diabetes mellitus in groups A and B was 22.90±13.08 and 23.50±13.94 years, respectively. Consistent with our findings, a nationwide study depicted that over 10 years after the diagnosis of diabetes was associated with painful DNP. Moreover, the presence of other co-morbid conditions like hypertension and ischemic heart disease was also related to the early development of diabetic neuropathy.[11] Bondar et al. also stated that DNP was the most prevalent microvascular complication in individuals with diabetes, affecting more than half of patients after 20 years of disease progression.[12]

Despite being on hypoglycemic medications, 43.3% of patients in the current study had uncontrolled diabetes, indicated by HbA1C levels above 7%. Previous literature emphasized that chronic hyperglycemia increased the risk of peripheral diabetic neuropathy.[13] Nozawa et al. also reported that higher 3-year mean HbA1c levels showed a significant association with the occurrence of DPN (adjusted odds ratio: 1.23; 95% CI: 1.06-1.42).[9] Another study observed that increasing HbA1c levels were significantly associated with the occurrence of DNP ($p < 0.05$).[11] Hepsen et al. found that even HbA1c levels of prediabetics showed a significant positive correlation ($r=0.188$, $p=0.014$) with VAS score.[14]

Despite the effectiveness of traditional treatments like pregabalin, duloxetine, or tricyclic antidepressants, neuropathic pain continued to be a considerable contributor to morbidity and disability.[13,15] When the mean post-treatment pain scores were evaluated, the lacosamide group exhibited a significant reduction in pain scores from 7.40±1.96 to 3.90±1.92 ($p < 0.001$), compared to the placebo group in our study. A study from Sindh, Pakistan reported that patients in the lacosamide group had a mean pre-trial pain score of 6.59±1.95, which declined to 3.39±1.94. In comparison, the placebo group showed a baseline score of 6.71±1.89, decreasing only to 6.35±1.52 after the 20-week maintenance phase ($p < 0.0001$).[7]

In a recent multicenter trial to study the effect of lacosamide on peripheral neuropathic pain, lacosamide reduced the pain intensity by up to 50% in patients with peripheral neuropathic pain.[16] In a meta-analysis, LCM was reported to be more effective than placebo in reducing the pain of DPN, but showed inferior efficacy when compared to 1st line drugs like duloxetine and pregabalin. However, it was more tolerable and had fewer side effects.[17] In a study conducted in Swat, Riaz et al. combined LCM with pregabalin and reported that the pregabalin group demonstrated a mean post-treatment score of 3.07±1.32, whereas the combination of pregabalin and lacosamide achieved a lower mean score of 2.30±1.16 ($p < 0.05$). Treatment effectiveness was observed in 58.2% of the pregabalin group compared to 80.6% in the combination group ($p < 0.05$).[18] In a recent study on the Indian population, Lacosamide significantly reduced pain (numeric rating score: 7.7 to 2.50) compared to pregabalin (7.6 to 4.27) ($p < 0.001$), indicating greater effectiveness. [19]

CONCLUSION

Lacosamide showed significantly higher efficacy in reducing pain intensity indicated by lower VAS scores among patients with diabetic neuropathy compared to placebo. When compared with placebo, lacosamide significantly lowered pain scores across age, gender, diabetes control, and obesity groups. The marked decrease in post-treatment VAS scores highlighted its potential as an effective adjunctive option for managing neuropathic pain in diabetic patients.

LIMITATIONS & RECOMMENDATIONS

Our study had a few limitations, including a single-centered study and a small sample size. Moreover, a fixed dose of lacosamide was studied. Further studies are recommended on lacosamide at various doses, with a special emphasis on its side effects and tolerability. Studies on combination treatments are also recommended for the future.

Conflict of interest: None.
Source of funding: None.

Authors Contributions:
A.A: Conception of the idea and data collection
S.A.K: Data collection and analysis
U.A: Manuscript writing and proofreading

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Original Article

Intestinal Parasitic Infections among Children and Young Adolescents Visiting Provincial Headquarter Hospital in Gilgit, Pakistan and their Associated Factors

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ABSTRACT

Objective: To detect the frequency and species distribution of intestinal parasites among children and young adolescents visiting a provincial Headquarter Hospital in Gilgit, Pakistan and determine their association with socio-demographic and environmental factors

Methodology: This descriptive, cross-sectional study was done among patients visiting the Provincial Headquarter Hospital in Gilgit-Baltistan, Pakistan after ethical approval. The study duration was 6 months from August 2024 to January 2025. After taking informed consent, 227 children and young adolescents with ages ranging from 1 to 18 years were included using non-probability convenience sampling technique. Data was collected using a structured questionnaire including demographic factors, hygiene practices, healthcare access, and other relevant factors. Specimen bottles labeled with participant names and identification numbers were provided to parents and they were guided for stool sample collection. The collected specimens were processed in the Pathology Department of a healthcare facility for stool routine analysis. The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.

Results: Intestinal parasitic infections (IPIs) were present in 74(32.6%) children and young adolescents. *Ascaris lumbricoides* (46%) and *Giardia lamblia* (29.7%) were the most prevalent intestinal parasites. Access to clean drinking water and hygienic conditions had a significant relation with IPIs (p-value=0.001). No significant association was seen with other variables such as gender, age, education level, and family income.

Conclusion: Intestinal parasitic infections were prevalent in 32.6% children and young adolescents. *Ascaris lumbricoides* and *Giardia lamblia* were the most common parasites. There was a statistically significant influence of environmental factors, particularly access to clean drinking water and poor personal hygienic conditions, on the frequency of these infections.

Keywords: *Parasitic infections. Ascariasis. Giardiasis.*

INTRODUCTION

Intestinal parasitic infections pose a significant threat to global health, affecting 30% of the world population. Around 3.5 billion people have parasitic infestations across the world, out of which 450 million cases present with signs and symptoms. Approximately 200,000 deaths are attributed to these infections. The parasitic infections by hookworms cause 45000, *Ascaris* causes 4300, and *Entamoeba* histolytica causes 54000 annual deaths.[1,2] Intestinal parasitic infections are responsible for 1.9 million disability-adjusted life years. The healthcare systems face significant financial constraints to cope with the rising number of IPIs.[3]

The major burden of IPIs lies in the developing countries.[1] The major reasons behind the greater prevalence of IPIs in these countries are poverty, overcrowding, insufficient handwashing practices, use of unwashed vegetables, lack of education & awareness, poor hygiene, shortage of clean water supply, and inadequate healthcare facilities.[4] Parasitic infections are caused by protozoans and helminths (worms). The main transmission route is fecal-oral, but transmission can also occur by larval penetration of skin.[5] Children are prone to acquire IPIs owing to their weak immunity and poor hygienic practices. These infections cause abdominal pain, anemia, and malnutrition in children. They can also impair their physical and mental growth, leading to a great influence on productivity and quality of life. Children should be routinely screened for IPIs & their associated malnutrition and prescribed proper therapy, not only to reduce the morbidity & mortality attributed to IPIs but also to boost the physical and mental health of children.[6]

The prevalence of intestinal parasitic infections is very high in Pakistan, varying from 25% to 70%. Combating this high burden of IPIs is challenging owing to lack of awareness among the public, inadequate healthcare facilities, and a lack of a monitoring system for IPIs.[7]

The mountainous location of Gilgit-Baltistan with its harsh climate makes it a hard-to-reach area, leading to limited healthcare infrastructure in the region. The traditional practices of fetching water from far areas, lack of clean water availability, defecating in the open environment, and other unhygienic lifestyle conditions contribute to the favorable transmission

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Received: September 5, 2025; Accepted: September 20, 2025

of parasites. In spite of the considerable risks involved, there is an absence of thorough data regarding the frequency and determinants of intestinal parasitic infections in Gilgit-Baltistan. The current study aims to address this critical gap by assessing the frequency of IPIs and associated factors in children and young adolescents in Gilgit-Baltistan to provide evidence for improving public health interventions, aligning with Pakistan's broader commitment to the Sustainable Development Goals.

METHODOLOGY

This descriptive, cross-sectional study was done on children and young adolescents visiting the Provincial Headquarter Hospital in Gilgit, Pakistan. The study duration was 6 months from August 2024 to January 2025. After ethical approval (Letter No. 1150/PHG/2023, 29-07-2024), 227 participants were included using non-probability convenience sampling technique. The sample size was estimated based on the expected prevalence rate of 30% IPIs, confidence level of 95% and margin of error of 6%.[8] The inclusion criteria were children and young adolescents with an age range of 1 to 18 years, who were willing to participate and give stool samples. Children/adolescents on anti-parasitic/deworming medication and those with chronic gastrointestinal conditions unrelated to IPIs were excluded. Informed written consent was obtained from the parents or guardians before participation and they were explained the purpose of the study. Data was collected using a semi-structured questionnaire including demographic factors, education level of guardian, family income, access to clean drinking water, and physical hygiene conditions. Based on family income, those with monthly income <30,000 rupees were labeled as having low income, 30,000 to 70,000 rupees were middle income, and >70,000 rupees were high income. The physical hygienic conditions were categorized according to handwashing practices (before meals and after defecation), trimmed nails, regular wearing of shoes, in-home sanitation facility, eating raw fruits and vegetables, playing with soil, and swimming habit.[9] Wide-mouthed, leak-proof specimen bottles labeled with participant names and identification numbers were provided to parents or guardians and they were guided for stool sample collection. Each participant was instructed to provide three stool samples on alternate days to increase the diagnostic sensitivity. The collected specimens were processed in the Pathology Department of a nearby healthcare facility for stool routine analysis by a trained laboratory technologist. The fresh specimens received were physically examined and then two wet preparations were made using normal saline on one side and Lugol's iodine on the other side of the same glass slide. They were examined under 10X and 40X objective lens to identify ova, cysts or trophozoites of various parasites. In addition, wet preparations were also made by using the formalin-ether concentration technique. In this technique, 0.5 g of the stool sample was mixed with 10 ml of normal saline. The suspension was strained using a gauze, centrifuged, and the supernatant was discarded. Around 2.5 ml of 10% formaldehyde and 1 ml of ether were added to the sediment. The suspension was again centrifuged for 1-2 minutes at 3000 rpm. The supernatant was discarded and wet preparation was prepared from the sediment and examined under microscope.[9] To ensure accuracy, each sample was examined independently by two trained microbiologists. In case of disagreement, the slides were re-examined together and senior microbiologists were also consulted for final confirmation. Positive cases were referred to the physician for treatment.

STATISTICAL ANALYSIS

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Categorical variables were presented as frequency & percentage, while numerical variables were summarized using mean and standard deviation. Association between categorical variables was determined using Pearson's Chi-square and Fisher's exact test. A p-value of <0.05 was considered statistically significant.

RESULTS

Out of 227 participants of our study, most (42.3%) were school-aged children (6-12 years), followed by young adolescents (33.5%), and children ≤5 years (24.2%). Most (55%) of the participants were males. A greater proportion of the participants (41.4%) had low income, 36.6% had middle income, and 22% had high income. Regarding the education status of guardians, 42.8% were illiterate, 34.8% were educated till secondary, and 22.4% had completed graduation. The majority (56.4%) of the population had no access to clean water and reported good physical hygienic conditions (62.1%).

Out of 227 participants, 74(32.6%) had parasitic infestations while 153(67.4%) showed no infestation. Access to clean drinking water and hygienic conditions were significantly associated with infestation rates (p-value=0.001). A higher

frequency of IPIs was observed among participants with no access to clean drinking water and poor physical hygienic conditions. No significant association was seen with other variables such as gender, age, education level, and family income (Table 1).

Regular swimming habits, playing with soil, and eating raw fruits & vegetables were significantly associated with the presence of parasitic infestations (p=0.001). More frequent IPIs were exhibited by those who did not trim nails, wear shoes or wash hands before meals, and after defecation regularly (p=0.001).

The most frequently reported parasite was *Ascaris lumbricoides* (46%), followed by *Giardia lamblia* (29.7%). Other parasites, such as *Hymenolepis nana*, *Taenia saginata*, *Trichuris trichiura*, and *Entamoeba histolytica*, had lower frequency rates (Figure 1).

Table 1: Association of Socio-Demographic and Environmental Factors with Parasitic Infestation

Socio-Demographic and Environmental Factors		Parasitic Infestation (Frequency & Percentage)			p-value
		Present (n=74)	Absent (n=153)	Total	
Gender	**Male**	38(16.7%)	87(38.3%)	125(55%)	0.43
	Female	36(15.9%)	66(29.1%)	102(45%)	
	Total	74(32.6%)	153(67.4%)	227(100%)	
Age Groups (Years)	**≤5**	23(10.1%)	32(14.1%)	55(24.2%)	0.18
	6 to 12	26(11.5%)	70(30.8%)	96(42.3%)	
	13 to 18	25(11%)	51(22.5%)	76(33.5%)	
	Total	74(32.6%)	153(67.4%)	227(100%)	
Education Level of Guardian	**Illiterate**	29(12.8%)	68(30%)	97(42.8%)	0.66
	Secondary	26(11.5%)	53(23.3%)	79(34.8%)	
	Graduation	19(8.3%)	32(14.1%)	51(22.4%)	
	Total	74(32.6%)	153(67.4%)	227(100%)	
Family Income	**Low**	29(12.8%)	65(28.6%)	94(41.4%)	0.89
	Middle	28(12.3%)	55(24.2%)	83(36.5%)	
	High	17(7.5%)	33(14.5%)	50(22%)	
	Total	74(32.6%)	153(67.4%)	227(100%)	
Access to Clean Drinking Water	**No**	65(28.6%)	63(27.8%)	128(56.4%)	0.001*
	Yes	9(4%)	90(39.6%)	99(43.6%)	
	Total	74(32.6%)	153(67.4%)	227(100%)	
Physical Hygienic Conditions	**Poor**	58(25.6%)	28(12.3%)	86(37.9%)	0.001*
	Good	16(7%)	125(55.1%)	141(62.1%)	
	Total	74(32.6%)	153(67.4%)	227(100%)	

**Significant p-value*

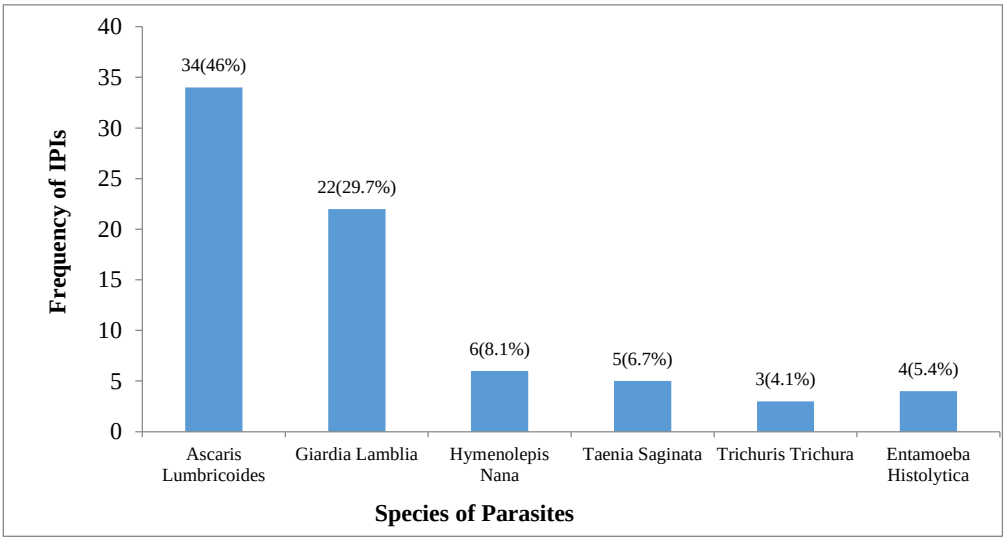

Figure 1: Species Distribution of Intestinal Parasitic Infections

DISCUSSION

Intestinal parasitic infections remain a critical public health challenge globally, especially in low-resource settings where factors such as inadequate sanitation, unsafe water, and poor hygiene practices are widespread. The prevalence of IPIs had also increased due to food globalization and frequent travel to various countries.[10,11] The findings of our study revealed a significant burden of IPIs (32.6%) among children and young adolescents in Gilgit-Baltistan, Pakistan. In two studies done in Ethiopia, IPIs were present in 24.4% of the children.[12,13] Other studies reported 28.27% and 29.4% prevalence of parasitic infestation among children in Ethiopia.[14,15] Sitotaw et al. reported a higher (62.40%) rate of parasitic infections among school children in Ethiopia.[16] This showed that the prevalence of IPIs can vary greatly from one area to another, even within the same country. In Argentina, 55.4% of the participants aged 1-15 years had IPIs.[17] In Somalia, IPIs were reported in 82.9% of the children.[18] A study from Lower Dir, Pakistan showed an 82% IPI rate among children. The high frequency of IPIs in children and young adolescents was attributed to their increased vulnerability due to unhygienic behaviors and greater interaction with contaminated environment.[19] On the other hand, a lower prevalence of IPIs had been found in Europe (5.9%).[20] In a study in India, the frequency of IPIs was 9.3%.[21]

The most common parasites in our study were *Ascaris lumbricoides* (46%) and *Giardia lamblia* (29.7%). Other parasites isolated were *Hymenolepis Nana* (8.1%), *Taenia saginata* (6.7%), *Trichuris trichiura* (4.1%), and *Entamoeba histolytica* (5.4%). In Lower Dir from Pakistan, *Ascaris* was the most common parasite isolated (57.7%), followed by hookworm (40.7%), *Taenia saginata* (20.9%), *Enterobius* (14.8%), *Trichuris* (14.5%), *Hymenolepis* (12.9%), and *Entamoeba* (9.25%).[19] Abebaw et al. and Scavuzzo et al. reported *Giardia lamblia* and *Hymenolepis nana* as the most common causes of parasitic infections.[12,17] In Ethiopia, parasitic infestations were mainly caused by *Entamoeba histolytica* (10.9%) and *Schistosoma mansoni* (7.4%).[13] According to a study by Duguma et al., *Ascaris* was the most common parasite (8%), followed by *Trichuris* (6.2%) and *Giardia* (4%).[15] In another study, the most common parasites were *Ascaris* (22.7%), Hookworms (20.6%), and *Entamoeba histolytica* (8.1%). Other parasites isolated were *Trichuris trichura* (7.6%), *Giardia* (6.5%), *Hymenolepis nana* (5.7%), and *Schistosoma mansoni* (4.4%).[16] In Somalia, the most common parasites were *Ascaris* (46.6%), *Giardia lamblia* (22.1%), and *Entamoeba histolytica* (17.6%).[18] In India, *Ascaris* (57%) and hookworm (42%) were the most common parasites.[21]

In our study, males comprised 55% of the population, and 45% were females. There was no statistically significant difference in parasitic infestation rates between males and females. Similarly, there were 53.2% males and 46.8% females in a study done by Yeshitila et al. Females were predominantly infected but with no statistical difference.[13] Similarly, another study revealed that IPIs affected males and females equally.[16] Our study showed that the frequency of IPIs was almost similar in various age groups and the age factor did not significantly affect infestation rates (p=0.18). Our results were in accordance with a study by Sitotaw et al., where no statistically significant difference in IPIs in different age groups was observed.[16] The IPIs affected a greater proportion of participants in the 10-14 years age groups (26.7%) in a study by Yeshitila et al.[13] In another study, there was a significant difference in the frequency of IPIs in different age groups, with <5 years most commonly affected, followed by 6-12 years.[17] Osman et al. from Somalia reported that IPIs were significantly prevalent in 13-36 months age group.[18] The results of the current study reported no significant association between the infestation rates and the education level of guardians (p=0.66). Similarly, family income did not significantly impact infestation rates (p=0.89). In contrast, a study revealed a significant association of IPIs with family income and education level. The rate of IPIs was significantly higher in the low income group and those with lower literacy.[16]

In our study, the factors significantly associated with IPIs were limited access to clean drinking water and poor physical hygienic conditions. Children without access to clean water (28.6%) had a significantly higher infection rate as compared to those with access to clean water (4%) (p=0.000). Poor hygienic conditions were significantly associated with higher infection rates (25.6%) as compared to only 7% rate among those with good hygienic practices. (p=0.000). Duguma et al. showed that access to clean drinking water, lack of handwashing, waste disposal methods, habit of wearing shoes, and poor hygiene were significantly associated with IPIs in Ethiopia.[15] In other studies, the most common risk factors associated with parasitic infections in children were untrimmed fingernails and lack of

handwashing.[12,14] The predisposing factors for parasitic infestation were lack of handwashing and swimming in contaminated water in a study.[13] Scavuzzo et al. reported that overcrowding and walking barefoot, were significantly associated with IPIs in Argentina.[17]

CONCLUSION

Intestinal parasitic infections were prevalent in 32.6% children and young adolescents. *Ascaris lumbricoides* and *Giardia lamblia* were the most common parasites. There was a statistically significant influence of environmental factors, particularly access to clean drinking water and poor hygienic conditions on the frequency of these infections.

LIMITATIONS & RECOMMENDATIONS

Our study had a few limitations, such as cross-sectional design, a single-centered study, and the use of convenience sampling, limiting the generalizability of the findings. The reliance on self-reported data for hygiene practices introduced the possibility of recall bias or social desirability bias. The study was conducted over 6 months, but parasitic prevalence may vary seasonally, which was not discussed.

The study recommended that targeted public health interventions focusing on improving water & sanitation infrastructure and promoting hygiene education should be implemented. Routine deworming programs, particularly in schools, are essential for reducing the burden of parasites such as *Ascaris lumbricoides*, etc. Health education campaigns focused on promoting hygiene practices, such as handwashing and safe food handling, can further reduce the spread of parasitic infections.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
U.A: Performed data analysis, interpretation, and drafted the initial manuscript.
S.N: Contributed to study design, methodology development, and critical revision of the manuscript.
A.Q: Conceived and designed the study, supervised data collection.
A.A: Participated in data collection, laboratory work, and tabulation of results.
N.Y: Assisted in literature review, data entry, and formatting of figures and tables.
Z.W: Supervised the overall project, reviewed the final manuscript critically for important intellectual content, and approved it for publication.

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Original Article

Diagnostic Accuracy of Retrograde Urethrogram in Determination of Urethral Stricture taking Cystoscopy as Gold Standard

Rafia Irum, Aneeza Qayyum, Hira Bushra, Hamna Mazhar

ABSTRACT

Objective: To assess the diagnostic accuracy of retrograde urethrogram in determination of urethral strictures taking cystoscopy as the gold standard.

Methodology: This cross-sectional study was conducted at the Department of Radiology, Sharif Medical & Dental College, Lahore from May to October 2024. After ethical approval and written informed consent, 189 patients meeting the inclusion criteria were recruited through non-probability convenience sampling technique. These patients underwent retrograde urethrogram (RUG) with contrast injection, followed by cystoscopy 4-5 days later. Demographic details and history of risk factors were recorded. Radiographic findings were assessed by a radiologist, and patients were classified as positive or negative for urethral strictures. Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25. A 2x2 table was made and diagnostic accuracy was calculated. Chi-square test was used to compare categorical variables.

Results: Retrograde urethrogram detected urethral strictures in 24.3% of cases with a sensitivity of 75.56%, specificity of 91.67%, positive predictive value (PPV) of 73.91%, and negative predictive value (NPV) of 92.31%. The overall diagnostic accuracy of RUG was 87.83%. Age groups, history of urinary tract infections, and prostate surgeries had significant association with the presence/absence of strictures on RUG ($p < 0.05$).

Conclusion: The diagnostic accuracy of retrograde urethrogram was high in determination of urethral strictures taking cystoscopy as the gold standard. Urethral strictures were significantly more prevalent among older males with history of urinary tract infections and prostate surgeries.

Keywords: *Urethral stricture. Cystoscopy. Contrast media. Iohexol.*

INTRODUCTION

The male urethra is an essential part of the urinary system, measuring approximately 20 cm in length, and it is surrounded by the corpus spongiosum, a vascular tissue that plays a critical role in maintaining the structure and function of the urethra. The urethra itself is divided into two primary sections: the anterior urethra and the posterior urethra, which are separated by the membranous urethra.[1] Each part of the urethra serves a unique function in the passage of urine from the bladder to the outside of the body.[2]

Urethral stricture is a condition characterized by the narrowing of the urethra, which can have a significant impact on a patient's quality of life. This condition develops slowly over time and can result in a variety of symptoms, including dysuria, weak urinary stream, incomplete bladder emptying, and urinary tract infections (UTIs).[3] In recent years, the incidence of iatrogenic urethral strictures has been increasing, primarily due to the rise in minimally invasive, transurethral urological procedures like cystoscopy and transurethral resection of the prostate (TURP).[4] Chronic inflammatory conditions such as lichen sclerosis, urinary tract infections, prolonged catheterization, and the increased cases of urethral traumas resulting from traffic accidents and workplace injuries are among other contributing factors.[5] Many complications including acute urinary retention, prostatitis, epididymo-orchitis, hydronephrosis, chronic kidney disease, peri-urethral abscess, and kidney stones can arise if the disease remains untreated for a longer duration.[6]

Various diagnostic techniques like uroflowmetry, cystoscopy, RUG, voiding cysto-urethrography (VCUG) can be useful in making diagnosis of urethral strictures and describing key characteristics like position & length of stricture and severity of condition. Cystoscopy, usually performed under anesthesia, makes the definitive diagnosis of urethral stricture. However, it cannot assess the length of the stricture and does not provide information about the condition of the surrounding tissue.[4] Retrograde urethrogram technique offers several advantages including its ability to provide real-time imaging of the urethra as contrast material is injected, allowing for dynamic assessment of the stricture's characteristics. It also enables the clinician to measure its length, which is a crucial factor in

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Received: July 10, 2025; Accepted: September 1, 2025

planning further treatment, such as urethral dilation, urethrotomy, or urethroplasty.[7]

A recent high number of urethral strictures is being reported in Pakistan due to increased prevalence of sexually transmitted diseases and improper catheterization techniques. Retrograde urethrogram is comparatively inexpensive, and less invasive technique for its diagnosis. It was pertinent to compare the diagnostic accuracy of RUG against the gold standard (cystoscopy) in our local setting to develop locally relevant diagnostic guidelines and improve patient outcomes.

METHODOLOGY

After approval from the institutional review board (Letter No. SMDC/SMRC/337-24, 22-05-2024), this cross-sectional study was carried out at the Department of Radiology, Sharif Medical & Dental College, Lahore from May to October 2024. A sample size of 189 was estimated using 90% confidence level, 7% margin of error, 100% sensitivity of RUG, 66.7% specificity, and prevalence of urethral strictures at 28.5%.[8] The male patients aged 18-75 years, who presented with restricted urinary flow from the bladder, urinary tract infection, or inflammation of the bladder, incomplete voiding, and/or painful urination were enrolled by using non-probability convenience sampling technique. Patients who had suggestive symptoms of acute urethritis, malignancy or metastatic disease, and received renal implant were excluded.

After obtaining written informed consent, demographic and risk factors detail [name, age, body mass index (BMI), duration of symptoms, marital status, occupation, history of diabetes, hypertension, smoking, urinary tract infection, and previous prostate surgery] were recorded on a questionnaire. The patients then underwent retrograde urethrogram in the right oblique or semi-lateral position after emptying the bladder. The right leg was partially flexed, with the left leg stretched above it and the left hip just above the table. A Foley's catheter was placed in the external meatus after disinfecting the glans, and 10-15 ml of 15% (w/v) Iohexol was injected through catheter. The patients were told to relax their pelvic floor muscles during the injection. The penile tip was pressed tightly around the catheter during injection to prevent the escape of contrast medium. A single spot film was taken with a constant film focus distance of 1 meter maintained for all radiographs. All scans were performed and interpreted by two consultant radiologists with at least 4 years of experience in radiology to improve accuracy. Patients were labeled as positive for urethral strictures if annular or longitudinal narrowing of the urethra was seen on radiographs.[9] After 4-5 days, cystoscopy was performed through the suprapubic tract, and the cystoscope was advanced through the bladder neck to the level of the stricture. Findings were recorded, and patients were confirmed for presence or absence of urethral strictures. The cases that were positive on both RUG and cystoscopy were labelled as true positives (TP). Those who were positive on RUG but negative on cystoscopy were false positives (FP). False negatives (FN) were negative on RUG but positive on cystoscopy. Those who were negative on both the tests were true negatives (TN).

STATISTICAL ANALYSIS

Data was entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics like mean±standard deviation and frequency (percentage) were used for numeric and categorical variables, respectively. A 2x2 table was made by taking cystoscopy as a gold standard. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of RUG were calculated. The categorical variables were compared using Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included 189 male participants and the mean age of the participants was 46.87±16.74 years, indicating a wide range of ages (from 30.9 to 63.6 years). Most of the participants (56.6%) belonged to 18-50 years age group. Nearly half (48.1%) of them were married and only 45% were employed. The mean BMI was 27.31±4.87 kg/m^2, suggesting that the majority of the participants were in the overweight range. The mean duration of symptoms was 11.70±6.72 weeks, reflecting that some participants experienced longer duration of symptoms than others. The frequency of urethral stricture on RUG was 24.3%. The age groups showed significant association with urethral strictures on RUG. Most of the patients with urethral strictures were older than 50 years (Table 1).

The risk factors profile of 189 participants revealed 47.6% diabetics, 40.7% hypertensive and 49.7% smokers. None of these factors had any significant association with urethral strictures on RUG ($p \geq 0.05$). Urethral stricture was significantly more prevalent among those with UTIs (16.9%) and history of prostate surgery (15.9%) (Table 1).

The cross-tabulation of cystoscopy and RUG outcomes showed significant results (Table 2).

Retrograde urethrogram showed a sensitivity of 75.56%, specificity of 91.67%, PPV of 73.91%, NPV of 92.31%, and an overall diagnostic accuracy of 87.83%.

DISCUSSION

This study aimed to evaluate the diagnostic accuracy of retrograde urethrography for detecting urethral strictures keeping cystoscopy as gold standard. The frequency of urethral stricture on RUG was 24.3%. The mean age of the participants was 46.87±16.74 years and most of the patients with urethral strictures on RUG were older than 50 years age (p=0.00001). Similarly, de Farias RB et al. showed that urethral strictures were significantly more frequent (82.2%) among patients over 40 years of age (p <0.001).[10] However, a previous study didn't reported any significant association of age with the occurrence of urethral strictures among post-TURP patients (p=0.932).[11] The results of the current study showed that hypertension, diabetes mellitus, and smoking had no significant association with the occurrence of urethral stricture on RUG. Contrary to our findings, diabetes mellitus (p=0.038) and hypertension (p=0.012) were significant risk factors in recurrence of urethral strictures among patients who underwent internal urethrotomy.[12]

Our significant results also revealed that the majority of cases of urethral strictures diagnosed on RUG had a history of UTI and prostate surgeries. Another study also reported that TURP represented 41% of all iatrogenic causes of urethral strictures. Infections accounted for 26.6% of cases.[13] Sekar et al. found that 12.8% patients who underwent TURP developed urethral strictures. They also revealed that the use of larger size Foley's catheter during this procedure was significantly associated with post-operative urethral strictures.[14]

When compared with cystoscopy as gold standard in our study, RUG had a sensitivity of 75.56%, specificity of 91.67%, positive predictive value of 73.91%, negative predictive value of 92.31%, and an overall accuracy of 87.83%. In a previous study, when RUG was compared with intraoperative findings as gold standard, it showed 100% sensitivity, 66.7% specificity and an overall accuracy of 83.3% in detecting urethral strictures.[8] Patel et al. also documented in their review of literature that RUG was the best technique in making diagnosis of urethral structures following urethral traumas.[15]

Table 1: Association of Risk Factors with Urethral Strictures on RUG (n=189)

Risk Factors		Urethral Stricture on RUG		Total	p-value
		Present (n=46)	Absent (n=143)		
Age Groups (Years)	**16-50**	09(4.8%)	98(51.9%)	107(56.7%)	0.00001*
	51-70	37(19.5%)	45(23.8%)	82(43.3%)	
	Total	46(24.3%)	143(75.7%)	189(100%)	
Urinary Tract Infections	**Yes**	32(16.9%)	57(30.2%)	89(47.1%)	0.0004*
	No	14(7.4%)	86(45.5%)	100(52.9%)	
	Total	46(24.3%)	143 (75.7%)	189(100%)	
History of Prostate Surgery	**Yes**	30(15.9%)	58(30.7%)	88(46.6%)	0.003*
	No	16(8.4%)	85(45%)	101(53.4%)	
	Total	46(24.3%)	143(75.7%)	189(100%)	

**Significant p-value*

Table 2: Cross Tabulation for Determining Diagnostic Accuracy of RUG in Diagnosis of Urethral Strictures taking Cystoscopy as Gold Standard

Retrograde Urethrogram	Cystoscopy (Gold Standard)		Total	p-value
	Positive	Negative		
Positive	34(18%) (TP)	12(6.3%) (FP)	46(24.3%)	0.00001*
Negative	11(5.8%) (FN)	132(69.9%) (TN)	143(75.7%)	
Total	45(23.8%)	144(76.2%)	189(100%)	

**Significant p-value*

In contrast to our findings, a study reported that RUG was used in combination with VCUG for the evaluation of urethral strictures. They found that combined preoperative use of RUG and VCUG underestimated urethral stricture measurements, especially in the membranous and bulbar regions, when compared with intraoperative results ($p < 0.05$).[16] A high level of diagnostic accuracy is especially important as the precise location and length of the stricture are critical for planning surgical interventions like simple urethral dilation, an internal urethrotomy, or a more complex urethral reconstruction, i.e. urethroplasty. Misjudging the length or location of the stricture can lead to suboptimal outcomes, such as incomplete stricture excision or recurrence of the stricture postoperatively.[16,17]

Despite its high diagnostic accuracy reported in the literature, RUG had limitations, particularly in its ability to provide critical and detailed information regarding the fibrosis of soft tissues surrounding the stricture, such as spongiofibrosis or periurethral fibrosis. This condition required a more extensive reconstruction, and failing to detect it preoperatively could result in inadequate treatment.[18] To address this limitation, alternative imaging modalities such as sonourethrography (SUG) and magnetic resonance urethrography (MRU) have been explored. Bogdanov et al. found that stricture measurements on RUG were significantly different than those of intraoperative findings. However, MRU results were significantly similar to those of intraoperative findings.[19] A study documented that MRU was significantly most accurate in preoperative evaluation of strictures, followed by cystourethrography (RUG and VCUG) when compared to intraoperative measurements. The least accurate was SUG in this regard.[9] In contrast, a previous study showed that SUG was the most accurate method with a sensitivity of 60% and specificity 87.8% when compared with VCUG and cystoscopy for determining the length of strictures.[17] Jesrani et al. also highlighted that SUG had a higher diagnostic accuracy in determination of urethral strictures as compared to RUG.[20] With advancements in technologies, artificial intelligence and machine learning were more accurate in the detection and reconstruction of urethral strictures.[21]

Our findings reflected the broad utility of RUG in clinical practice, where it can be used for assessing urethral strictures providing crucial information about the location, length, and severity of the stricture.

CONCLUSION

When compared with cystoscopy as gold standard, retrograde urethrography had a good diagnostic accuracy in determination of urethral strictures among males. Urethral strictures were significantly more prevalent among older males with history of urinary tract infections and prostate surgeries.

LIMITATIONS & RECOMMENDATIONS

This study had a few limitations: cross-sectional design, single-centered study, non-probability convenience sampling technique limiting the generalizability of results. This study also lacked information on detailed characteristics of the stricture and post-operative follow-up. Further research is needed to explore the role of advanced imaging modalities and the integration of RUG with other techniques in the comprehensive evaluation of urethral strictures, particularly in complex cases where precise assessment of soft tissue involvement is necessary.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
R.I: Supervised the overall project, reviewed the final manuscript critically for important intellectual content, and approved it for publication.
A.Q: Contributed to study design, methodology development, and critical revision of the manuscript.
H.B: Performed data analysis, interpretation, and drafted the initial manuscript.
H.M: Conceived and designed the study, supervised data collection.

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Original Article

Comparison of Effectiveness between Diclofenac Suppositories and Injection Diclofenac in Abdominal Surgeries

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ABSTRACT

Objective: To compare the effectiveness of diclofenac suppositories and injection diclofenac in pain relief after abdominal surgeries.

Methodology: This quasi-experimental study was conducted at the West Surgical Ward, Mayo Hospital, Lahore from June 2022 to January 2023 after taking approval from ethical committee. Total 136 patients undergoing elective and emergency abdominal surgeries were enrolled in the study via non-probability convenience sampling technique. Informed written consent was taken from all the patients. The patients were divided into two groups (group A & B). Group A was given diclofenac suppositories and group B was given injection diclofenac via the intramuscular (I/M) route. The pain scores were recorded by using visual analogue scale (VAS) at 0, 8, 16, and 24 hours. The data was analyzed using Statistical Package for the Social Sciences (SPSS) version 26.

Results: There was a significant decrease in mean pain scores at 0, 8, 16, and 24 hours post-operatively in group A as compared to group B. The maximum difference in the means was observed at 16 hours post-operatively ($p < 0.001$). Only 15(11.1%) patients in group A required rescue analgesia, while more than half the patients in group B required rescue analgesia for effective pain relief ($p=0.001$). The proportion of patients experiencing adverse effects of the drug in group A was significantly smaller (8.1%) as compared to group B (25.7%) ($p=0.001$).

Conclusion: Rectal suppositories of diclofenac were significantly more effective for post-operative pain relief among patients undergoing abdominal surgeries as compared to diclofenac intramuscular injection.

Keywords: *Pain. Post-operative. Visual Analog Scale. Analgesia. Diclofenac.*

INTRODUCTION

Abdominal surgeries have a major role in the treatment of cases of non-traumatic acute abdominal pain. Appendicitis is the leading cause of acute abdominal pain, followed by cholecystitis and others.[1] The major complaint of surgical patients is the post-operative pain that occurs due to trauma to the tissues during surgery and activates pain pathways by the release of chemical mediators. Almost 22-67% patients experience moderate to severe pain during the first 24 hours after abdominal surgery as reported by various studies. The management of post-operative pain is the foremost challenge for surgeons as it is necessary for early mobilization and recovery as well as the psychological satisfaction of the patient.[2] Pain activates the sympathetic nervous system and renders the patient immobile. It also cripples the patient psychologically. All of this leads to more burden on the economy, hospitals, and healthcare resources. In the modern era, post-operative pain relief is directed towards maximum comfort of the patient using safe and cost-effective analgesics.[3]

Diclofenac sodium belongs to the class of non-steroidal anti-inflammatory drugs (NSAIDs). They inhibit cyclooxygenase enzymes and prostaglandin synthesis. Diclofenac in particular inhibits both cyclooxygenase 1 and 2 enzymes as well as lipoxygenase and phospholipase A2. It is a potent analgesic for musculoskeletal and spasmodic pain.[4] It has antipyretic effect and also helps in the reduction of inflammation.[5]

Diclofenac can be given orally as a tablet, through intramuscular injection or as a rectal suppository. Administration of the drug via the rectal route is easier and does not require a trained personnel as compared to the intramuscular route.[6] Intramuscular administration should be done by following proper protocol & aseptic techniques, and failure to do so may result in localized infection or abscess formation.[7] Administration of drug via the rectal route has the benefits of decreased first-pass metabolism, no gastric irritation, and higher local and systemic levels.[8]

Assessing the difference in pain relief and the need for rescue analgesia between diclofenac suppository and injectable diclofenac can guide clinicians in selecting the most effective and patient-friendly route of administration. This study aimed to compare the analgesic efficacy of diclofenac

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Received: October 3, 2025; Accepted: October 24, 2025

suppository versus injectable diclofenac in patients undergoing abdominal surgeries, to determine which route provides optimal post-operative pain control with reduced dependency on additional analgesics.

METHODOLOGY

This quasi-experimental study was conducted at the West Surgical Ward, Mayo Hospital, Lahore over a period of 8 months from June 2022 to January 2023 after taking approval from the ethical committee (Letter No. 233/RC/KEMU, 15-03-2021). A sample size of 136 participants was determined based on 80% power, 95% confidence interval, and the post-operative mean visual analog scale (VAS) pain scores for the diclofenac suppository and intramuscular injection groups reported as 3.88±1.90 and 4.76±1.75, respectively.[9] Patients were enrolled by using non-probability convenience sampling technique and were randomly divided into 2 groups of 68 each. Males and females, ≥18 years of age undergoing elective or emergency abdominal surgeries were included in the study. Patients with history of any previous abdominal surgery, NSAIDs contraindication (patients with gastritis, gastric or duodenal perforation), and patients on central nervous system (CNS) depressants or warfarin treatment were excluded.

Informed written consent was taken from all patients. The demographic data and body mass index (BMI) were recorded. Patients with BMI less 25 kg/m^2 were labeled as normal and those with ≥25 kg/m^2 were categorized as having deranged BMI. Group A was given diclofenac suppositories [Voltral suppository by DVAGO-100 mg twice daily (BD)] and group B was given intramuscular diclofenac [Injection Voren by DVAGO-75 mg or 1.5 mg/kg three times a day (TDS)]. If the pain was not relieved with diclofenac by either route**,** rescue analgesia was given in the form of injection nalbuphine via intravenous route at the dose of 10 mg.

Visual analog scale was used to measure pain at 0, 8, 16, and 24 hours post-operatively. Patients graded the severity of pain on VAS from 0 (no pain) to 10 (severe pain).[9] The proportion of patients undergoing any adverse event (gastrointestinal tract discomfort, headache, itching) and requiring rescue analgesia were also recorded.

STATISTICAL ANALYSIS

Data entry and analysis was done by using Statistical Package for the Social Sciences (SPSS) version 26. Quantitative variables such as age, body mass index (BMI), and VAS were presented as mean±standard deviation (SD). Qualitative variables such as gender and adverse events were presented by frequency & percentages. The results for quantitative and qualitative variables were compared by using independent sample t-test and chi-square, respectively. A p-value <0.05 was taken as significant.

RESULTS

The mean age of patients in group A and group B was 33.22±9.58 years and 34.05±10.70 years, respectively. The mean BMI of patients in group A was 25.71±2.35 kg/m^2 and the mean BMI of group B patients was 26.38±2.70 kg/m^2. Both groups didn't significantly differ in terms of age, gender, and BMI distribution (p >0.05). In group A, only 15(11.1%) patients needed rescue analgesia as compared to 39(28.7%) patients in group B (p=0.001). Also, 35(25.7%) patients faced adverse events in group B as compared to group A, where only 11(8.1%) patients suffered from adverse events (p=0.001) (Table 1).

The patients receiving diclofenac suppositories showed significantly better pain relief compared to those who received Injection diclofenac via I/M route. Group A showed a reduction in mean pain scores at 0, 8, 16, and 24 hours post-operatively as compared to group B (p <0.001) (Table 2). Pain reduction was greater in group A across all age categories. Participants aged 18-35 years had lower mean pain scores in group A (3.86±0.89) compared to group B (4.13±1.10) (p=0.028). Similarly, in those aged ≥35 years, group A (3.75±1.09) reported significantly less pain than group B (4.17±1.27) (p=0.0043). Both males and females in group A had significantly lower mean pain scores compared to their counterparts in group B (p <0.05). The analgesic effect of group A treatment remained superior regardless of side effects. Among participants who experienced adverse effects, group A (3.75±1.08) reported lower pain than group B (4.38±1.16) (p <0.001). The same pattern was observed in those without adverse effects (p <0.001). Participants who required rescue analgesia had higher pain scores, but group A (3.85±1.12) still showed significantly lower pain than group B (4.65±1.30) (p <0.001). Even among those not needing rescue analgesia, group A had better pain control (p <0.001). When stratification was done for BMI, patients with normal & deranged BMI in group A had significantly lower mean pain score as compared to group B (p-value <0.001) (Table 3).

Table 1: Demographic and Clinical Parameters of Groups A & B

Variables		Group A Diclofenac Suppositories (Frequency & Percentage)	Group B Injection Diclofenac (Frequency & Percentage)	Total	p-value
Age Groups (Years)	**18 to <35**	25(18.4%)	30(22.1%)	55(40.5%)	0.38
	≥35	43(31.6%)	38(27.9%)	81(59.5%)	
	Total	68(50%)	68(50%)	136(100%)	
Gender	**Male**	46(33.8%)	49(36.1%)	95(69.9%)	0.57
	Female	22(16.2%)	19(13.9%)	41(30.1%)	
	Total	68(50%)	68(50%)	136(100%)	
Adverse Events	**Yes**	11(8.1%)	35(25.7%)	46(33.8%)	0.001*
	No	57(41.9%)	33(24.3%)	90(66.2%)	
	Total	68(50%)	68(50%)	136(100%)	
Patients who Needed Rescue Analgesia	**Yes**	15(11.1%)	39(28.7%)	54(39.7%)	0.001*
	No	53(38.9%)	29(21.3%)	82(60.3%)	
	Total	68(50%)	68(50%)	136(100%)	

**Significant p-value*

Table 2: Comparison of Post-Operative Mean Pain Scores between Study Groups

Time (Hours)	Group A (Mean Pain Scores)	Group B (Mean Pain Scores)	p value
0	4.94±0.96	5.67±0.79	<0.001*
8	4.4±0.99	5.25±1.09	<0.001*
16	3.95±0.89	5.06±1.53	<0.001*
24	3.75±1.09	4.69±1.05	<0.001*

**Significant p-value*

Table 3: Comparison of Mean Post-Operative Pain Scores between Groups A & B regarding Demographic & Clinical Variables

Variables		Group A (Mean Pain Scores after 24 Hours) (Mean±SD)	Group B (Mean Pain Scores after 24 Hours) (Mean±SD)	p-value
Age Groups (Years)	**18 to <35**	3.86±0.89	4.13±1.1	0.028*
	≥35	3.75±1.09	4.17±1.27	0.004*
Gender	**Male**	3.7±1.07	4.16±1.07	0.0004*
	Female	3.88±1.16	4.46±1.08	<0.001*
Adverse Effects	**Yes**	3.75±1.08	4.38±1.16	<0.001*
	No	3.6±1.0	4.55±1.28	<0.001*
Rescue Analgesia	**Yes**	3.85±1.12	4.65±1.3	<0.001*
	No	3.58±1.1	4.49±1.32	<0.001*
BMI (kg/m^2)	**Normal (18.5-24.9)**	3.65±1.43	4.49±1.35	<0.001*
	Deranged (≥25)	3.86±0.51	4.62±1.1	<0.001*

**Significant p-value*

DISCUSSION

The foremost challenge after a surgery is effective relief in pain with minimum possible side effects and cost-effectiveness.[10] This study aimed to compare the effect of diclofenac suppositories and injection in the management and relief of pain after abdominal surgeries.

The mean age of patients in group A and group B was 33.22±9.58 years and 34.05±10.70 years, respectively. Pain reduction was significantly greater in group A in both age groups as compared to group B. Aleem et al. also reported that the mean age of patients who received diclofenac suppositories was 43.50±5.72 years and those who received diclofenac injections was 44.16±5.31 years. They reported

better pain control and relief with diclofenac suppositories; the most significant differences were recorded at 24 hours (p=0.001).[11] However, in our study, the most significant difference in score has been recorded at 16 hours, followed by 24 hours; this can be attributed to the difference in mean age of the populations in these studies.

In our study, 69.9% of the participants were males, whereas 30.1% were females. Pain reduction was significantly greater in group A across both gender categories as compared to group B. A previous study conducted in Faisalabad included approximately two-third males and one-third females. The study showed that diclofenac suppository was more effective at 12th hour (p <0.001) as compared to 2nd and 6th hour in relief of post-operative pain.[12] A study conducted on pediatric patients with mean age of 6.05±2.33 years for the relief of post-operative pain showed that patients who received diclofenac suppositories had lower pain scores (p-value=0.03) on VAS which corresponded to our study results.[13] Another study was conducted to assess pain relief in the first 24 hours after cesarean section delivery. The study results showed better pain relief with diclofenac suppositories, similar to our study despite the fact that the sample population consisted of females only.[14] Rab et al. included 72.45% males and showed effective pain relief with diclofenac suppositories after abdominal surgery.[15] Another study compared the effects of the two forms of the drug in relief of the pain after vaginal delivery. The study showed that the patients who received diclofenac suppositories reported mild to moderate pain, while a few patients who received injection diclofenac reported severe pain as well, besides others who had mild to moderate pain (p-value=0.002 at 6 hours).[16]

In our study, the mean BMI of patients in group A & B was not significantly different. However, when stratification was done for BMI, patients with normal & deranged BMI in group A had significantly lower mean pain score as compared to group B (p-value <0.001). A study conducted in Iran compared the effect of diclofenac suppositories with placebo group in relief of post-operative pain in patients undergoing laparoscopic cholecystectomy. Similar to our study, the placebo and diclofenac group did not significantly differ in terms of BMI distribution. The study showed significant reduction in mean pain scores on VAS of the patients who received diclofenac suppositories as compared to the other group (p-value <0.05) but they did not reported the association of post-operative pain scores and BMI categories.[17] Saeed et al. conducted a study on females undergoing gynecological and obstetrical surgeries and reported that rectal diclofenac suppositories were effective for post-operative pain relief in patients with any BMI category.[3]

In our study, the results showed that mean pain on VAS was significantly lower for those who received diclofenac suppositories as compared to those who were given injection diclofenac at 0, 8, 16, and 24 hours (p-value <0.0001). Altaf et al. compared the effectiveness of diclofenac suppositories versus injections in pain relief after perineal repair in primipara. Mean pain score on VAS in the suppositories group was 2.08±0.96 and the score in the injection group was 5.92±1.08 (p-value <0.0001).[18] A study compared rectal diclofenac suppository and transdermal diclofenac patch in the relief of pain after open cholecystectomy. The study concluded that the suppository form of the drug is more effective than transdermal patch (p-value <0.05).[19] These findings strongly support the results of our study. A study conducted in Nigeria compared rectal and intramuscular diclofenac for pain relief after abdominal surgery. The results showed significantly lower pain scores on VAS at 24 hours in the rectal suppository group. A statistically significant difference was found between the two groups (p-value <0.001).[20] Elahabadi et al. conducted a study in Iran in which they compared diclofenac with acetaminophen suppositories in post-hemorrhoidectomy pain relief. Diclofenac suppositories had better analgesic effect and showed more satisfactory results.[21] A study comparing oral and rectal diclofenac in pain relief after episiotomy and concluded that suppositories are far better in pain control. The mean pain score in the suppositories group was 2.93 as compared to 3.98 in the oral diclofenac group.[22]

In our study, significant results showed that fewer (11.1%) patients in group A needed rescue analgesia as compared to 28.7% patients in group B. Hosny et al. conducted a study for relief of post-episiotomy pain and reported that only 1.1% patients (p-value=0.01) required rescue analgesia.[23] This was proportionately less as compared to our study and may be due to less extensive procedure and hence requiring lesser need for analgesia.

CONCLUSION

Rectal suppositories of diclofenac were significantly more effective for post-operative pain relief among patients undergoing abdominal surgeries as compared to diclofenac intramuscular injection. Diclofenac suppositories had shown significantly better pain relief as measured by VAS mean scores

at 0, 8, 16, and 24 hours. It was also observed that a smaller number of patients in the diclofenac suppositories group required rescue analgesia while more than half patients in the injection group demanded for rescue analgesia.

LIMITATIONS & RECOMMENDATIONS

The few limitations of this study included a single study setting and non-probability convenience sampling technique. Pain measurement by VAS introduced the risk of measurement bias since it is subjective and may vary from person to person. Multi-centered RCT with blinding should be done to further ascertain the results of this study. The groups should be further subdivided and matched for severity and type of abdominal surgery.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
M.A.U: Conceived the study, drafted the manuscript & coordinated data collection
F.L: Proofread the manuscript & ensured reference accuracy
F.M: Supervised the research & reviewed the manuscript
M.F: Performed statistical analysis & contributed to results interpretation
S.S.Z.J: Managed patient enrollment & clinical data verification
H.Z.A: Assisted in literature review & data organization

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Original Article

Association of Radial Artery Diameter with Radial Artery Spasm in Patients Undergoing Transradial Cardiac Catheterization

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ABSTRACT

Objective: To assess the association of radial artery spasm (RAS) with radial artery diameter and other factors in patients undergoing transradial cardiac catheterization.

Methodology: This descriptive, cross-sectional study was conducted at the Fauji Foundation Hospital, Rawalpindi from June to September 2025 after ethical approval. After taking informed written consent, 150 patients who underwent coronary angiography or percutaneous coronary intervention using transradial approach were included. Prior to the procedure, radial artery diameter was assessed by the linear probe of Xario 100g Ultrasound machine. Radial artery spasm was assessed clinically by the operator and radial artery angiograms. Patients were divided into two groups: group I with no RAS and group II with RAS. The association of RAS with the radial artery diameter and other variables were determined. Statistical Package for the Social Sciences (SPSS) version 26 was used for data analysis.

Results: Radial artery spasm occurred in 35(23.3%) patients. The time to vascular access was significantly higher (150.60±49.77 seconds) in patients with RAS as compared to those without spasm (43.69±29.61 seconds) (p=0.001). The number of procedure attempts, episodes of vasovagal syncope (3.3% versus 0%) and access site crossover (6% versus 0%) were also significantly higher in patients with RAS. The radial artery spasm had a significant positive association with radial artery diameter, ejection fraction, angiographic findings, and treatment plan. The ROC curve showed an area under the curve of 0.876, showing the excellent ability of radial artery diameter to predict RAS.

Conclusion: Radial artery spasm affects a significant proportion of patients (23.3%) undergoing transradial cardiac catheterization. The radial artery diameter, vascular access time, need for ultrasound assistance to secure vascular assistance, additional vasodilator & glide wire, vasovagal syncope, and access site crossover were significantly higher in patients with RAS.

Keywords: *Radial Artery. Cardiac catheterization. Percutaneous coronary intervention. Coronary angiography.*

INTRODUCTION

Cardiac catheterization is an important and potentially lifesaving diagnostic and therapeutic modality, with the purpose to diagnose and treat conditions like coronary artery disease (CAD). It includes procedures such as diagnostic coronary angiography and percutaneous coronary intervention (PCI).[1] Various access sites can be used for left heart catheterization, such as the radial artery, ulnar artery, and femoral artery. In the current times, the radial artery is used as the access site of preference in diagnostic and therapeutic left heart catheterization procedures including diagnostic coronary angiography and percutaneous coronary intervention. This is because of ease of access, patient comfort, lower risk of vascular complications, shorter hospital stay, and early patient mobilization proven by various clinical trials.[2] However, intraprocedural and postprocedural complications can still occur via transradial access. Intraprocedural complications are radial artery spasm, kinking of the catheter, arterial dissection & perforation and vasovagal syncope. On the other hand, postprocedural complications include occlusion of the radial artery, pseudoaneurysm, hematoma formation, arteriovenous fistula, and nerve damage. These complications can potentially contribute to morbidity and mortality. They can lead to patient discomfort, limb dysfunction, long procedure duration, high chances of access site crossover, and life-threatening complications such as compartment syndrome.[3]

Radial artery spasm is generally identified when the operator feels resistance while advancing the sheath or catheter through the radial artery, causing pain in the forearm or arm. This complication is very common and is one of the leading causes of access site crossover. The spasm of the radial artery occurs frequently owing to the vasoreactivity of the vessel. Most of the cases are mild that can be prevented and treated. Pain relief and sedation can markedly decrease the incidence of RAS. Proper selection of equipment also reduces the chances of RAS.[4]

The risk factors of RAS include female gender, young or old age, diabetes mellitus, hypertension, deranged lipid profile, smoking, anxiety, and tachycardia. Radial artery spasm has been associated with both radial artery characteristics and procedural

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Received: September 29, 2025; Accepted: October 15, 2025

factors. The radial artery parameters associated with RAS are small caliber of the radial artery and low intensity of the radial pulse. Emergency procedures, multiple attempts, use of multiple catheters, and large sheaths can lead to RAS.[5]

The association of radial artery spasm with clinical parameters such as co-morbids have been studied in detail, there is paucity of local data regarding the association of radial artery diameter with radial artery spasm, and while logic dictates that smaller radial artery diameter should be a significant contributor to this rather common complication. This study aimed to bridge this gap in knowledge that can potentially serve to identify patients at risk of radial artery spasm and its subsequent vascular complications, and hence reduce morbidity and mortality in patients undergoing transradial cardiac catheterization.

METHODOLOGY

This descriptive, cross-sectional study was conducted at the Fauji Foundation Hospital, Rawalpindi from June to September 2025. After ethical approval (Letter No. 977/RC/FFH/RWP, 23-06-2025), the sample size of 150 was estimated using 11% frequency of radial artery spasm, 95% confidence interval, and 5% margin of error.[6] The patients were included using non-probability convenience sampling.

All the patients who underwent coronary angiography or percutaneous coronary intervention using transradial approach were included in the study. Exclusion criteria were patients with absent radial pulse, prior abnormal modified Allen's test, history of radial artery occlusion, known radial artery abnormalities, arteriovenous fistulas involving the radial artery, peripheral artery disease involving upper limbs, history of vascular complications in prior transradial cardiac catheterization, hemodynamic instability, and patients undergoing procedure from an alternative access site. Informed written consent was taken from the patients and their demographics, co-morbidities, electrocardiographic changes, and ejection fraction were noted.

Modified Allen's test was performed to check the patency of the radial artery and the adequacy of collateral supply from the ulnar artery. After occluding both arteries and then releasing the ulnar artery, return of hand color within ≤5 seconds indicated adequate collateral flow and a normal result.[7] Patients with abnormal test results were excluded from the study as per the defined exclusion criteria.

Prior to the procedure, radial artery diameters were assessed by the linear probe of Xario 100g Ultrasound machine, set on vascular mode at a frequency of 10 MHz. Measurements were taken in cross-sectional plane in 2D mode at optimal gain settings, at a depth of 2-3 centimeters, keeping the arterial lumen in the middle third of the screen, with the calipers positioned in a manner to measure the anterior-posterior diameter from inner wall to inner wall. All measurements were taken 1cm proximal to the styloid process. As per the hospital's cardiac catheterization lab protocols, 5000 IU of I/V unfractionated heparin along with 200 mcg of I/V nitrates mixed in 10 ml of normal saline was injected via the sheath after securing the vascular access.

Radial artery spasm was assessed clinically by the operator performing the procedure on the basis of pain or resistance encountered during manipulation of sheath, catheters or guidewires. In such instances, radial artery angiograms were performed to document radial artery spasm and differentiate it from other possible causes of pain and resistance, such as radial artery loops or tortuosity.[5] The total number of attempts, time, and need of ultrasonographic (USG) assistance in securing vascular access, flouroscopy time and coronary angiographic findings were recorded. Similarly, in the event of radial artery spasm, the need of additional vasodilators, the use of hydrophilic guidewires, or the need and location of access site crossover were also recorded. Any procedural complication, such as vasovagal syncope was also noted.

To eliminate interobserver bias, modified Allen's test, assessment of radial artery diameter on ultrasound and assessment of radial artery spasm were done by the consensus of 2 interventional cardiologists with experience of more than 200 transradial cardiac catheterizations per year.

STATISTICAL ANALYSIS

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Categorical and numerical variables were presented as frequency (percentage) and mean (standard deviation), respectively. Independent t-test was used for the association of numerical variables. Chi-square and Fisher's exact test was used to analyze categorical variables. The receiver operating characteristic (ROC) curve was drawn for radial artery diameter to evaluate its ability to predict radial artery spasm. The area under the curve (AUC) of greater than 0.6 is considered meaningful,

graded as poor if >0.6 but <0.7, fair if >0.7 but <0.8, good if >0.8 but <0.9, and excellent if >0.9.[8] The cut-off value of radial artery diameter was estimated using the Youden Index. The Youden index (J) is used to calculate the threshold value of a parameter with maximum sensitivity and specificity using the formula: sensitivity + specificity – 1.[8] The results were considered significant at the p-value of <0.05.

RESULTS

The mean age of the patients was 59.21±10.52 years with a range of 26 to 89 years. There were 115(76.7%) females and 35(23.3%) males. Most of the patients (42.6%) had stable angina, 26.7% had non-ST-elevation myocardial infarction (NSTEMI), 24% had ST-elevation myocardial infarction (STEMI), and 6.7% had unstable angina. Seventy seven (51.3%) patients were diabetic, 115(76.7%) were hypertensive, 9(6%) were smokers, and 22(14.7%) had a history of prior PCI. Most of the patients had triple vessel coronary artery disease (TVCAD) (26%) and double vessel coronary artery disease (DVCAD) (26%), followed by single vessel coronary artery disease (SVCAD) (18.7%). The majority of the patients were managed with medical treatment (38%), followed by PCI (36.7%).

The mean radial artery diameter of all patients was 2.25±0.35 mm. The mean angiographic fluoroscopic time was 3.05±3.45 minutes. In patients who underwent PCI, the mean PCI fluoroscopic time was 9.89±6.63 minutes, and in these patients, the total fluoroscopic time was 12±6.7 minutes.

Radial artery spasm occurred in 35(23.3%) patients. The mean time to vascular access was significantly higher (150.60±49.77 seconds) in patients with radial artery spasm as compared to those without spasm (43.69±29.61 seconds). Whereas the angiographic, PCI, and total fluoroscopic time were not statistically different (p >0.05). A significantly higher proportion of patients with RAS required ultrasound assistance for vascular access (10.6%), use of additional vasodilators (18%), guidewire insertion (14.7%) and crossover to other site (6%) compared to those without RAS. The frequency of RAS also increased with increasing number of procedure attempts. Moreover, episodes of vasovagal syncope (3.3%) were also significantly higher in patients with RAS (p=0.001) (Table 1).

The radial artery spasm had a significant positive association with radial artery diameter. The mean radial artery diameter was much lower in patients with radial artery spasm. The ejection fraction was significantly lower in patients with spasm than with no spasm. Triple vessel disease was significantly associated with RAS (30.8%), followed by DVCAD (25.6%) and SVCAD (21.4%). The patients who underwent PCI had the highest proportion of RAS (29.1%) as compared to coronary artery bypass grafting (CABG) and medical treatment. The radial artery spasm had no significant link with age, gender, diabetes mellitus, hypertension, smoking, and prior PCI (p >0.05). (Table 2).

The ROC curve drawn for radial artery diameter to predict radial artery spasm showed an area under the curve of 0.876. This shows that the radial artery diameter has an excellent ability to predict radial artery spasm. The cut-off value of radial artery diameter for predicting radial artery spasm was estimated to be 2.05 mm. At this cut-off value, the sensitivity of radial artery diameter was 77% and the specificity was 88% (Figure 1).

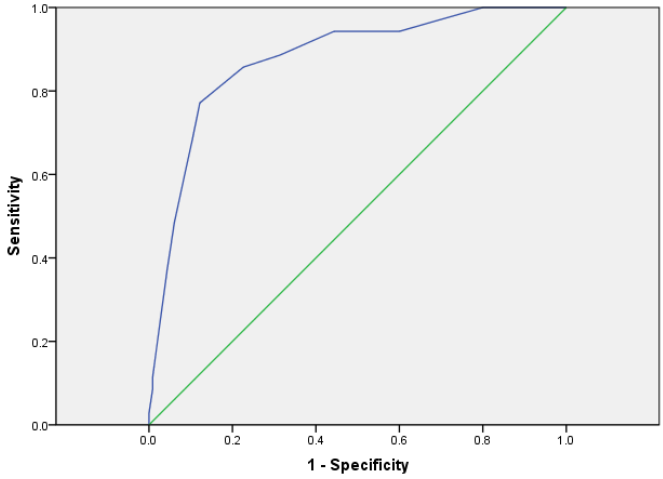

Figure 1: ROC Curve for Radial Artery Diameter to Predict Radial Artery Spasm

Table 1: Procedural Outcomes in Patients with or without Radial Artery Spasm

Parameters		Radial Artery Spasm (Frequency & Percentage)		Total	p-value
		No	Yes		
Number of Attempts	1	102(68%)	11(7.3%)	113(75.3%)	0.001*
	2	11(7.3%)	14(9.4%)	25(16.7%)	
	3	2(1.3%)	8(5.4%)	10(6.7%)	
	4	0(0%)	2(1.3%)	2(1.3%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Need for USG Assistance to Secure Vascular Access	No	111(74%)	19(12.7%)	130(86.7%)	0.001*
	Yes	4(2.7%)	16(10.6%)	20(13.3%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Need of Additional Vasodilator	No	115(76.7%)	8(5.3%)	123(82%)	0.001*
	Yes	0(0%)	27(18%)	27(18%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Need of Guide wire	No	112(74.7%)	13(8.6%)	125(83.3%)	0.001*
	Yes	3(2%)	22(14.7%)	25(16.7%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Vasovagal Syncope	No	115(76.7%)	30(20%)	145(96.7%)	0.001*
	Yes	0(0%)	5(3.3%)	5(3.3%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Crossover	No	115(76.7%)	26(17.3%)	141(94%)	0.001*
	Yes	0(0%)	9(6%)	9(6%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Time to Vascular Access (Seconds)	Mean±SD	43.69±29.61	150.60±49.77	-	0.001*

**Significant p-value*

Table 2: Association of Radial Artery Spasm with Radial Artery Diameter and Clinical Parameters

Parameters		Radial Artery Spasm		Total	p-value
		No	Yes		
Radial Artery Diameter (mm)	Mean±SD	2.36±0.29	1.88±0.26	-	0.001*
Ejection Fraction	Mean±SD	50.96±9.93	45.86±10.87	-	0.01*
Angiographic Findings (Frequency & Percentage)	Normal Coronaries	19(12.7%)	4(2.6%)	23(15.3%)	0.001*
	Minor CAD	9(6%)	2(1.3%)	11(7.3%)	
	Subcritical CAD	9(6%)	1(0.7%)	10(6.7%)	
	SVCAD	22(14.7%)	6(4%)	28(18.7%)	
	DVCAD	29(19.3%)	10(6.7%)	39(26%)	
	TVCAD	27(18%)	12(8%)	39(26%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	
Treatment Plan (Frequency & Percentage)	Medical Rx	46(30.7%)	11(7.3%)	57(38%)	0.001*
	PCI	39(26%)	16(10.7%)	55(36.7%)	
	CABG	30(20%)	8(5.3%)	38(25.3%)	
	Total	115(76.7%)	35(23.3%)	150(100%)	

**Significant p-value*

DISCUSSION

The frequency of RAS in our study was 23.3%. Roczniak et al. also reported symptomatic angiographic RAS in 24.3% of patients.[9] This was higher than 11% reported in a previous study.[6] The reported incidence of radial artery spasm ranges from 1% to 34%, while radial artery occlusion occurred in up to 19.7% of cases. This wide variation may be attributed to differences in arterial size, operator experience, and the equipment used during the procedure.[10] Patel et al. observed the RAS rate of 5.5% and emphasized that the type of vasodilator used in transradial access can also contribute to a wide difference in the occurrence of radial artery spasm.[11]

The mean radial artery diameter of patients was 2.25±0.35 mm in our study. Similarly, Hasan et al. observed that the mean radial artery diameter was 2.35±0.41 mm. Moreover, literature showed that the diameter of the radial artery was smaller in Asians (2.63±0.35mm) as compared to the western population (3.6±0.8 mm). The smaller caliber of the radial artery and its resultant tendency to develop spasms may lead to higher procedural failure in the transradial approach.[12]

In the current study, patients with RAS had a significantly smaller mean radial artery diameter (1.88±0.26 mm vs. 2.36±0.29 mm) (p=0.001). Sanketh et al. found that the frequency of radial artery occlusion was 24% in patients with small radial artery diameter (<2.5 mm) as compared to 6.7% in patients with larger diameter (p=0.03).[13] Radial artery dimension was smaller among RAS patients as compared to those without RAS but the results were not significant in another study.[9]

The average patient age was 59.21±10.52 years in our study and most of the patients were females (76.7%). The age and gender distribution had no significant association with RAS incidence. In another study, the average age was 62.5±11.2 years with 62.3% males. The patients with smaller radial artery diameters were generally older and had a lower proportion of males. However, multivariate analysis revealed that age and gender were not significant predictors of radial artery occlusion.[13] In a study by Mazhar et al., age was not significantly associated with RAS however, RAS showed a significant association with the female gender.[6] Another study reported that the frequency of RAS was significantly higher among females (66.6%; p=0.003) and those aged ≤65 years (62.5%; p=0.001).[14] Roczniak et al. also found that women were significantly more likely to experience radial artery spasm as compared to men (OR = 2.94, p=0.02).[9]

In our study, 76.7% of the patients were hypertensive and 51.3% were diabetic. Only 6% were smokers. The association of RAS with hypertension, diabetes mellitus, smoking, and prior PCI was insignificant. Previous studies didn't find any significant association of RAS with diabetes and hypertension.[6,15] Hasan et al. also reported that radial artery diameter wasn't significantly linked to diabetes and hypertension.[12] In addition to diabetes and hypertension, smoking was also not considered a predictor of RAS.[14]

Our results showed that the fluoroscopic time was not significantly different in patients with RAS as compared to patients without RAS. Procedural factors like puncture attempts, longer vascular access time, more frequent use of ultrasound, guide wire, additional vasodilators, as well as higher rates of vasovagal episodes and access site crossover were strongly linked to RAS in our participants (p ≤0.001). Another study reported that first-attempt failure significantly predicted spasm.[9] Roy et al. reported increased procedural time and access site crossover in patients who developed radial artery spasm while undergoing transradial access.[16] More than one procedural attempts were linked with RAS in a study conducted in 2023.[15] Another study was conducted to compare radial artery diameter pre and post-radial coronary angiography and a change in radial artery diameter was significantly associated with the number of puncture attempts.[17] Our data reinforce that minimizing puncture attempts can reduce spasm risk.

A majority of RAS patients needed additional vasodilators in our study. Vasodilators such as nitric oxide donors and calcium channel blockers can be administered individually or in combination with other agents to create an anti-spasmolytic radial "cocktail" aimed at preventing or reducing radial artery spasm.[10] Roczniak et al. used nitroglycerine and lidocaine cocktail but administration of the radial cocktail did not result in a statistically significant reduction in the odds of spasm (p=0.48).[9]

CONCLUSION

Radial artery spasm affects a significant proportion of patients (23.3%) undergoing transradial cardiac catheterization. The vascular access time, need for ultrasound assistance to secure vascular access, additional vasodilator & guide wire, vasovagal syncope, and access site crossover were significantly higher in patients with RAS. It had a significant association with small radial artery diameter, ejection fraction, angiographic findings, and treatment plan.

LIMITATIONS & RECOMMEDATIONS

The small sample size and conduction of the study at a single center affect the generalizability of the results. Future multicenter studies should be conducted on a large scale in Pakistan.

Small radial artery diameter is an associated factor of radial artery spasm. These patients must be considered at high-risk and managed optimally to reduce the chances of RAS.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
I.A.K: Conceived and designed the study, supervised data collection, and critically reviewed the manuscript.
U.S: Contributed to study design, performed data analysis and interpretation, and drafted the manuscript.
S.A: Assisted in data collection, clinical evaluation, and literature review.
Z.A: Participated in patient selection, data acquisition, and manuscript formatting.
W.L: Contributed to data analysis and interpretation of results.
W.H: Assisted in statistical analysis and preparation of tables and figures.
A.M: Supervised the overall research process, reviewed the final manuscript for intellectual content, and approved it for publication.

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Original Article

Early Clinical Exposure through Modular Curriculum in Undergraduate Medical Students: Student Experiences

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ABSTRACT

Objective: To explore experiences and perceptions of early clinical exposure (ECE) in undergraduate medical students under a modular curriculum through a mixed-methods approach.

Methodology: This cross-sectional mixed-methods study was conducted at Rashid Latif Khan University Medical College, Lahore from July to September 2025, following a recently introduced modular curriculum after ethical approval. The participants were second-year MBBS students who had completed at least one year of learning under the modular system with early clinical exposure components. After obtaining written, informed consent, 100 students were included using non-probability convenience sampling technique. Quantitative data was collected through a structured questionnaire using 5-point Likert scale assessing integration of basic and clinical sciences, motivation to learn, communication with patients, and overall satisfaction. Qualitative perceptions were obtained through focus group discussions (FGDs), transcribed verbatim and analyzed thematically using NVivo software. Quantitative data was analyzed using Statistical Package for the Social Sciences (SPSS) version 25.

Results: The majority of the students were of the opinion that ECE resulted in enhanced incorporation of basic and clinical sciences (mean Likert score 4.3/5), it also improved the motivation to learn (4.5/5), and better-quality communication skills with patients (4.2/5). Qualitative data analysis with thematic analysis discovered four major themes, i.e. (1) Linking theory and practice; students recognized the significance of learning in a specific context (2) Motivation through realistic exposure - clinical learning environment stimulated them for enhanced learning (3) Professionalism and communication - students felt an improvement in their self-confidence, communication skills and empathy with the patients; and (4) Challenges and barriers - despite major positive outcomes overcrowding, lack of time, and inconsistent faculty input posed difficulties.

Conclusion: The majority of the students perceived early clinical exposure within modular curricula positively. It enhanced students' motivation, understanding, and communication skills. Fixing the logistical and faculty training challenges can maximize the impact.

Keywords: *Clinical competence. Professionalism. Empathy. Curriculum.*

INTRODUCTION

Globally, medical education has shifted from traditional, discipline-based curricula to modular and competency-based frameworks for the undergraduate medical and dental students. Such an integrated curriculum incorporates basic science disciplines with clinical subjects from early years, allowing the bridging of knowledge with clinical application. The majority of such curriculum designs have a key feature of early clinical exposure (ECE), providing them a learning experience of patient care and communication from the initial years of medical education.[1]

Early clinical exposure is believed and proven to bridge the gap between basic medical learning and actual patient interaction. It enhances students' motivation, understanding, and learning in clinical contexts by providing them an exposure to clinical environments from the beginning. It not only enhances context specific learning and professionalism but also helps in early acquisition of communication skills and empathy among the medical students. Literature review suggests that a structured early clinical exposure improves self-assessed professional competence and confidence in clinical skills.[2] Studies conducted within Pakistan have almost similar findings, providing evidence of benefits to the undergraduate medical students perceiving it as a helpful tool of instruction in concept building and enhancing engagement during the pre-clinical years.[3]

Apart from bridging the gap between theory and practice, ECE has the advantage of contributing significantly to the holistic professional progress of medical students by building their professional identity and emotional endurance. Learning in clinical contexts indirectly inculcates empathy, ethical values, and reflective thinking. Such qualities are expected to be essential in a lifelong learner who is providing compassionate care.[4] Early clinical exposure in a specific clinical environment not only helps the students in a better understanding of the complexities of healthcare systems but also provides

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Received: October 8, 2025; Accepted: October 30, 2025

insight to interprofessional collaboration, and social determinants of health in the local context. The opportunity of working and learning in an authentic clinical situation during early educational years provides an additional benefit of adopting the values and responsibilities of the medical profession by the students. Hence, it incorporates a sense of determination and belonging that provides continuous motivation throughout their training.[5]

The University of Health Sciences (UHS), Lahore has introduced the modular integrated curriculum 2k23 in 2023 in its affiliated medical colleges. Data pertaining to ECE is limited to the introduction of clinical lectures in the first two years, while the modular integrated curriculum 2k23 provides a real-time clinical interaction with students learning relevant clinical skills in a specific clinical setting.[6] The responses across institutions are variable, and students' perception has not yet been explored in the local context. Therefore, we decided to conduct a mixed-method study to explore experiences and perceptions of the students undergoing ECE in the modular integrated curriculum 2k23. This mixed-method study seeks to explore the perceptions, experiences, and challenges of the undergraduate medical students undergoing ECE within the UHS modular integrated curriculum 2k23. By integrating quantitative survey data with qualitative insights, the study aims to provide a comprehensive understanding of how ECE contributes to learning, motivation, and professionalism in the early years of medical education. We believe that the conclusions from this research will not only provide guidelines to curriculum organizers but will also suggest measures for faculty development and capacity building. It will also assist the policymakers and degree awarding bodies in promoting the early clinical learning experiences across Pakistani medical schools.

METHODOLOGY

This cross-sectional mixed-methods study was conducted at Rashid Latif Khan University Medical College, Lahore from July to September 2025 that implemented a modular MBBS curriculum in 2023, after ethical approval (Letter No. RLKUMC/IRB/0063, 24-06-2025). The participants were second-year MBBS students who had completed at least one year of learning under the modular system with early clinical exposure components. After obtaining informed written consent, 100 students were included using non-probability convenience sampling technique.

Data was collected through a structured, pretested questionnaire. It was developed following AMEE Guide No. 87 for developing questionnaire, the literature review, development of relevant items, and preliminary questionnaire, pilot testing with revision and refining based upon the feedback of pilot testing. This was followed by pre-testing to validate the questionnaire. A Cronbach's alpha of 0.7 was obtained indicating internal consistency of the item. It was a structured questionnaire consisting of statements rated on a 5-point Likert scale (1=strongly disagree, 2=disagree, 3=neutral, 4=agree, 5=strongly agree). The survey covered four key domains of the ECE experience: integration of basic and clinical sciences, motivation to learn, communication with patients, and overall satisfaction.

In-depth qualitative insights were gathered through two FGDs with students (n=10 in each) enrolled through purposive sampling. Each FGD was facilitated using a semi-structured guide that encouraged students to discuss the benefits, challenges, and suggestions regarding early clinical exposure. Open-ended questions were designed to explore experiences corresponding to themes. These questions related to themes are given in Table 1.

Table 1: Qualitative Research Questions Aligned with Themes

Theme	Qualitative Research Question
Bridging Theory and Practice	In what ways has early clinical exposure helped you connect with what you learn in lectures with actual patient care?
Motivation through Real-Life Exposure	How did meeting real patients early in your training affect your motivation or interest in learning medicine?
Professionalism and Communication	Can you describe how early patient interactions have influenced your communication skills or professional behavior?
Challenges and Barriers	What difficulties or barriers have you encountered during your early clinical exposure sessions?

STATISTICAL ANALYSIS

Quantitative data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. The descriptive data, including frequencies (percentages) and mean±standard deviation (SD) for each item and domain of the questionnaire (integration, motivation, communication, and overall satisfaction) were calculated. These are mentioned in Table 2. As the study population comprised only 2nd year MBBS students, the analysis focused on summarizing response trends rather than subgroup comparisons. To analyze the trends of students' perceptions, combined scores from each domain were calculated.

For qualitative data, NVivo software (version XX) was used. We followed the principles of Braun and Clarke for qualitative data analysis to generate themes and thematic analysis. Audio recordings from the two focus group discussions were transcribed verbatim and introduced into NVivo for coding and organization. Utilizing thematic analysis approach, repeated patterns and categories were identified inductively from the data (Figure 1). This was followed by iterative coding to draft emerging themes connected to students' perceived advantages, challenges, and proposals for improvement regarding early clinical exposure. For refining and validation of final themes, thematic maps and query functions in NVivo were used to safeguard reliability and uniformity of interpretation.

RESULTS

Hundred students gave consistently positive ratings to their early clinical exposure. Most of them agreed that ECE improved their understanding of the relevance of basic sciences in a clinical context (82% agreement; mean Likert score 4.3/5), enhanced their motivation to learn (88% agreement; mean 4.5/5), and increased their confidence in communicating with patients (76% agreement; mean 4.2/5). In terms of overall impact, 80% of the students rated the ECE experience as beneficial to their education (Table 2).

Data examination through NVivo-assisted thematic analysis revealed that ECE not only improved integration between basic and clinical sciences, but it also improved student motivation and enhanced professional and communication skills. There were however, some challenges and contextual barriers that were identified by the students including overcrowding in clinical settings, time restraints, and unpredictable faculty guidance. In general, the findings in this study support the inclusion of structured and well-supervised ECE sessions in the early medical curriculum (Table 3).

Figure 1: Word Cloud Depicting Key Themes Emerging from Students Perspectives on Medical Education

Table 2: Mean Scores of Quantitative Domains of ECE

Domain	Description	Likert Score (out of 5) (Mean±SD)	Agree/Strongly Agree (Percentage)	Interpretation
Integration of Basic & Clinical Sciences	ECE enhanced the linkage between theory and practice	4.3±0.55	82%	Strongly positive
Motivation to Learn	ECE improved students' enthusiasm and engagement in learning	4.5±0.48	88%	Very positive
Communication Skills	ECE improved student–patient communication and confidence	4.2±0.6	76%	Positive
Overall Satisfaction with ECE Experience	ECE was perceived as a useful tool with positive impact on learning	4.33±0.54	80%	Positive

Table 3: Thematic Analysis of Qualitative Data

Theme	Subthemes (Identified Through NVivo Coding)	Representative Verbatim Comments
Linking Theory and Practice	Comprehending the significance of basic sciences through the incorporation of clinical examples	"When I saw the patient with anemia, I could eventually connect what we studied in physiology to the tangible problem. ECE facilitated me to understand why basic sciences actually matter."
	Strengthened classroom learning leading to context-based learning	"I couldn't understand the significance of studying physiology in so much detail in lectures unless I observed the clinical cases in ECE, everything started connecting in my mind"
	Augmented knowledge retention	"The anatomy of brachial plexus became so clear and easy when I saw a patient with a fractured humerus, I could visualize exactly which nerve was affected and why".
Motivation Through Realistic Exposure	Enhanced internal motivation of students	"I felt like a real doctor in training. After the ECE sessions, I went home and read more because I wanted to know what I had seen."
	Appealing, relevant, and meaningful learning	"When I learnt how to examine a patient's pulse and blood pressure, I instantly was eager to recall the physiology behind it. I wanted to comprehend what was happening inside the body."
	Clinical learning environment increased curiosity and self-study.	"After examining a patient with anemia in the ward, I felt inquisitive to understand the biochemical basis. For the first time, I read metabolism not for the test, but to connect it with real life."
Professionalism and Communication	Enhanced self-confidence during patient interaction	"Initially, I was under confident to talk, but now I can communicate more confidently with patients. I realized that patients are people, not just cases, ECE taught me compassion."
	Development of empathy and professionalism	"When I saw patients with multiple health problems, I realized how much empathy matters & it made me think beyond books and marks."
	Understanding the ethical aspects of care	"I learnt my first lesson about secrecy, patient confidentiality, and ethics during ECE, we were told not to discuss patient details outside the ward".
Challenges and Barriers	Overcrowding in clinical settings; limited time for observation	"The clinical batches had too many students at one bedside resulting it difficult to learn. Small batches might help in a better understanding"
	Inconsistent faculty facilitation	"Each teacher had a different approach in clinical methodology, it got confusing sometimes."
	Lack of structured debriefing	"There was generally no discussion on how we performed in ECE session. The sessions would have been more fruitful if there was a short debrief so we could clear our doubts and reflect on what we learned"

DISCUSSION

Early clinical exposure (ECE) is an educational approach that familiarizes medical students with patient interactions during the early stages of the MBBS program. It encourages students to enhance their academic knowledge, clinical abilities, and communication skills, thereby boosting their confidence.[7]

The findings of our study demonstrate that early clinical exposure serves as an effective pedagogical approach in bridging the gap between basic and clinical sciences in the early years of medical education. The higher mean Likert scores across all domains; motivation to learn, integration of basic & clinical sciences, communication skills, and overall satisfaction underscore the strong positive perception of students towards ECE. Similar outcomes have been reported in other studies. In a study by Oshiro et al., integrated modular curriculum in Tokyo led to improved self-assessment scores of medical students in various professional competencies. The students were able to correlate basic sciences with the practical knowledge, contributing to long-term retention of concepts and better efficacy.[8] Another study from Ethiopia reported a positive role of ECE on the motivation of students to learn, problem-solving abilities, professional knowledge, and orientation towards the community.[9] Ahire et al. stated that ECE improved students' understanding of concepts, enhanced knowledge retention, and increased interest in the subject.[10] In a study, ECE positively influenced cognitive and affective learning domains. Students described a deeper comprehension of concepts of basic sciences when encountered in clinical contexts. The ability to visualize theoretical content in patient scenarios appeared to reinforce meaningful learning, aligning with the principles of constructivist and experiential learning theories. The sense of curiosity and intrinsic motivation described by students after ECE reflects self-directed learning behaviors, which is a key outcome desired in outcome-based medical curricula.[11] A study conducted at the Rawal Institute of Health Sciences, Islamabad assessed the effects of early clinical exposure in 3rd to final year MBBS students. The results of the study showed that ECE is associated with enhanced confidence, communication, and clinical skills of the students.[12] Similar to our study, a study revealed that 90% of the medical students were satisfied with the ECE program. Students reported that ECE facilitated adaptation to the clinical environment, increased confidence in communicating with supervisors & patients, and enhanced their abilities to learn clinical skills.[13]

In our study, another important finding was the improvement in empathy and professional attitude among medical students. According to a study from Dubai, early patient exposure fosters emotional intelligence and nurtures empathy, allowing students to view patients as individuals rather than disease entities. It contributes significantly to the development of professionalism and ethical awareness in undergraduate medical students.[14] In another study, ECE has also been shown to promote professional development in the initial stages of medical education.[15] Ingale et al. reported that ECE helps the students to learn clinical skills by providing an engaging learning environment, cultivate empathy, foster a patient-focused approach to care, and develop professional attitudes such as the value of teamwork, effective communication, and ethical decision-making.[16]

However, our study identified that despite the overall positive impact, students found challenges such as overcrowding during sessions, inconsistent facilitation, and lack of structured debriefing. These issues are consistent with other studies. A study pointed out that ECE has complex dynamics depending on a large extent on student-teacher relationship. This is because the students consider their clinical teachers as mentors and role models. Insufficient guidance and poorly structured programs can hinder the effectiveness of ECE.[16] Another study highlighted several barriers to implementing ECE, with increased workload of the clinical doctors as the most common challenge. Other significant obstacles included poor coordination between academic & healthcare institutions and inadequate orientation on the implementation process.[9] A study reported a decline in student satisfaction with ECE, attributed to the absence of structured programs in hospitals.[13]

CONCLUSION

The majority of the students perceived ECE within modular curricula positively. Early clinical exposure, when implemented systematically with adequate faculty support, can enhance motivation to learn, integration of basic & clinical sciences, communication skills, and overall satisfaction in early years of medical students. It also contributes to improvement in empathy and professional attitude among medical students. Its incorporation into the preclinical curriculum of Pakistani medical colleges should be encouraged to promote active, reflective, and patient-centered learning.

LIMITATIONS & RECOMMENDATIONS

The study included only second-year MBBS students from a single medical institution. Future research should include students from different academic years and involve multiple medical colleges following UHS integrated curriculum to provide a more comprehensive evaluation of ECE-integrated curricula.

It is recommended that smaller group rotations, faculty development workshops, and structured debriefing sessions be implemented to address existing barriers and enhance the effectiveness of ECE in improving learning outcomes.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
L.Y: Concept and study design, data analysis, final proofreading, and approval of the manuscript.
A.A: Literature review, and questionnaire administration, data validation, results compilation, and critical manuscript review.
M.A: Data collection, statistical analysis and interpretation of quantitative data.
M.F.A: Data collection, facilitation of focus group discussions and qualitative data analysis.
M.H.K: Literature review, bibliography, data collection, and formatting.
M.B.A: Literature review, bibliography, data collection, and formatting.

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Original Article

Ticagrelor versus Clopidogrel in Complex Percutaneous Coronary Intervention in terms of Mortality and Stent Thrombosis

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ABSTRACT

Objective: To compare the effects of ticagrelor and clopidogrel on major adverse cardiovascular events (MACE), 30 day mortality, and stent thrombosis in patients with ST-elevation myocardial infarction (STEMI) undergoing complex percutaneous coronary intervention (PCI).

Methodology: This quasi-experimental study was conducted at the Rawalpindi Institute of Cardiology, Rawalpindi in 3 months from June to August 2025 after ethical approval. After obtaining informed written consent, 376 patients with STEMI treated with complex PCI were included by non-probability convenience sampling technique. The patients were assigned to two groups: Group A received aspirin & clopidogrel, whereas group B received aspirin and ticagrelor. The outcomes assessed were MACE, 30 day mortality, and stent thrombosis. Follow-up was done till 1 month. Data analysis was performed using the Statistical Package for the Social Sciences **(**SPSS) version 25.

Results: Bifurcation stenting was present in 80(42.6%) patients in clopidogrel group, while it was seen in 46(24.5%) patients in ticagrelor group. The left main PCI was also more prevalent in the ticagrelor group [81(43.1%)]. The thrombolysis in myocardial infarction (TIMI) 3 flow was restored in 53.7% versus 30.3% of the patients taking ticagrelor and clopidogrel, respectively. Stent thrombosis and MACE were significantly higher in the clopidogrel group (8.5% versus 2.7%) and (19.1% versus 11.2%), respectively. In contrast, no substantial difference was noted regarding 30 day mortality (9% vs. 8%) between the two groups.

Conclusion: Ticagrelor is associated with improved post-PCI TIMI flow, lower incidence of MACE and stent thrombosis in STEMI patients who underwent complex PCI as compared to clopidogrel. However, 30 day mortality is not significantly different in the two groups.

Keywords: *Ticagrelor. Clopidogrel. Percutaneous coronary intervention.*

INTRODUCTION

Primary percutaneous coronary intervention (P-PCI) with stent insertion is the preferred treatment in patients with ST-elevation myocardial infarction. However, stent thrombosis (ST) continues to be a rare but catastrophic event that can present in the initial 30 days after implantation.[1] Aspirin and clopidogrel are given as conventional antiplatelet drugs. Aspirin inhibits the enzyme cyclooxygenase-1, thereby stops thromboxane A2 production, which facilitates platelet plug formation. Clopidogrel is a P2Y12 receptor inhibitor. These receptors are present on platelets and bind adenosine diphosphate (ADP). So, P2Y12 inhibitors block the ADP-mediated platelet activation and hence clot formation.[2,3]

One of the disadvantages of clopidogrel is its variable efficacy. Even with ongoing oral antiplatelet therapy, atherothrombotic events still occur in some patients. Evidence from several studies suggests that residual platelet activity may be associated with these clinical outcomes, implying that "resistance" to antiplatelet therapy could play a role.[4] Long-term dual antiplatelet therapy decreases the occurrence of ischemic complications, but is also related to high bleeding risk, contributing to greater morbidity, mortality, and increasing healthcare costs.[5] The new P2Y12 receptor antagonist, ticagrelor, has good oral bioavailability. It has a quicker onset of action, more potency, and reversibly inhibits platelet aggregation when compared to conventional P2Y12 inhibitors like clopidogrel and prasugrel.[6]

This study was conducted to compare the effects of ticagrelor and clopidogrel on major adverse cardiovascular events, 30 day mortality, and stent thrombosis in patients with STEMI undergoing complex PCI. Having more efficacy, ticagrelor would be associated with lower frequency of complications and mortality. Over the past few years, there have been controversial results from complex PCI cohorts. In some studies, it has been reported that ticagrelor lowers the incidence of MACE than clopidogrel in complex PCI, whereas others claim that the two drugs are not significantly different. These uncertainties underline the

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Received: September 27, 2025; Accepted: October 27, 2025

requirement for additional assessment of antiplatelet treatment in this high-risk population.

METHODOLOGY

This quasi-experimental study was conducted at the Rawalpindi Institute of Cardiology, Rawalpindi in 3 months from June to August 2025 after approval from the institution ethical review board (Letter No. RIC/RERC/14/25, 17-07-2025). The sample size of 376 was calculated using the incidence of stent thrombosis of 5% with ticagrelor and 13.3% with clopidogrel, 80% power, and 95% confidence interval.[7] After obtaining informed written consent, patients with STEMI treated with complex PCI were included by non-probability convenience sampling technique. Patients of both genders and age >18 years were eligible for inclusion. The diagnosis of STEMI was made from clinical history and ECG findings. Patients complaining of chest pain consistent with myocardial ischemia and a duration of ≥20 minutes along with either ST-segment elevation of ≥1 mm in two contiguous limb leads, or ≥2 mm in two contiguous chest leads, or a new left bundle branch block, were diagnosed with STEMI.[8] Complex PCI was defined by the presence of any of the following: chronic total occlusion, >60 mm stent length, bifurcation stenting, left main PCI, bypass graft, use of multiwires, atherectomy, guiding catheter extensions or multiple stents.[9] The exclusion criteria were patients with known allergy or intolerance of antiplatelet therapy, concomitant anticoagulant use, prior bare-metal stent implantation, and history of coronary artery bypass grafting. The patients were assigned to two groups, with 188 patients in each: group A received 75 mg of aspirin once daily and 75 mg of clopidogrel once daily, whereas group B received 75 mg of aspirin once daily and 90 mg of ticagrelor twice daily. Emergency diagnostic coronary angiography and immediate P-PCI were done if the duration from symptom onset was less than 12 hours. The interventional approach (arterial access, stent type, aspiration thrombectomy) was at the discretion of Interventional Cardiologists. The TIMI flow was evaluated in the infarcted vessel pre- and post-procedure. Afterwards, patients were continuously monitored for at least 1 day, and were hospitalized for a minimum of 72 hours. The outcomes assessed were MACE, 30 day mortality, and stent thrombosis. Follow-up was done after 1 month. Major adverse cardiovascular events included myocardial infarction, stroke, or cardiovascular death.[10]

STATISTICAL ANALYSIS

Data analysis was performed using the Statistical Package for the Social Sciences **(**SPSS) version 25. Categorical variables are reported as frequencies & percentages, and continuous variables as mean±standard deviation (SD)**.** Group comparisons were conducted using Pearson's Chi-square test and a p-value <0.05 was considered statistically significant.

RESULTS

Patients had a mean age of 58.4±10.2 years in the clopidogrel group and 57.9±9.8 years in the ticagrelor group. Patients had a mean body mass index (BMI) of 26.1±3.7 kg/m^2 in the clopidogrel group and 26.4±3.5 kg/m^2 in the ticagrelor group. The mean ejection fraction was 46.2±8.5 and 47.1±8.2 in the clopidogrel and ticagrelor groups, respectively. Regarding gender, the clopidogrel group contained 50.6% of males and 49.4% of females, whereas the ticagrelor group comprised 49.4% of males and 50.6% of females. Diabetes mellitus was more common in the clopidogrel group (50% vs. 39.4%) and so was hypertension (53.3% vs. 46.7%). In the clopidogrel group, 44.4% of the patients had hyperlipidemia versus 47.2% of the patients in the ticagrelor group. The proportion of smokers was 46.1% in the clopidogrel and 47.8% in the ticagrelor group. The history of previous PCI was positive in 50% and 49.4% of the patients in the clopidogrel and ticagrelor groups, respectively.

The procedural characteristics of the two groups are given in Table 1. Significant differences were seen in arterial access, post-PCI TIMI flow 3, bifurcation stenting, and left main PCI.

Major adverse cardiovascular events were significantly higher in the clopidogrel group [36(19.1%)] as compared to the ticagrelor group [21(11.2%)] with a p-value=0.03. In contrast, no substantial difference was noted in 30 day mortality (9% vs. 8%; p-value=0.71) between the two groups. In terms of the stent thrombosis, the clopidogrel group had higher number of cases (8.5%) versus ticagrelor group (2.7%) and this was statistically significant (p=0.01). These data emphasize that despite a similar incidence of mortality between the two groups, ticagrelor was related with a lower incidence of MACE and stent thrombosis, suggesting a possible clinical benefit to clopidogrel (Table 2).

Table 1: Procedural Characteristics of the Study Participants

Variables		Clopidogrel Group (n=188)	Ticagrelor Group (n=188)	Total	p-value
		Frequency and Percentage			
Arterial Access	**Radial**	80(42.6%)	100(53.2%)	180(47.9%)	0.04*
	Femoral	108(57.4%)	88(46.8%)	196(52.1%)	
Severity of Coronary Artery Disease (CAD)	**Single Vessel CAD (SVCAD)**	68(36.2%)	63(33.5%)	131(34.8%)	0.79
	Double Vessel CAD (DVCAD)	53(28.2%)	52(27.7%)	105(28%)	
	Triple Vessel CAD (TVCAD)	67(35.6%)	73(38.8%)	140(37.2%)	
Treated Vessel	**Left Anterior Descending**	55(29.3%)	47(25%)	102(27.1%)	0.69
	Left Main	44(23.4%)	44(23.4%)	88(23.5%)	
	Left Circumflex	47(25%)	56(29.8%)	103(27.4%)	
	Right Coronary	42(22.3%)	41(21.8%)	83(22%)	
Type of Stent	**Drug Eluting Stents (DES)**	95(50.5%)	88(46.8%)	183(48.7%)	0.47
	Bare Metal Stents	93(49.5%)	100(53.2%)	193(51.3%)	
GP2b/3a Inhibitor use	**Yes**	90(47.9%)	91(48.4%)	181(48.1%)	0.92
	No	98(52.1%)	97(51.6%)	195(51.9%)	
Pre-PCI TIMI Flow	**0**	51(27.1%)	41(21.8%)	92(24.5%)	0.23
	1-3	137(72.9%)	147(78.2%)	284(75.5%)	
Post-PCI TIMI Flow 3	**Yes**	57(30.3%)	101(53.7%)	158(42%)	<0.00001*
	No	131(69.7%)	87(46.3%)	218(58%)	
Bifurcation Stenting	**Yes**	46(24.5%)	80(42.6%)	126(33.5%)	<0.0002*
	No	142(75.5%)	108(57.4%)	250(66.5%)	
Left Main PCI	**Yes**	45(23.9%)	81(43.1%)	126(33.5%)	0.00008*
	No	143(76.1%)	107(56.9%)	250(66.5%)	
Bypass Graft as Target	**Yes**	98(52.1%)	83(44.1%)	181(48.1%)	0.12
	No	90(47.9%)	105(55.9%)	195(51.9%)	

**Significant p-value*

Table 2: Clinical Outcomes in Patients Taking Clopidogrel versus Ticagrelor

Outcomes		Clopidogrel Group (n=188)	Ticagrelor Group (n=188)	Total	p-value
		Frequency and Percentage			
MACE	**Yes**	36(19.1%)	21(11.2%)	57(15.2%)	0.03*
	No	152(80.9%)	167(88.8%)	319(84.8%)	
30 day Mortality	**Yes**	17(9%)	15(8%)	32(8.5)	0.71
	No	171(91%)	173(92%)	344(91.5%)	
Stent Thrombosis	**Yes**	16(8.5%)	5(2.7%)	21(5.6%)	0.01*
	No	172(91.5%)	183(97.3%)	355(94.4%)	

**Significant p-value*

DISCUSSION

Patients with acute coronary syndrome receive conventional antiplatelet regimen consisting of aspirin and P2Y12 receptor inhibitor. However, determining the optimal agent among available P2Y12 inhibitors remains a subject of debate.[11] In our study, patients had a mean age of 58.2±10 years and the mean BMI of 26.3±3.6 kg/m^2. The males constituted 50% of the study population. There were 44.7% diabetics, 50% hypertensive, 45.8% dyslipidemic, 46.9% smokers, and 49.7% had previous PCI. In a study, patients had an average age of 59.1±10.1 years with the majority (80.3%) of males. Their mean BMI was 26.1±3.3 kg/m^2. Most of the patients had dyslipidemia (82.8%) followed by hypertension (63.1%), smoking (59.9%), diabetes mellitus (34.3%), and prior PCI (18.8%).[12] In another study, the average age was 54.8±10.1 years with 87.3% males and the mean BMI was 26.9±12.3 kg/m^2. There were 38.4% hypertensive, 30.7% diabetic, 39.5% smokers, 0.4% hyperlipidemic, and 9.6% patients with the history of previous PCI.[13]

In our study, femoral access was predominantly used (52.1%), with the majority of the patients having TVCAD (37.2%), followed by SVCAD (34.8%). In a study by Hakeem et al., radial access was used in 89.9% of the patients. Most of the patients had SVCAD (36.2%) and DVCAD (36.5%).[13] According to our study, 33.5% of the patients had bifurcation lesions and DES were used in 48.7% of the participants. Around 17.7% had bifurcation lesion and DES were used in 94.1% of the study population according to Hakeem et al.[13] In our study, bifurcation stenting and left main PCI were more frequently performed in patients taking ticagrelor. Another study reported that ticagrelor did not reduce periprocedural adverse events compared to clopidogrel. Bifurcation stenting was done in 64.6% and 43.4% of the patients taking ticagrelor and clopidogrel, respectively, whereas left main stenting was done 32.4% and 49.4% of the patients taking ticagrelor and clopidogrel, respectively.[9] Xi et al. also found that ticagrelor was associated with complex procedural outcomes.[12]

Our results revealed that pre-PCI TIMI flow showed no significant variation between the groups, whereas TIMI flow after the procedure was significantly improved in patients taking ticagrelor. A trial reported no variation in TIMI flow before and after procedure in the ticagrelor and clopidogrel groups.[14] In our study, there was a significantly marked reduction in MACE (11.2% versus 19.1%) and stent thrombosis (2.7% versus 8.5%) in the patients taking ticagrelor. In contrast, 30 day mortality was almost the same in the two groups (8% versus 9%). Our results were comparable to other studies. The results of a study showed that ticagrelor was linked to lower incidence of all-cause deaths (1.38% versus 2.85%) and MACE (6.53% versus 9.48%) and the findings were statistically significant.[15] In another study, MACE occurred in 8.6% of patients taking ticagrelor in contrast to 11.2% of the patients taking clopidogrel with a significant difference. Cardiac deaths occurred in 1.2% versus 1.7% in the ticagrelor and clopidogrel groups, respectively with statistically insignificant results.[12] A study by Yan et al. concluded significant reduction in all-cause deaths and stent thrombosis with ticagrelor but there was no difference in cardiovascular deaths between patients taking ticagrelor and clopidogrel.[16] Qiu et al. and Bari et al. showed a marked reduction in MACE with ticagrelor as compared to clopidogrel.[17,18] On contrary, another study revealed no statistical variation in MACE (15% versus 11.8%) and deaths (1% versus) in patients treated with ticagrelor and clopidogrel, respectively.[9] Another study also showed that 30 day all-cause mortality (14.6% versus 13.5%) and MACE (16.1% versus 14.7%) did not differ statistically in patients taking ticagrelor and clopidogrel.[19] Other studies also showed that MACE was not different in the two groups.[14,20] In a study, the frequency of MACE was 2.2% versus 2.9%, all-cause deaths were 1.5% versus 1.8%, and stent thrombosis was 1.6% versus 2.1% in the ticagrelor and clopidogrel groups, respectively but with no significance.[13]

CONCLUSION

Ticagrelor is associated with improved post-PCI TIMI flow, lower incidence of MACE, and stent thrombosis in STEMI patients who underwent complex PCI as compared to clopidogrel. However, 30 day mortality is not significantly different in the two groups.

LIMITATIONS & RECOMMENDATIONS

Our findings suggest that ticagrelor may be preferable to clopidogrel, particularly in patients undergoing complex PCI. However, further multicenter randomized trials with larger sample sizes and longer follow-up periods are required to confirm these results and to more accurately assess mortality, bleeding, and long-term ischemic outcomes. The quasi-experimental design of this study may introduce selection bias. Additionally, bleeding events, which are important when evaluating the safety profile of ticagrelor, were not comprehensively assessed.

Cost-effectiveness analyses are also needed, especially in low- and middle-income countries, where issues of affordability and drug accessibility are significant. Incorporation of individualized risk assessment tools (ischemic vs. bleeding risk stratification) may help guide the selection and duration of antiplatelet therapy in clinical practice.

Conflict of interest: None.
Source of funding: None.

Authors' Contributions:
M.M: Conceived and supervised the study.
T.A.R: Reviewed study design and clinical interpretation.
H.A.G: Collected data and performed analysis.
M.U.F: Assisted in data collection and literature review.
E.S: Contributed to data analysis and interpretation.
M.H.Y: Edited and finalized the manuscript.

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OTHER SECTIONS: The journal also accepts manuscripts for other sections such as diagnostic & therapeutic challenges, clinicopathological correlations, surgical techniques, and new instruments. Diagnostic & therapeutic challenges require no abstract and have no limit for figures and references. Surgical techniques and clinicopathological correlations are treated as a full manuscript and require an abstract. All correspondence and new instruments should have a standard title page with a full-length title, running title, and author information. Keywords anti summary statement should be on the second page. An abstract is not required by the journal for correspondence and new instruments. A summary statement of 50 words is necessary for publication and indexing and must be included at the time of submission. All pages must be numbered starting with the title page being page one. Each figure must be submitted separately.

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