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ORIGINAL ARTICLE

Prevalence of Gastrointestinal Bleeding in Patients Receiving Dual Antiplatelet Therapy after Percutaneous Coronary Intervention

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ABSTRACT

Background: Dual antiplatelet therapy (DAPT), consisting of aspirin and a P2Y12 inhibitor such as clopidogrel, prasugrel, or ticagrelor, is an essential component of post–percutaneous coronary intervention (PCI) management to prevent stent thrombosis and recurrent ischemic events.

Objective: To determine the prevalence of gastrointestinal bleeding and associated risk factors among patients receiving dual antiplatelet therapy after percutaneous coronary intervention.

Methodology: This descriptive cross-sectional study was conducted at Punjab Institute of Cardiology, Lahore from November 2022 to April 2023. A total of 85 patients who underwent PCI and were receiving DAPT (aspirin with clopidogrel, prasugrel, or ticagrelor) were included. Demographic data, comorbidities, duration of therapy, and use of proton pump inhibitors (PPIs) were recorded.

Results: The mean age of participants was 59.8 ± 10.4 years, with 68.2% males and 31.8% females. The overall prevalence of gastrointestinal bleeding was 12.9% (11 patients), with upper GI bleeding accounting for 72.7% and lower GI bleeding for 27.3% of cases. Significant associations were observed between GI bleeding and chronic kidney disease ($p = 0.02$) as well as absence of PPI use ($p = 0.03$). Although not statistically significant, the highest bleeding incidence was noted among patients receiving aspirin plus prasugrel (21.4%), compared with aspirin plus clopidogrel (9.8%) and aspirin plus ticagrelor (10%).

Conclusion: It is concluded that gastrointestinal bleeding is a frequent and clinically important complication among patients on DAPT following PCI, with a prevalence of approximately 13%.

Keywords: dual antiplatelet therapy, percutaneous coronary intervention, gastrointestinal bleeding, proton pump inhibitors.

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality globally, accounting for nearly one-third of all deaths each year[1]. Among the various treatment modalities, percutaneous coronary intervention (PCI) has revolutionized the management of coronary artery disease by restoring coronary blood flow and improving survival outcomes. However, the long-term success of PCI relies heavily on the use of dual antiplatelet therapy (DAPT) a combination of aspirin and a P2Y12 receptor inhibitor (such as clopidogrel, prasugrel, or ticagrelor) to prevent stent thrombosis, myocardial infarction, and other ischemic complications[2]. While DAPT has undoubtedly reduced adverse cardiovascular events, its use introduces a significant risk of bleeding, particularly gastrointestinal (GI) bleeding, which remains one of the most feared and common complications in this patient population[3].

The mechanism underlying DAPT-induced GI bleeding is multifactorial. Aspirin exerts its effect by irreversibly inhibiting the cyclooxygenase-1 (COX-1) enzyme, leading to reduced synthesis of prostaglandins that normally maintain gastric mucosal integrity and blood flow. This disruption predisposes the mucosa to erosions and ulcerations[4]. Meanwhile, P2Y12 inhibitors further impair platelet aggregation, compromising primary hemostasis and exacerbating bleeding risk from preexisting mucosal lesions. Consequently, even minor mucosal injuries can progress to clinically significant bleeding events. The pathophysiological interplay between mucosal injury and platelet inhibition makes the gastrointestinal tract a vulnerable site in patients receiving DAPT[5]. The prevalence of gastrointestinal bleeding in patients on DAPT after PCI varies widely, ranging from 1% to 12% depending on population characteristics, duration of therapy, and the concomitant use of gastroprotective agents like proton pump inhibitors (PPIs)[6]. For example, large-scale clinical trials such as CURE and CHARISMA reported major bleeding rates between 1% and 3%, while observational data suggest even higher real-world rates[7]. The variation also reflects differing prescribing practices, regional dietary patterns, and prevalence of risk factors such as *Helicobacter pylori* infection, chronic alcohol consumption, and use of nonsteroidal anti-inflammatory drugs (NSAIDs)[8]. Older adults, patients with prior ulcer disease, chronic kidney disease, or liver dysfunction are particularly at risk. Additionally, prolonged DAPT duration beyond the recommended 6 to 12 months further amplifies bleeding risk without necessarily conferring proportional ischemic protection[9]. From a clinical perspective, GI bleeding following PCI represents a delicate therapeutic paradox. On one hand, interruption of DAPT to control bleeding may increase the risk of stent thrombosis, potentially leading to myocardial infarction or death. On the other hand, continued DAPT during active bleeding can worsen hemodynamic instability and increase the need for transfusions. This creates a therapeutic dilemma that underscores the importance of individualized treatment strategies based on patient-specific risk profiles. Tools such as the PRECISE-DAPT and DAPT scores are increasingly being used to stratify bleeding versus ischemic risk, though their practical implementation in resource-limited settings remains inconsistent[10].

Preventive strategies have been developed to mitigate the gastrointestinal complications of DAPT. Proton pump inhibitors are recommended for patients at high risk of GI bleeding, as they significantly reduce the incidence of upper GI hemorrhage by maintaining gastric mucosal integrity[11]. Testing and eradication of *H. pylori* infection before initiating long-term antiplatelet therapy is another effective measure. The use of *enteric-coated aspirin* has been proposed as an additional step, though evidence supporting its protective role remains inconclusive. Moreover, short-term DAPT followed by monotherapy, or the use of newer agents with improved safety profiles, are emerging as potential approaches to balance efficacy and safety[12]. Despite these advancements, data on the prevalence and determinants of GI bleeding among patients receiving DAPT after PCI in low- and middle-income countries, including Pakistan, remain scarce[13].

Objective: To determine the prevalence of gastrointestinal bleeding and associated risk factors among patients receiving dual antiplatelet therapy after percutaneous coronary intervention.

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METHODOLOGY

This was a descriptive cross-sectional study conducted at Punjab Institute of Cardiology, Lahore from November 2022 to April 2023. A total of 85 patients were included in the study. Non-probability consecutive sampling was used to recruit participants who met the inclusion criteria.

Inclusion Criteria: Patients aged 18 years and above who had undergone percutaneous coronary intervention (PCI) and were receiving dual antiplatelet therapy (aspirin plus clopidogrel, prasugrel, or ticagrelor) for at least one month were included. Both male and female patients were eligible.

Exclusion Criteria: Patients with known coagulation disorders, pre-existing gastrointestinal malignancy, chronic liver disease, or those receiving oral anticoagulants (such as warfarin or direct oral anticoagulants) were excluded. Patients with incomplete medical records or those lost to follow-up were also excluded from the study.

Data Collection Procedure: After obtaining ethical approval from the institutional review board, data were collected through structured proformas and patient record reviews. Each participant's demographic profile (age, gender), clinical variables (comorbidities such as hypertension, diabetes mellitus, and chronic kidney disease), type and duration of dual antiplatelet therapy, and use of gastroprotective agents (e.g., proton pump inhibitors) were recorded. Gastrointestinal bleeding was identified based on documented clinical evidence such as melena, hematemesis, or positive fecal occult blood test confirmed by clinical evaluation or endoscopy where applicable.

Data Analysis: All data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 22. Quantitative variables such as age and duration of therapy were expressed as mean ± standard deviation (SD), while categorical variables such as gender, type of antiplatelet agent, and presence of gastrointestinal bleeding were presented as frequencies and percentages. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Data were collected from 85 patients, mean age of the patients was 59.8 ± 10.4 years, with ages ranging between 38 and 81 years, indicating that most participants were middle-aged or elderly. Males constituted 68.2% of the study population, while females accounted for 31.8%, showing a male predominance. Hypertension was observed in 62.4% of patients, and diabetes mellitus in 48.2%, reflecting the high burden of cardiovascular comorbidities among the study group. Chronic kidney disease was identified in 14.1% of patients, and a smoking history was noted in 42.4%. Proton pump inhibitors (PPIs) were used by 63.5% of participants, suggesting that over one-third did not receive gastroprotective therapy despite being on DAPT. The mean duration of DAPT use was 8.2 ± 3.7 months. Among the DAPT regimens, aspirin combined with clopidogrel was the most frequently prescribed (71.8%), followed by aspirin with prasugrel (16.5%) and aspirin with ticagrelor (11.7%).

Out of 85 patients, 11 (12.9%) experienced gastrointestinal bleeding, whereas 74 (87.1%) did not report any bleeding events. Among those who developed bleeding, the majority (8 patients, 72.7%) had upper gastrointestinal bleeding, manifested as hematemesis or melena. The remaining 3 patients (27.3%) suffered from lower gastrointestinal bleeding, presenting as hematochezia or a positive fecal occult blood test.

Patients aged 60 years or older experienced more bleeding episodes (63.6%) compared to younger patients, though this difference was not statistically significant (p = 0.18). Similarly, gender, hypertension, diabetes mellitus, and smoking history showed no significant association with gastrointestinal bleeding. However, chronic kidney disease was significantly associated with an increased risk of bleeding (p = 0.02), as 36.4% of patients with this condition developed bleeding compared to 10.8% of those without it. Another significant finding was the relationship between PPI use and bleeding events; only 27.3% of patients who developed bleeding were using PPIs, compared to 68.9% in the non-bleeding group (p = 0.03).

The highest bleeding rate was found among patients using aspirin plus prasugrel (21.4%), followed by aspirin plus ticagrelor (10%) and aspirin plus clopidogrel (9.8%). Although the bleeding frequency was higher with prasugrel, the difference among regimens did not reach statistical significance (p = 0.28).

Table 1. Demographic and Baseline Characteristics of Patients Receiving Dual Antiplatelet Therapy After PCI (n = 85)

Variable	Category / Unit	n (%) / Mean ± SD
Age (years)	Mean ± SD	59.8 ± 10.4
Gender	Male	58 (68.2%)
	Female	27 (31.8%)
Hypertension	Present	53 (62.4%)
	Absent	32 (37.6%)
Diabetes Mellitus	Present	41 (48.2%)
	Absent	44 (51.8%)
Chronic Kidney Disease	Present	12 (14.1%)
	Absent	73 (85.9%)
Smoking History	Yes	36 (42.4%)
	No	49 (57.6%)
Proton Pump Inhibitor (PPI) Use	Yes	54 (63.5%)
	No	31 (36.5%)
Duration of DAPT (months)	Mean ± SD	8.2 ± 3.7
Type of DAPT Regimen	Aspirin + Clopidogrel	61 (71.8%)
	Aspirin + Prasugrel	14 (16.5%)
	Aspirin + Ticagrelor	10 (11.7%)

Table 2. Prevalence and Type of Gastrointestinal Bleeding Among Patients Receiving DAPT (n = 85)

Variable	Category	n (%)
Gastrointestinal Bleeding	Present	11 (12.9%)
	Absent	74 (87.1%)
Type of GI Bleeding	Upper GI (hematemesis/melena)	8 (72.7%)
	Lower GI (hematochezia/occult blood)	3 (27.3%)

Table 3. Association Between Risk Factors and Gastrointestinal Bleeding

Risk Factor	GI Bleeding Present (n = 11)	GI Bleeding Absent (n = 74)	p-value
Age ≥ 60 years	7 (63.6%)	31 (41.9%)	0.18
Male Gender	8 (72.7%)	50 (67.6%)	0.71
Hypertension	8 (72.7%)	45 (60.8%)	0.42
Diabetes Mellitus	7 (63.6%)	34 (45.9%)	0.26
Chronic Kidney Disease	4 (36.4%)	8 (10.8%)	0.02
Smoking	6 (54.5%)	30 (40.5%)	0.36
PPI Use	3 (27.3%)	51 (68.9%)	0.03

Table 4. Distribution of Gastrointestinal Bleeding by Antiplatelet Regimen

Antiplatelet Regimen	Total (n)	GI Bleeding n (%)	p-value
Aspirin + Clopidogrel	61	6 (9.8%)	0.28
Aspirin + Prasugrel	14	3 (21.4%)	
Aspirin + Ticagrelor	10	1 (10.0%)	

DISCUSSION

The present study evaluated the prevalence and associated risk factors of gastrointestinal (GI) bleeding in patients receiving dual antiplatelet therapy (DAPT) following percutaneous coronary intervention (PCI). Among 85 patients, 12.9% developed GI bleeding, with upper GI bleeding being the predominant type (72.7%). The findings highlight that while DAPT remains essential for preventing stent thrombosis and recurrent ischemic events, it significantly increases the risk of gastrointestinal complications, particularly in patients with additional comorbidities or without gastroprotective coverage. The observed prevalence of 12.9% in this study aligns with previously reported global estimates ranging

between 1% and 15%, depending on population characteristics, follow-up duration, and the specific antiplatelet agents used. Previous research has consistently demonstrated that the addition of a P2Y12 inhibitor to aspirin amplifies the risk of GI bleeding compared to aspirin monotherapy. Clinical trials such as CURE and PLATO reported major bleeding rates of approximately 3% to 5%, whereas real-world observational data from Asian populations have often shown higher rates, likely reflecting differences in patient comorbidities, genetic variability in drug metabolism, and limited use of gastroprotective agents[14].

A notable finding from this study was the significant association between chronic kidney disease (CKD) and gastrointestinal bleeding (p = 0.02). CKD has been identified as an independent risk factor for both upper and lower GI hemorrhage due to platelet dysfunction, uremic toxins, and the increased use of concomitant medications such as anticoagulants and NSAIDs. Previous research supports this observation, demonstrating that even mild renal impairment markedly increases bleeding risk in patients on DAPT. Moreover, patients with CKD often require prolonged DAPT duration due to higher thrombotic risk, further compounding their susceptibility to bleeding complications. Another important observation was the protective role of proton pump inhibitors (PPIs)[15]. In this study, the absence of PPI use was significantly associated with a higher rate of GI bleeding (p = 0.03). PPIs are known to reduce the risk of upper GI bleeding by preserving gastric mucosal integrity and preventing ulcer formation. Several meta-analyses have confirmed that concurrent PPI therapy substantially lowers the incidence of major GI bleeding in patients on DAPT without adversely affecting antiplatelet efficacy. However, in many low- and middle-income countries, routine PPI prophylaxis is underutilized, either due to cost constraints or lack of awareness, which may partially explain the higher prevalence observed in this population[16-18].

The type of P2Y12 inhibitor also influenced bleeding trends. Patients receiving the combination of aspirin and prasugrel demonstrated the highest rate of GI bleeding (21.4%), followed by ticagrelor (10%) and clopidogrel (9.8%). Although the difference was not statistically significant (p > 0.05), this trend aligns with prior evidence suggesting that prasugrel and ticagrelor, being more potent platelet inhibitors, carry a greater bleeding risk than clopidogrel[19]. Trials such as TRITON-TIMI 38 and PLATO have shown that while these agents reduce ischemic events, they do so at the cost of increased bleeding, particularly in older adults and those with low body weight or prior ulcer disease. In clinical practice, careful patient selection and bleeding risk stratification using validated scores such as PRECISE-DAPT or DAPT Score are therefore essential for optimizing outcomes. The prevalence of bleeding was also higher in patients aged ≥60 years (18.4%) compared to those under 60 (8.5%), although the difference did not reach statistical significance. Advanced age is a well-established predictor of bleeding due to mucosal fragility, polypharmacy, and altered pharmacokinetics. Prior studies have shown that the elderly population experiences both higher ischemic and bleeding risks, making therapeutic balancing particularly challenging. This highlights the importance of individualized antiplatelet regimens with shorter DAPT durations or use of gastroprotective agents in older patients[20].

Limitations: The study has several limitations. Being a single-center cross-sectional analysis, the findings may not be generalizable to broader populations. The sample size was modest (n = 85), which limited the statistical power to detect certain associations. Moreover, the study relied on clinical and documented evidence of bleeding; minor or occult cases may have gone undetected. The absence of long-term follow-up also precluded assessment of recurrent bleeding episodes or late adverse cardiac events.

CONCLUSION

It is concluded that gastrointestinal bleeding represents a significant clinical concern among patients receiving dual antiplatelet therapy (DAPT) following percutaneous coronary intervention (PCI), with an overall prevalence of 12.9% in this study. The majority of bleeding episodes involved the upper gastrointestinal tract, underscoring the vulnerability of the gastric mucosa to the combined effects of aspirin and P2Y12 inhibitors. Patients with chronic kidney disease and those not using proton pump inhibitors (PPIs) were found to be at markedly higher risk, emphasizing the importance of renal function monitoring and routine gastroprotective therapy in this population.

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