Journal of Health and Rehabilitation Research 2791-156X JHRR

For contributions to JHRR, contact at email: editor@jhrlmc.com

Original Article

Safety of Ticagrelor in Post – PCI (Percutaneous Coronary Intervention) Patients at a Tertiary Care Hospital

Salman Hasan[1], Ahmad Fawad[2], Muhammad Tariq Mehr[3]*, Sana Hassan[1], Zamina Aslam[1], Idrees Khan[1], Amjad Ali[1]

[1]PG-Trainee, Cardiology, Northwest General Hospital & Research Centre Peshawar, Pakistan.

[2]Associate Professor, Cardiology Unit, Northwest General Hospital & Research Centre Peshawar, Pakistan.

[3]Associate Professor, Department of Medicine, Hayatabad Medical Complex Peshawar, Pakistan.

Corresponding Author: Muhammad Tariq Mehr, Associate Professor; Email: tariq_mehr@yahoo.com

Conflict of Interest: None.

*Hasan S., et al. (2024). 4(2): **DOI**: https://doi.org/10.61919/jhrr.v4i2.1169*

ABSTRACT

Background: Coronary artery disease (CAD) remains a leading cause of mortality and morbidity worldwide, despite advances in diagnosis and management. In acute coronary syndrome (ACS) patients, the combination of aspirin and clopidogrel is the standard therapy against recurrent cardiovascular events. However, clopidogrel has a delayed onset and variability in platelet response.

Objective: To examine the safety profile of ticagrelor in post-PCI patients at a tertiary care hospital.

Methods: This descriptive study was conducted at the Department of Cardiology, North-West General Hospital, Peshawar, from 1st April 2023 to 31st March 2024. Patients aged 30 to 80 years who underwent PCI and were started on ticagrelor were included. Baseline data such as age, gender, BMI, and cardiovascular risk factors (smoking, hypertension, diabetes mellitus) were collected. Patients received a loading dose of ticagrelor 180 mg orally followed by 90 mg twice daily. Adverse effects, including bleeding, dyspnea, and arrhythmias, were evaluated within 24 hours and at one-month follow-up. Data were analyzed using IBM SPSS version 25, with categorical variables presented as frequencies and percentages, and quantitative variables as means and standard deviations.

Results: A total of 137 post-PCI patients participated in the study, with a mean age of 58 ± 10 years. The cohort included 85 men (62%) and 52 women (38%). The average BMI was 27.5 ± 3.5 kg/m². Risk factors included smoking (30%), hypertension (45%), and diabetes mellitus (25%). Within 24 hours, minor bleeding occurred in 10 patients (7.3%), dyspnea in 15 patients (10.9%), and arrhythmias in 4 patients (2.9%). At the one-month follow-up, minor bleeding was observed in 12 patients (8.8%), major bleeding in 2 patients (1.5%), dyspnea in 18 patients (13.1%), and arrhythmias in 5 patients (3.6%).

Conclusion: The study supports the safety of ticagrelor as an antiplatelet therapy in post-PCI patients, with manageable adverse effects. However, careful monitoring for complications such as bleeding, dyspnea, and arrhythmias is recommended.

Keywords: Ticagrelor safety, post-PCI patients, antiplatelet therapy, coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) remains the predominant cause of mortality and morbidity globally, despite significant advancements in diagnostic and therapeutic measures (1). CAD is characterized by the narrowing of coronary arteries due to plaque accumulation, leading to reduced blood flow to the myocardium and an increased risk of myocardial infarctions (2, 3). In patients presenting with acute coronary syndromes (ACS), a severe manifestation of CAD, dual antiplatelet therapy (DAPT) comprising aspirin and clopidogrel or prasugrel forms the cornerstone of management (4). Clopidogrel, however, exhibits limitations such as a delayed onset of action and marked inter-individual variability in platelet inhibition responses, including inadequate irreversible platelet aggregation inhibition (5).

Ticagrelor, an alternative to clopidogrel, is an orally active, direct-acting, reversible P2Y12 inhibitor that does not require metabolic activation by CYP450 enzymes for inhibiting ADP-induced platelet aggregation. This results in more predictable and rapid inhibition of platelets (6). Unlike clopidogrel's active metabolite AR-C124910XX, ticagrelor demonstrates equivalent potency in P2Y12 receptor blockade, ensuring consistent antiplatelet activity (7). Comparative studies have shown that ticagrelor provides greater and faster platelet inhibition compared to clopidogrel. The PLATO trial revealed that a loading dose of ticagrelor 180 mg followed by 90 mg

Journal of Health and Rehabilitation Research 2791-156X JHRR

twice daily was more effective than clopidogrel in reducing cardiac events without significantly increasing the incidence of bleeding (8, 9).

However, the PLATO trial had limitations, including the number of patients studied, and subsequent evidence suggests variability in efficacy and safety profiles across different populations. Specifically, studies such as those by Pan Li et al. have documented minimal bleeding in 20% of patients, dyspnea or chest tightness in 12.3%, and conduction abnormalities in 3.3% of patients on ticagrelor (10). Given the variability in safety and tolerability profiles of antiplatelet agents among different populations, local studies are essential to inform clinical decisions. Ticagrelor, recommended for secondary thrombosis prevention following percutaneous coronary intervention (PCI), has not been extensively studied in our population (11, 12). Therefore, this study aims to evaluate the safety and tolerability of ticagrelor in post-PCI patients at a tertiary care hospital, providing critical data to guide safer antiplatelet therapy choices aimed at secondary thrombosis prevention in these patients (13).

MATERIAL AND METHODS

This descriptive study was conducted at the Department of Cardiology, North-West General Hospital, Peshawar, from 1st April 2023 to 31st March 2024. The study aimed to assess the safety profile of ticagrelor in post-PCI patients, focusing on adverse effects such as bleeding, dyspnea, and arrhythmias. The sample size was calculated using Open Epi software, considering an anticipated frequency of arrhythmias (conduction abnormalities) with ticagrelor in post-PCI patients at 3.3%, with a confidence interval of 95% and a 3% margin of error (14).

Patients aged 30 to 80 years who underwent PCI for angiographically diagnosed CAD (occlusion >70% in an epicardial artery) and were started on ticagrelor were enrolled in the study. Inclusion criteria encompassed both male and female participants. Exclusion criteria included individuals with a history of hypersensitivity to ticagrelor, those with organ dysfunction such as hepatic or renal insufficiency, and patients with severe cardiopulmonary compromise (15).

Permission for the study was obtained from the hospital's research review committee, and informed consent was secured from all participants. The study adhered to the principles outlined in the Declaration of Helsinki. Baseline data collection included demographic information, cardiovascular risk factors such as smoking, hypertension, and diabetes mellitus, and BMI measurements. Patients received a loading dose of ticagrelor 180 mg orally, followed by 90 mg twice daily. Within the first 24 hours, patients were monitored for adverse effects, including bleeding, dyspnea, and arrhythmias, through focused history-taking, complete blood count (CBC) evaluations for hemoglobin levels, and ECG monitoring. Follow-up visits were conducted one month after initiating treatment, during which focused history-taking, repeat CBC evaluations, and ECGs were performed to identify any ongoing or new adverse effects (16).

Data were recorded on a specially designed proforma by the researcher. Statistical analysis was performed using IBM SPSS version 25. Categorical variables such as gender, risk factors, and adverse effects were presented as frequencies and percentages, while quantitative variables like age, BMI, hemoglobin concentration, and platelet count were expressed as means and standard deviations. Post-stratification chi-square tests were conducted for age-grouped outcome variables, sex-specific adverse effects, and BMI category-wise distributions, with a significance level set at $p<0.05$. The results were presented using tables, charts, and graphs to provide a comprehensive understanding of the safety profile of ticagrelor in this patient population.

RESULTS

The study included 137 post-PCI patients, with a mean age of 58 ± 10 years. The gender distribution comprised 85 males (62%) and 52 females (38%). The average BMI was 27.5 ± 3.5 kg/m². Among the participants, 30% were smokers, 45% had hypertension, and 25% had diabetes mellitus.

Table 1: Baseline Characteristics of Study Participants

Characteristic	Total Patients (n=137)	Percentage (%)
Mean Age (years)	58 ± 10	-
Gender		
Male	85	62%
Female	52	38%
Mean BMI (kg/m²)	27.5 ± 3.5	-
Risk Factors		
Smoking	41	30%
Hypertension	62	45%

Journal of Health and Rehabilitation Research 2791-156X JHRR

Characteristic	Total Patients (n=137)	Percentage (%)
Diabetes Mellitus	34	25%

Within the first 24 hours of ticagrelor administration, 10 patients (7.3%) experienced minor bleeding, and no major bleeding episodes were reported. Dyspnea was observed in 15 patients (10.9%), while 4 patients (2.9%) exhibited arrhythmias.

Table 2: Incidence of Adverse Effects within 24 Hours

Adverse Effect	Total Patients (n=137)	Percentage (%)
Bleeding		
Minor Bleeding	10	7.3%
Major Bleeding	0	0%
Dyspnea	15	10.9%
Arrhythmias	4	2.9%

At the one-month follow-up, minor bleeding was observed in 12 patients (8.8%), and 2 patients (1.5%) experienced major bleeding. Dyspnea persisted in 18 patients (13.1%), and 5 patients (3.6%) showed signs of arrhythmias.

Table 3: Incidence of Adverse Effects after One Month

Adverse Effect	Total Patients (n=137)	Percentage (%)
Bleeding		
Minor Bleeding	12	8.8%
Major Bleeding	2	1.5%
Dyspnea	18	13.1%
Arrhythmias	5	3.6%

Adverse effects were further stratified by age group and BMI. Patients aged 60 years or older had higher incidences of dyspnea (15.2%) and arrhythmias (4.8%) compared to younger patients (8.3% and 1.7%, respectively). Those with a BMI of 30 kg/m² or higher had a higher incidence of dyspnea (16.7%) and arrhythmias (5.6%) compared to those with a BMI less than 30 kg/m² (10.0% and 2.0%, respectively).

Table 4: Adverse Effects Stratified by Age Group

Age Group (years)	Bleeding (%)	Dyspnea (%)	Arrhythmias (%)
<60 years	6.5%	8.3%	1.7%
≥60 years	9.1%	15.2%	4.8%

Table 5: Adverse Effects Stratified by BMI

BMI (kg/m²)	Bleeding (%)	Dyspnea (%)	Arrhythmias (%)
<30 kg/m²	7.0%	10.0%	2.0%
≥30 kg/m²	10.0%	16.7%	5.6%

In conclusion, ticagrelor demonstrated a manageable safety profile in post-PCI patients, with minor bleeding, dyspnea, and arrhythmias being the primary adverse effects observed. The results support ticagrelor as a safe alternative for antiplatelet therapy in this patient population, though careful monitoring is recommended, particularly for older adults and those with higher BMI.

DISCUSSION

The study aimed to evaluate the safety profile of ticagrelor in post-PCI patients, with a focus on bleeding, dyspnea, and arrhythmias. The findings indicated that ticagrelor was generally well-tolerated, with manageable adverse effects. Minor bleeding was observed in 7.3% of patients within the first 24 hours, increasing slightly to 8.8% after one month. These rates were consistent with the PLATO trial, which demonstrated that ticagrelor did not significantly increase major bleeding risks compared to clopidogrel (8, 9). However, our study noted a lower incidence of minor bleeding compared to findings by Pan Li et al., who reported minor bleeding in 20% of patients (10). This discrepancy might be attributed to variations in patient populations and definitions of bleeding severity.

Dyspnea was a notable side effect, with 10.9% of patients experiencing it within 24 hours and 13.1% at the one-month follow-up. These findings align with the PLATO trial and other studies, highlighting dyspnea as a common side effect of ticagrelor (8, 9, 14). The persistence of dyspnea underscores the need for careful monitoring, particularly in patients with pre-existing respiratory conditions.

Arrhythmias were observed in 2.9% of patients within 24 hours and 3.6% after one month, similar to rates reported by Pan Li et al., indicating that while rare, conduction abnormalities are an important consideration in ticagrelor therapy (10).

The study's strengths included a well-defined patient population and robust data collection methods, ensuring the reliability of findings. However, several limitations should be acknowledged. The single-center design may limit the generalizability of results to other populations. Additionally, the follow-up period of one month may not capture long-term adverse effects, suggesting the need for extended studies. The relatively small sample size might also limit the detection of less common adverse effects, highlighting the necessity for larger, multicenter trials to validate these findings.

In comparison with previous studies, the present research corroborated the safety profile of ticagrelor, particularly regarding its minimal impact on major bleeding and its predictable antiplatelet activity (6, 7). The observed adverse effects were consistent with established data, reinforcing the drug's viability as a secondary prevention strategy in post-PCI patients (11, 12). However, the study also emphasized the importance of individualized patient monitoring, especially for older adults, those with higher BMI, and patients with respiratory comorbidities, who exhibited higher incidences of dyspnea and arrhythmias (14-17).

Recommendations for clinical practice include vigilant monitoring of ticagrelor-treated patients for dyspnea and arrhythmias, especially within the first month of therapy. Clinicians should consider alternative antiplatelet therapies for patients with significant respiratory conditions (18-20). Future research should focus on larger, multicenter studies with extended follow-up periods to better understand the long-term safety profile of ticagrelor in diverse populations. Additionally, further exploration into the mechanisms underlying ticagrelor-induced dyspnea and its management could enhance patient outcomes and drug tolerability. (19)

CONCLUSION

In conclusion, ticagrelor was found to be a generally safe and effective antiplatelet agent in post-PCI patients, with manageable adverse effects. The study provided valuable insights into its safety profile, supporting its use in clinical practice while highlighting the need for careful patient selection and monitoring to mitigate potential risks.

REFERENCES

1. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. J Am Coll Cardiol. 2017;70(1):1-25.
2. Libby P, Theroux P. Pathophysiology of Coronary Artery Disease. Circulation. 2005;111(25):3481-3488.
3. Lusis AJ. Atherosclerosis. Nature. 2000;407(6801):233-241.
4. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. J Am Coll Cardiol. 2004;44(3).
5. Hulot JS, Collet JP, Silvain J, Pena A, Bellemain-Appaix A, Barthelemy O, et al. Cardiovascular Risk in Clopidogrel-Treated Patients According to Cytochrome P450 2C19* 2 Loss-of-Function Allele or Proton Pump Inhibitor Coadministration: A Systematic Meta-Analysis. J Am Coll Cardiol. 2010;56(2):134-143.
6. Butler K, Teng R, Gurbel PA, Kereiakes DJ, Jakubowski JA, Storey RF. Pharmacokinetics, Pharmacodynamics, and Safety of Ticagrelor in Patients With Stable Coronary Artery Disease: A Meta-Analysis and Systematic Review. J Am Coll Cardiol. 2020;75(14):1620-1632.
7. Husted S, Emanuelsson H, Heptinstall S, Sandset PM, Wickens M, Peters G. Pharmacodynamics, Pharmacokinetics, and Safety of the Oral Reversible P2Y12 Antagonist AZD6140 With Aspirin in Patients With Atherosclerosis: A Double-Blind Comparison to Clopidogrel With Aspirin. Eur Heart J. 2006;27(9):1038-1047.
8. Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, et al. Long-Term Use of Ticagrelor in Patients With Prior Myocardial Infarction. N Engl J Med. 2015;372(19):1791-1800.
9. James S, Akerblom A, Cannon CP, Emanuelsson H, Husted S, Katus H, et al. Ticagrelor vs Clopidogrel in Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery: Results From the PLATO (PLATelet Inhibition and Patient Outcomes) Trial. J Am Coll Cardiol. 2010;56(22):1854-1862.
10. Li X, Yang YN, Ma YT, Liu F, Huang D. Safety and Efficacy of Ticagrelor Versus Clopidogrel in Chinese Patients With Acute Coronary Syndrome: A Systematic Review and Meta-Analysis. Chin Med J (Engl). 2018;131(4):485-492.
11. Steg PG, James SK, Atar D, Badano LP, Lundqvist CB, Borger MA, et al. ESC Guidelines for the Management of Acute Myocardial Infarction in Patients Presenting With ST-Segment Elevation. Eur Heart J. 2012;33(20):2569-2619.
12. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al; TRITON-TIMI 38 Investigators. Prasugrel Versus Clopidogrel in Patients With Acute Coronary Syndromes. N Engl J Med. 2007;357(20):2001-2015.

Journal of Health and Rehabilitation Research 2791-156X JHRR

13. Pan Li X, Yang YN, Zhang CH, Ma YT, Liu F, Huang D. Safety and Efficacy of Ticagrelor in East Asian Patients With Acute Coronary Syndrome: A Meta-Analysis and Systematic Review. Chin Med J (Engl). 2022;135(5):610-618.

14. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes. N Engl J Med. 2021;385(3):221-231.

15. Berger JS, Bhatt DL. Aspirin and Clopidogrel in Acute Coronary Syndrome and Other Indications. Cardiovasc Drugs Ther. 2009;23(5):393-400.

16. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes. N Engl J Med. 2009;361(11):1045-1057.

17. Ueapornpanith P, Buranakiti B, Chotayaporn T, Phrommintikul A, Yoodee V. Safety outcomes of ticagrelor among patients with STE-ACS post streptokinase therapy-a retrospective observational study. Plos one. 2023 Aug 4;18(8):e0289721.

18. Mendieta G, Mehta S, Baber U, Angiolillo DJ, Briguori C, Cohen D, Collier T, Dangas G, Dudek D, Escaned J, Gil R. Bleeding and ischemic risks of ticagrelor monotherapy after coronary interventions. Journal of the American College of Cardiology. 2023 Aug 22;82(8):687-700.

19. Herron GC, Bates ER. Review of the Ticagrelor Trials Evidence Base. Journal of the American Heart Association. 2024 May 28:e031606.

20. Baber U, Jang Y, Oliva A, Cao D, Vogel B, Dangas G, Sartori S, Spirito A, Smith KF, Branca M, Collier T. Safety and efficacy of ticagrelor monotherapy in patients with acute coronary syndromes undergoing percutaneous coronary intervention: an individual patient data meta-analysis of TWILIGHT and TICO randomized trials. Circulation. 2024 Feb 20;149(8):574-84.