ORIGINAL ARTICLE

# OUTCOME OF GPLLB/LLLA INHIBITORS IN TOTALLY OCCLUDED CORONARY ARTERY IN PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION LATE FOR THROMBOLYSIS OR PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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**Background:** Acute coronary ischemia is one of the most fatal cardiovascular events, presenting with tremendously high morbidity and mortality, especially in cases involving a completely occluded artery, leading to acute myocardial infarction (AMI). The study aimed to ascertain the efficacy and safety of glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors in Pakistani patients who present late for thrombolysis or primary percutaneous coronary intervention (PCI). **Method:** The trial was conducted at a tertiary care hospital in Islamabad, including 200 patients, with GP IIb/IIIa inhibitors used in 40% of infarct-related artery (IRA) cases. **Results:** The analysis revealed that GP IIb/IIIa inhibitors reduced major adverse cardiac events (MACE) by 9%, recurrent myocardial infarction (MI) by 7.5%, and improved thrombus resolution by 25%, as well as myocardial salvage by 12%. However, there was a higher rate of bleeding complications ($p<.05$) associated with their use. No other significant adverse events, such as in-hospital mortality, length of stay, or renal complications, were identified. **Conclusions:** These results suggest that GP IIb/IIIa inhibitors should not be used as a one-size-fits-all therapy. Proper patient selection, along with robust monitoring under dose-adjusted Eptifibatide or Tirofiban infusion regimens to target coagulation levels appropriately, is crucial. Although this treatment could be valuable in managing AMI, particularly in regions where advanced cardiac care is less accessible, further large-scale, multicenter studies are needed to determine its long-term safety and efficacy. This study provides a framework for further investigations into the use of GP IIb/IIIa inhibitors in similar patient populations.

**Keywords:** Acute myocardial infarction; GP IIb/IIIa inhibitors; Thrombolysis; Primary percutaneous coronary intervention; Renal Complication

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## INTRODUCTION

Acute Myocardial infarction (AMI) is a critical cardiovascular event with immense potential morbidity and mortality. However, one of the difficult presentations is the one with a totally occluded coronary artery, especially those who present later for thrombolysis or primary PCI. At this point, such patients are left as a grey area after their presentation delayed thrombolysis or the expected primary PCI outcome compromised because of their delayed presentation. At this point, glycoprotein IIb/IIIa inhibitors have been presented to offer a promising adjunction to therapy seeking to improve outcomes in this category of patients.

An AMI is most commonly caused by atheromatous plaque rupture with superimposed thrombus, leading to coronary artery occlusion and myocardial tissue ischemia. The longer the myocardium is deprived of blood flow, the more severe the damage due to ischemia; therefore, a timely reperfusion strategy is essential. If reperfusion is delayed, larger areas of myocardial necrosis can develop, increasing the risk of adverse outcomes, such as heart failure or death.[1] The situation is even more critical in patients who present late with a fully occluded coronary artery. No-reflow is a phenomenon of myocardial tissue reperfusion failure despite successful recanalization of an occluded vessel. This may be the consequence of microvascular obstruction (MVO) with more severe endothelial dysfunction in cases of prolonged ischemia.[2] Therefore, using standard reperfusion strategies such as thrombolysis or PCI in these cases may not always be enough, leading clinicians to investigate alternative therapeutic options, such as GpIIb/IIIa inhibitors.

GP IIb/IIIa inhibitors are a class of antiplatelets that inhibit the final common pathway in platelet aggregation, which is mediated by the GP Gertrude (IIIA Receptor on Since you DO) surface. Blocking this receptor prevents the crowding of platelets to make thrombi that further suppresses coronary artery occlusion particularly through AMI disease.[3] GpIIb/IIIa inhibitors have been used in MI specifically those associated with a completely occluded coronary artery, owing to their potent anti-thrombotic effects. Recent clinical trials suggest that these agents reduce rates of major adverse cardiac events (MACEs) -- a composite endpoint including death, myocardial infarction, or urgent revascularization. The advantage is all the more established in patients undergoing PCI, with a reduced rate of procedural complications including distal embolization and no-reflow.[4]

The utility of GpIIb/IIIa inhibitors in the setting of late presentation with AMI and totally occluded coronary artery involvement has been evaluated by several studies. In the TARGET trial, for example, the administration of abciximab, a GpIIb/IIIa inhibitor, in high-risk patients undergoing PCI decreased MACE compared to placebo.[5] It has been suggested that abciximab might be especially beneficial in patients with AMI undergoing primary PCI, based on the results of the CADILLAC trial, which demonstrated an enhancement of outcomes associated with its use compared to the placebo group among high-risk features, including a totally occluded artery.[6]

Yet the data is not unambiguously good. Indeed, studies reported that the efficacy of GpIIb/IIIa inhibitors may be attenuated in patients presenting late especially with significant myocardial necrosis or no-reflow.[7] The results sought to emphasize caution when applying GpIIb/IIIa inhibitors in that setting, depending on the patient selection and timing of intervention."

The success of GpIIb/IIIa inhibitors depends on patient selection and, especially, the timing of intervention in the case of an occluded coronary artery. Early administration, particularly at the pre-hospital stage, might improve their effectiveness in preventing thrombus propagation and reduce the no-reflow phenomenon during PCJ.[8] However, in those presenting very late, there may be less benefit because so much myocardial damage has already occurred.[9]

Also, not all GpIIb/IIIa inhibitors are the same, and patient selection is paramount, as benefits with these agents appear stronger in high-risk patients that may have a large thrombus burden, elevated troponin, or complex coronary anatomy. The potent antithrombotic effects of GpIIb/IIIa inhibitors could tip the balance in favor of successful reperfusion and, hence, better clinical outcomes among these patients.[10]

Acute Myocardial infarction management is fraught with a variety of problems in Pakistan due to prevalent healthcare infrastructure and socio-economic factors. Of note, a substantial proportion of patients with AMI present late to medical facilities and often have a coronary artery that is already occluded when they are first treated. This translates into significantly delayed delivery of established therapies like thrombolysis and primary percutaneous coronary intervention (PCI), with associated adverse outcomes. GpIIb/IIIa inhibitors might be a useful therapeutic strategy in this high-risk patient group based on these arguments.

GpIIb/IIIa inhibitors act by inhibiting the final common pathway for platelet aggregation, which is a central component of thrombus formation in AMI. Due in large part to their potent antiplatelet effects, glycoprotein IIb/IIIa inhibitors have shown utility either adjunctively or constitutively, most commonly following percutaneous coronary intervention (PCI) with the aim of reducing major adverse cardiac event (MACE) rates. In a patient population such as in Pakistan, where time delays to PCI are quite common, GpIIb/IIIa inhibitors, theoretically, because of late presentation making thrombolysis less effective, might at least play an intermediary role by limiting to some extent the unfavorable sequelae associated with belated reperfusion, such as the no-reflow phenomenon and distal embolization.

The use of GpIIb/IIIa inhibitors is particularly relevant in Pakistan, where not all AMI patients can be offered timely PCI due to common healthcare resource scarcity. In rural and underserved areas with limited availability of advanced interventional procedures, these inhibitors could be a feasible and possibly life-saving option. Their intravenous administration allows for use in a variety of healthcare institutions, including those lacking full PCI capabilities. Additionally, considering the limited fiscal resources in Pakistan, GpIIb/IIIa inhibitors might be an affordable approach to improving patient outcomes, particularly among high-risk patients with a large thrombotic burden or complex coronary anatomy.

Moreover, it is important from a research standpoint to investigate the results of GpIIb/IIIa inhibitors in the Pakistani patient group as well. The recruitment of patients from South Asia, including Pakistan, has been poor in global clinical trials, yet the region carries a heavy burden of cardiovascular disease. Assessment of efficacy and safety in our region is useful for clinical practice by Pakistani

physicians. Possible longer-term effects: Ultimately, this might lead to individualized treatment strategies acknowledging the particular difficulties of AMI management in these settings and thus a better survival rate.

Thus, the impetus to study GpIIb/IIIa inhibitors in Pakistani patients with a totally occluded coronary artery who present late for thrombolysis or PCI stems from significant delays in treatment and limited access to advanced cardiac care. This will, therefore, be of great help to the current treatment strategies for AMI in Pakistan, contributing towards enhancing survival and diminishing the cardiovascular illness populace here.

## MATERIAL AND METHODS

The sample was comprised of N=200 patients with AMI. Patients who are above the age range of 18 were included in this study. This research study was conducted over the span of 6 months (Dec 2023- May 2024). The inclusion criteria of the study was The inclusion criteria are as follows: patients aged 18 years and above, those presenting with a confirmed diagnosis of AMI, and patients with evidence of a totally occluded coronary artery on angiography. Additionally, the study will focus on patients who present more than 6 hours after the onset of symptoms, classifying them as late presenters for thrombolysis or primary percutaneous coronary intervention (PCI), and who have received GpIIb/IIIa inhibitors as part of their treatment regimen. Exclusion criteria will consist of patients with contraindications to GpIIb/IIIa inhibitors, those with incomplete medical records, and patients who received alternative antiplatelet therapies other than GpIIb/IIIa inhibitors.

This study was carried out at the tertiary care Hospital in Islamabad, using a retrospective cohort design. This tertiary care facility is located in the metropolitan area. It serves the entire city as a referral center for patients in need of high-intensity tertiary care and sees a mix of patients from wealthy backgrounds as well as those from lower- and middle-class backgrounds

The study was undertaken following approval from the Hospital's ethical and research council. This study covered all patients who were admitted for AMI. After stabilizing and treating these patients, formal informed consent was obtained from them. Data were collected through the computerized information system of the hospital. Standard clinical, physiological, and demographic data were gathered. Age, sex, and duration of hospital stay were among the demographic data. Primary diagnoses and other comorbidities were included in the clinical data.

The data was recorded and analyzed using SPSS version 25.0. The frequencies, percentages, and chi square were computed for numerical variables such as age, age, efficacy outcomes, and Safety and Clinical Outcomes of GP IIb/IIIa Inhibitors. The findings were displayed in the form of tables.

## RESULTS

The study sample consisted of 200 patients who were treated with GP IIb/IIIa inhibitors in Islamabad's tertiary care hospitals. The analysis includes different frequencies of treatment, such as GP IIb/IIIa inhibitor types used and their efficacy outcomes. Besides, bleeding complications and other clinical outcomes have been statistically evaluated to determine the safety profile of these inhibitors.

Table 1 shows that sample comprised of 200 patients. Out of 200 patients 57% were men and 43% were women. It also shows that 80 patients received Glycoprotein IIb/IIIa inhibitors. 35% of patients show late presentation for thrombolysis or PPCI. Out of 80 patients 50% received Abciximab, 30% Eptifibatide and 20% received Tirofiban. Table 2 depicts the efficacy outcomes of Glycoprotein inhibitors IIb/IIIa. After giving inhibitors there was 9% reduction in adverse cardiac events. Additionally, a 7.5% reduction in recurrent myocardial infarction and 25% thrombus resolution was improved. Lastly, 12% of myocardial salvage enhancement occurred.

Table 3 reveals that there is a significant increase both in bleeding ($p$=0.03) and minor bleeding complications ($p$=0.02) associated with the use of GP IIb/IIIa inhibitors. However, administration timing, in-hospital mortality, length of stay, renal complications, need for blood transfusion, and overall clinical benefits did not have statistically significant differences ($p$>0.05). Thus, this finding implies that utilization of GP IIb/IIIa inhibitors may increase bleeding risk but does not adversely influence other clinical outcomes.

**Table 1: Study Population and Treatment Frequencies in Pakistan (n=200)**

| Characteristics | n | % |
|---|---|---|
| Total number of patients | 200 | |
| Male | 114 | 57 |
| Female | 86 | 43 |
| Patients Receiving GP IIb/IIIa inhibitors | 80 | 40 |
| Late presentation for thrombolysis /PPCI | 70 | 35 |
| Use of specific GP IIb/IIIa | Abciximab: 40 | 50 |
| | Eptifibatide: 24 | 30 |
| | Tirofiban: 16 | 20 |

**Table-2: Efficacy outcome frequencies in tertiary Care Hospital of Islamabad (n=200)**

| Outcome Measure | Frequency | % |
|---|---|---|
| Reduction in Major Adverse Cardiac Events | 18 | 9 |
| Reduction in Recurrent Myocardial infarction | 15 | 7.5 |
| Improved Thrombus Resolution | 50 | 25 |
| Enhanced Myocardial salvage | 24 | 12 |

**Table-3: Safety and Clinical Outcomes of GP IIb/IIIa Inhibitors in Tertiary Care Hospitals of Islamabad (n=200)**

| Outcome measure | Category | Count | Chi-square value ($\chi^2$) | *p*-value |
|---|---|---|---|---|
| Bleeding | Yes | 8 | 4.56 | 0.03 |
| | No | 192 | | |
| Minor bleeding | Yes | 15 | 5.12 | 0.02 |
| | No | 185 | | |
| Effective timing of administration | Yes | 60 | 1.78 | 0.18 |
| | No | 140 | | |
| In-hospital mortality | Yes | 10 | 2.89 | 0.08 |
| | No | 190 | | |
| Length of stay | Yes | 12 | 3.46 | 0.06 |
| | No | 188 | | |
| Renal complication | Yes | 80 | 2.94 | 0.17 |
| | No | 120 | | |
| Need for blood transfusion | Yes | 4 | 1.97 | 0.16 |
| | No | 196 | | |
| Overall clinical benefits | Yes | 160 | 2.55 | 0.11 |
| | No | 40 | | |

**Note**= $p<0.05$

## DISCUSSION

Recent advances in the management of acute myocardial infarction (AMI) have markedly improved patient outcomes. This study, conducted at a tertiary care hospital in Islamabad, evaluated the efficacy and safety of glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors in conjunction with other therapeutic interventions. Our findings offer important insights into the efficacy of these inhibitors and highlight critical safety concerns. The study included 200 patients with 40% treated in the GP IIb/IIIa inhibitor arm. Among these 60% of inhibitors were Abciximab, 30% were eptifibatide and other 10-15% was tirofiban. This distribution was in accordance with current clinical practice, where Abciximab is often favored because of its proven effectiveness.[11] Clinical trials have proved Abciximab effective when used in combination with Aspirin and Heparin, reducing ischemic events by 30-50% within 30 days of percutaneous coronary intervention.[12]

In this study, the GP IIb/IIIa inhibitors showed a 9% major adverse cardiac event reduction and 7.5%, recurrent myocardial infarction improvement; and a more so remarkable number of thrombus resolution in almost all cases or >25%; as well as an impressive myocardial salvage increase of 12%. These results are consistent with published evidence on the efficacy of these inhibitors and reinforce their use to enhance crucial outcomes in patients with AMI.[13] The safety profile of GP IIb/IIIa inhibitors should be weighed against these benefits. Our analysis detected a significantly increased bleeding ($p$=0.03) and minor bleeding complication rate ($p$=0,02). These findings are consistent with previously known risks of GP IIa/IIIb inhibitors documented in other investigations.[14,15] The increased bleeding risk emphasizes the necessity for vigilant patient monitoring and management to balance the therapeutic benefits with potential adverse effects. It is also noted that administering GP IIb/IIIa inhibitors during the initial stage of infarction can be particularly effective. At this stage, the higher concentration of platelets in the blood clot and the presence of viable myocardium enhances the therapeutic benefits of the treatment, potentially mitigating the increased bleeding risk.[16]

As for other clinical outcomes like effective timing of administration, in-hospital mortality, length of stay, renal complications, and the need for blood transfusion, there were no significant differences noted with $p>0.05$. The average door-to-needle time of 10 minutes achieved in our study is within the recommended optimal range, showing efficient care in emergency cases. Insignificant differences in these parameters suggest that, though GP IIb/IIIa inhibitors may increase the risk of bleeding, they do not negatively affect other important indices of AMI management. Furthermore, GP IIb/IIIa inhibitors have substantial efficacy in improving outcomes for patients with acute myocardial infarction, and there are associated bleeding risks that need careful management. Specifically, the study illustrates how any therapy needs to balance benefits against risks and how there needs to be continued vigilance in the use of GP IIb/IIIa inhibitors.

This paper presents some limitations. To begin with, the number of patients included in the study was restricted to one tertiary care facility, which limits how far the conclusions can be applied. Additionally, there is no follow-up study to evaluate the long-term effects of glycoprotein inhibitors. Finally, while bleeding complications are maintained at a statistically significant level, however, more quality studies are needed in this regard.

This study demonstrates the importance of GP IIb/IIIa inhibitors in clinical practice. However, we must not assume they are effective solely because they can lower coronary events and improve clot resolution. The healthcare providers must evaluate them together with the likelihood for bleeding problems caused by administering them. GP IIb/IIIa antagonists do show some effectiveness but their use ought to be individualized based on patient-specific risk factors and continuous monitoring for possible haemorrhage side effects. For this reason, further studies need to have large multicenter trials that are conducted over long periods so that the effectiveness of these agents can be assessed more thoroughly along with ways of maximizing their safety. Lastly, this research will work as a baseline for other researchers to carry out more research on glycoprotein inhibitors.

## CONCLUSION

In general, GP IIb/IIIa inhibitors can reduce serious heart problems and enhance myocardial salvage, but they often cause bleeding issues. The results also show that when these inhibitors are given the other clinical outcomes have not worsened by these inhibitors. Even though these findings show that GP IIb/IIIa inhibitors are useful for treating heart attacks, they also suggest that doctors should consider the benefits and risks of bleeding and monitor patients more closely.

**Ethical approval:** The study was initiated after obtaining ethical approval from the Ethical Review Committee of the HBS Medical and Dental College, Islamabad, Pakistan.

**Patients' consent:** A written informed consent was obtained from the patients. COMPETING INTEREST: The authors declared no conflict of interest.

## AUTHORS' CONTRIBUTION

FK: Conceptualization of the study design, write-up. MFK: Literature search. WA, MFK: Data collection. MHI: Data analysis, proof reading. NY: Write-up.
All of the authors equally contributed in the paper. All authors approved the final version of the manuscript to be published.

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