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Relationship of Admission Glucose level with No-Reflow or Slow Flow in STEMI patients Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Objective: To evaluate the association of admission blood glucose levels with no-reflow or slow flow in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing Primary Percutaneous Coronary Intervention (PPCI).

Study Design: Analytic Cross-sectional study.

Place & Duration of Study**:** Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, Pakistan, from Jan 2023 till Jun 2023

Methodology: Total 141 STEMI patients (regardless of age and gender) presented in the emergency department with the time duration of 12 hours after onset of chest pain were included in the study by using non-probability Consecutive Sampling technique. Admission glucose levels were measured, and the occurrence of no-reflow or slow flow was assessed using the Thrombolysis in Myocardial Infarction (TIMI) flow score. Statistical analysis, including t-test and Chi-square tests were applied to evaluate the association between glucose levels and no-reflow or slow flow. Level of significance taken was ≤0.05.

Results: Out of total 141 patients, mean age of the patients was 61.74+10.87 years and majority were males, 118(83.7%). 101(71.6%) were hypertensive and 69(48.9%) were diabetic. The average admission glucose level was 181.13+112.16mg/dl. Patients with no-reflow or slow flow had significantly higher admission glucose levels compared to those with normal flow (p=0.031). Additionally, a significantly higher number of patients developed no-reflow 4(9.3%) or slow flow 24(55.8%) in the group with admission glucose levels >200 mg/dl (p=0.01).

Conclusion: Admission glucose levels may serve as a simple predictor of no-reflow or slow flow in STEMI patients undergoing PPCI, emphasizing the importance of adequate glucose management in these patients.

Keywords: Admission Glucose Levels, No-Reflow, Primary Percutaneous Coronary Intervention, Slow Flow, ST-Elevation Myocardial Infarction.

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INTRODUCTION

Coronary Artery Disease (CAD) is the most common cause of illness and death in the entire world, & caused 8.9 million deaths globally in the year 2015.[1-3] One out of every four individuals in Pakistan are affected by CAD.[4] Both modifiable and non-modifiable risk factors contribute to the development of CAD. Some of the most important risk factors for CAD includes hypertension, smoking, obesity, diabetes mellitus, and hypercholesterolemia.[5]

Acute Coronary Syndrome (ACS) encompasses different conditions, including ST-Segment Elevation Myocardial Infarction (STEMI), Non-ST Elevation Myocardial Infarction (NSTEMI), and unstable angina. These conditions are diagnosed based on specific criteria such as enzyme rise, presence of ischemic symptoms, and ECG changes. Diagnostic tests play a crucial role in detecting myocardial ischemia, particularly in patients with an intermediate pretest probability of CAD. They are recommended for individuals with an intermediate or high probability of CAD and can include exercise treadmill tests, stress echocardiography, magnetic resonance imaging, Coronary Artery Computed Tomography (CCT), and coronary angiography.[4]

The exercise treadmill test involves the measurement of heart's response to exercise-induced stress, assessing changes in the ECG, heart rate, and blood pressure. Stress echocardiography utilizes ultrasound imaging before and after exercise or pharmacological stress to evaluate regional wall motion abnormalities, providing insights into myocardial perfusion and function. Magnetic Resonance Imaging (MRI) offers detailed visualization of the heart and coronary

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arteries, enabling the detection of myocardial ischemia and assessment of ventricular function.[6]

CCT is a non-invasive imaging technique that provides high-resolution images of the coronary arteries, aiding in the detection of stenosis and plaque burden. Lastly, coronary angiography is an invasive procedure that involves injecting contrast dye into the coronary arteries, allowing direct visualization of vessel occlusions or stenosis.[6,7]

Stress hyperglycemia is a known entity, which as the name suggests can occur due to any stressful event in the body. This refers to glucose level of more than 180 mg/dl with no pre-existing diabetes. It is a temporary increase in blood sugars level and occurs even in non-diabetics.[6] Patients with acute Myocardial Infarction (MI) may also develop stress related hyperglycemia that worsens the outcomes[7] and may occur in as much as 50% of the individuals with STEMI. Stress hyperglycemia is associated with both in-hospital and long-term negative outcomes in patients with STEMI, irrespective of their diabetic status. This increased risk of mortality may be attributed to factors such as larger infarct size, higher incidence of congestive heart failure, and cardiogenic shock.[8]

There is a list of complications associated with Primary Percutaneous Coronary Intervention (PPCI) and one of those complications is no-reflow phenomenon. No-reflow is one of the major complications of PPCI and is associated with poor prognosis, leading to greater morbidity and mortality, adverse left ventricular remodeling, and congestive heart failure. Limited local data is available on this subject in our population. The exact mechanism responsible for the no-reflow phenomenon is not known. The most probable pathophysiological mechanisms attributed to this complication include distal athero-thrombotic embolization, ischemic damage, reperfusion injury, and individual susceptibility to micro vascular damage. It occurs in 10% of the STEMI patients treated with Primary PCI.[9]

Therefore, identifying the predictors of no-reflow and the high risk patients undergoing PPCI for STEMI is essential to avoid this complication and to improve outcomes.[10] Our study aimed at investigating the impact of hyperglycemia on the no-reflow phenomenon in both diabetic and non-diabetic patients after PPCI.

METHODOLOGY

Present study was an Analytical Cross-sectional study, carried out at Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, Pakistan from January 2023 till June 2023 after approval from IERB (IERB letter#9/2/R&D/2023/248).

Calculated sample size was 139 and it was calculated by using WHO calculator by taking 95% confidence level and 5% margin of error and 10% prevalence of no-reflow.[9] However, data was collected from 141 patients.

Inclusion Criteria: All STEMI patients presented in the Emergency Department with the time duration of 12 hours after onset of chest pain who underwent primary PCI irrespective of age and gender were included in the study.

Exclusion Criteria: Patients with unstable angina, stable angina, NSTEMI, non-ischemic dilated cardiomyopathy, and valvular heart diseases were excluded from the study. Additionally, those who presented after 12 hours of symptom onset, post-CABG patients, stent thrombosis, and had history of PCI were also excluded.

The diagnosis of STEMI was made using the criteria mentioned in ESC 2017 STEMI guidelines i.e. at least two contiguous leads with ST-segment elevation 2.5 mm in men < 40 years, 2 mm in men 40 years of age, or 1.5mm in women in leads V2–V3 and/or 1 mm in the other leads [in patients without having Left Ventricular (LV) hypertrophy or left bundle branch block (LBBB)].[11]

The coronary artery perfusion was assessed using the TIMI score. The no-reflow or slow flow was defined as any flow less than TIMI-3 after post-dilatation in the absence of dissection, vasospasm, & stenosis.[12-13] Patients' blood glucose levels were assessed in the lab from the initial blood sample taken in the emergency department before proceeding with the PPCI. No-reflow was assessed on Dicom in the catheterization laboratory by two experienced cardiologists.

Gathered data was entered and analyzed in statistical software; Statistical Package For Social Sciences version 24:00. Normality of data was assessed by Shapiro Wilk test. Chi-square and Independent samples t-test were applied to find the association of admission glucose level with no-reflow phenomenon and TIMI flow. *p*-value ≤0.05 was considered as significant.

RESULTS

The study included a total of 141 patients with a mean age of 61.74±10.87 years. Among study participants, 118(83.7%) were males, while 23(16.3%) were females. Hypertension was present in 101(71.6%) patients, while 69(48.9%) patients were diabetic. A small proportion of participants 4(2.8%) had Chronic Kidney Disease. The average blood glucose level at baseline was 181.13±112.16 mg/dl (Table-I).

Table-I: Baseline Characteristics of Study Participants (n=141)

Variables		Frequency (%)
Gender	Male	118(83.7%)
	Female	23(16.3%)
Age(years) (Mean± SD)		61.74±10.87
Comorbids	Hypertension	101(71.6%)
	Diabetes	69(48.9%)
	CKD	4(2.8%)
Blood Glucose (mg/dl) (Mean±SD)		181.13±112.16

CKD=Chronic Kidney Disease

Regarding procedural characteristics, the culprit vessel was predominantly the Left Anterior Descending artery (LAD) in 70(49.6%) cases, followed by Right Coronary Artery (RCA) in 50(35.5%) cases, Left Circumflex Artery (LCx) in 19(13.5%) cases and Posterior Descending Artery (PDA) in 2(1.4%) cases. In terms of disease distribution, patients presented with SVCAD were 52(36.9%), with DVCAD were 42(29.8%) of cases, and TVCAD cases were 47(33.3%). Regarding TIMI flow, 10(7.1%) of patients had TIMI flow grade-1, 52(36.9%) had TIMI flow grade-2, & 79(56.0%) had TIMI flow grade-3 (Table-II).

Table-II: Procedural Characteristics of Study Participants (n=141)

Variables		Frequency(%)
Culprit Vessel	LAD	70(49.6%)
	RCA	50(35.5%)
	LCx	19(13.5%)
	PDA	2(1.4%)
Disease Type	SVCAD	52(36.9%)
	DVCAD	42(29.8%)
	TVCAD	47(33.3%)
TIMI Flow(Grade)	TIMI-1	10(7.1%)
	TIMI-2	52(36.9%)
	TIMI-3	79(56.0%)

LAD=Left Anterior Descending, LCx=Left Circumflex, RCA=Right Coronary Artery, PDA=Posterior Descending Artery, SVCAD=Single Vessel Coronary Artery Disease, DVCAD=Double Vessel Coronary Artery Disease, TVCAD=Triple Vessel Coronary Artery Disease, TIMI=Thrombolysis In Myocardial Infarction.

Findings of the association of sugar levels with slow/no flow showed that for the "no/slow flow" group, the mean blood sugar level was 204.77±126.08 mg/dl, while for the "normal flow" group, it was 162.58±96.70 mg/dl (p=0.03). This indicates that, on average, patients with "no/slow flow" had higher blood sugar levels compared to those with normal flow. To evaluate further, patients were divided into 3 groups based on sugar levels: <100mg/dl, 101-200 mg/dl, & >200 mg/dl respectively. Cross tabulation revealed no-flow and slow-flow in (4(9.3%) and 24(55.8%) patients out of 43 respectively) in the group with sugar levels of >200mg/dl while normal flow was noted in 15(34.96%) patients (p=0.01) (Table-III).

Table-III: Mean Difference/Association of Admission Glucose Levels in No-Flow/Slow-Flow and Normal Flow Group (n=141)

Variables	No/Slow Flow (n =62)		Normal Flow (n=79)	*p*-value
Admission Glucose Level (Mean±SD) (mg/dl)	204.77±126.08		162.58±96.70	0.031
Sugar Level (mg/dl)	**TIMI 1 Frequency (%)**	**TIMI 2 Frequency (%)**	**TIMI 3 Frequency (%)**	***p*-value**
<100 (n=23)	1(4.3%)	7(30.4%)	15(65.2%)	0.01
101-200 (n=75)	5(6.7%)	21(28.0%)	49(65.3%)	
>200 (n=43)	4(9.3%)	24(55.8%)	15(34.9%)	

TIMI=Thrombolysis In Myocardial Infarction

DISCUSSION

The aim of this study was to investigate the relationship between admission glucose levels and the occurrence of no-reflow or slow flow in STEMI patients undergoing PPCI. Our study concluded that the occurrence of no-reflow or slow flow is strongly associated (p=0.01) with sugar levels at admission in patients with STEMI who underwent PPCI.

The findings of this study were consistent with previous studies that had reported a relationship between admission glucose levels and the occurrence of no-reflow or slow flow in STEMI patients undergoing PPCI. Liu *et al.* reported the similar findings of increased no reflow phenomenon in patients with raised sugar levels at admission.[14] Similarly, a study by Bahrehmand *et al*. found that admission hyperglycemia and diabetes mellitus were independent predictors of no-reflow in AMI patients undergoing PPCI.[15] Another study done by Khalfallah *et al.*, included patients specifically with stress hyperglycemia, also reported a higher incidence of no reflow or slow flow in patients with raised sugar levels at admission.[16]

The mechanism underlying the association between admission glucose levels and the occurrence of no-reflow or slow flow is not entirely clear. However, it is believed that hyperglycemia may exacerbate the ischemic-reperfusion injury that occurs during PPCI. Hyperglycemia is known to increase oxidative stress, inflammation, and endothelial dysfunction, all of which may contribute to impaired myocardial perfusion and the occurrence of no-reflow or slow flow.[16,17]

The management of no-reflow or slow flow in STEMI patients undergoing PPCI remains a challenge. The use of pharmacological agents such as Adenosine, Verapamil, and Nitroprusside, and mechanical devices such as thrombectomy catheters and distal protection devices have been shown to be effective in improving myocardial perfusion and reducing the incidence of no-reflow or slow flow.[18] However, the optimal management strategy for individual patients may vary depending on the severity and extent of the underlying disease, the patient's clinical condition, and the availability of resources.

The goal was to recognize the predictors of no reflow or slow flow & then limiting those predictors to prevent the occurrence of this complication. As concluded by our study and similar previous studies, raised admission sugar levels is one of the predictors and treating the sugars adequately may help prevent this complication.

LIMITATIONS OF STUDY

Few limitations of our study were small sample size, single centered study and the lack of data depicting long-term outcomes. Additionally, our study did not involve the mechanisms that cause no reflow in hyperglycemic patients. More similar studies are required in future to support these findings.

CONCLUSION

This study adds to the existing evidence of the relationship between admission glucose levels and the occurrence of no-reflow or slow flow in STEMI patients undergoing PPCI. Admission glucose levels may serve as a simple and readily available predictor of no-reflow or slow flow in these patients.

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Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript:

JA, SKS, & IA: Intellectual contribution, Study design, Manuscript writing, Data Analysis.

ARJ, BUK, & AZK: Proof reading, Intellectual contribution, Data Analysis, Editing.

HY, FUR: Data Analysis, Editing, Data Acquisition, Formatting, Approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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