Original Article

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Effects of hyperglycemia on coronary perfusion & left ventricular function in patients treated with primary percutaneous coronary intervention for acute ST elevation myocardial infarction

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ABSTRACT

Objective: To observe the effect of hyperglycemia on coronary perfusion and left ventricular function in patients treated with primary percutaneous coronary intervention for acute ST elevation myocardial infarction (STEMI).

Methodology: This descriptive case series study was conducted at Cardiology Department of Gulab Devi Chest Hospital, Lahore from October 2017 to November 2018. Consecutive patients presenting with acute ST elevation myocardial infarction were included in this study. After coronary angiography and revascularization, coronary perfusion was assessed using TIMI flow grade method. Glycosylated hemoglobin levels were also measured on the same day. Hyperglycemia was defined as HbA1c >7%. A comprehensive transthoracic echocardiogram was performed to assess the left ventricular ejection fraction (LVEF) 24 hours after procedure.

Results: Hyperglycemia was observed in 91 (39.2%) patients presented with acute STEMI. Patients with hyperglycemia had significantly lower LVEF than normoglycemic patients (55.00 ± 19.00 vs 45.00 ± 15.00, *p*-value=0.001). Multivariate analysis showed that hyperglycemia is an independent predictor of LV dysfunction, defined as LVEF ≤40% 24 hours after the procedure (OR=2.522, *p*-value =0.002). While no statistically significant association was observed between hyperglycemia and post PPCI impaired coronary perfusion (p=0.492).

Conclusion: The association between hyperglycemia (HbA1c >7%) upon hospital admission and left ventricular dysfunction in acute MI patients treated with PPCI is explained by lower left ventricular ejection fraction (≤ 40%) 24 hours after the procedure. But there is no statistically significant effect of hyperglycemia on post PCI coronary perfusion. Thus, we conclude that persistent hyperglycemia influences the post PPCI left ventricular functions in STEMI patients.

Key Words: *Hyperglycemia, LV function, Primary percutaneous coronary intervention, STEMI*.

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Introduction

Hyperglycemia can be found in patients with acute ST elevation myocardial infarction (STEMI) irrespective of the previous history of diabetes mellitus. It is a potent reason of diminished Thrombolysis in Myocardial Infarction (TIMI) flow grade in infarct related artery. Diminished myocardial blood flow despite revascularization can present during primary percutaneous coronary intervention (PPCI) in patients with STEMI and is predictive of poor outcomes. Slow or no-reflow has been reported during angiography of 14%-25% patients with

acute MI.[1,2] Several studies have shown that inflammatory markers such as C-reactive protein, peripheral white blood cell count, and plasma glucose level may surmise increased risk of vulnerability caused by atherosclerotic plaque. An increase in these serum markers after the onset of acute MI has been associated with a significantly diminished coronary blood flow.[3,4,5] Elevated blood sugar levels causing impaired TIMI flow are significantly associated with an increased risk of left ventricular dysfunction, congestive heart failure, cardiogenic shock & subsequent death.[6] Glycosylated hemoglobin (HbA1c) shows mean fasting & postprandial blood glucose levels over 3 months. HbA1c is a strong inflammatory marker.[7] Elevated HbA1c levels are associated with a higher incidence of micro & macrovascular complications in patients with acute MI.[8]

Although hyperglycemia may result in more complications and poor prognosis, no local data concerning admission HbA1c levels, TIMI flow & left ventricular function is available. Therefore, we conducted this study to investigate the relationship among HbA1c levels, coronary flow rate determined by TIMI flow grade and cardiac functions in patients with acute myocardial infarction undergoing primary PCI in our settings.

Methodology

The descriptive case series study was conducted at the Catheterization laboratory of Gulab Devi Chest Hospital, Lahore from October 2017 to November 2018. 232 consecutive patients of either gender, with acute STEMI, who were treated with primary PCI in were enrolled. Purposive sampling technique was used to collect the data through a pre designed questionnaire.

Patients with documented end stage renal failure, hepatic failure, non STEMI, patients with metastatic disease having life expectancy of less than 1 year and those with missing HbA1c levels or echocardiography were excluded from the study. Laboratory, echocardiographic and angiographic findings were also verified from the patients' file.

After taking approval from the institutional ethical review committee Al Aleem Medical College, informed verbal consent from all the patients, baseline data on age, presence of the following risk factors was collected:

Diabetes Mellitus was considered as already diagnosed diabetic cases or newly diagnosed cases with fasting blood sugar level >120 mg/dL at 3 separate occasions.

A high systolic (140 and over) or diastolic (90 and over) on 3 separate occasions was considered as hypertension.

Smoking was defined as smoking at least 100 cigarettes during one's life time.

Family History was considered positive if one's father or brother had a presentation of ischemic heart disease (IHD) before 55 years of age or if mother or sister had a known history of IHD before 65 years of age.

The diagnosis of acute myocardial infarction was based on typical chest pain lasting for more than 30 minutes and a ≥2 mm ST elevation in 2 or more adjacent leads.

Both descriptive and inferential statistical analyses were performed using SPSS version 20. The qualitative data were presented in the form of frequency tables along with its percentage. The quantitative data were presented in the form of mean, standard deviation, median and interquartile range by simple descriptive analysis. The normality of the continuous data was assessed and Mann Whitney U test was applied to compare the data. Chi square analysis or Fisher's exact test was used to comparing categorical variables. A p-value <0.05 was considered statistically significant. Multivariate analysis was done to examine determinants of LV dysfunction and poor coronary perfusion. Dependent variables were LV dysfunction, defined as LVEF <40%, and poor coronary perfusion, defined as TIMI 0/1 or 2 flow grade. Age >60 years, male gender, time to recanalization >2 hours, hypertension, diabetes mellitus, smoking, presence of multivessel disease, and hyperglycemia, defined as HbA1c > 7%, were the independent variables. Odds ratio (OR) and 95% confidence intervals (CI) were calculated.

Results

Of the study group, 91 (39.2%) patients had admission hyperglycemia (defined as HbA1c levels ≥ 7%) whereas. 141 (60.8%) patients did not.

232 consecutive patients with median age 50 years (IQR 35 to 65 years) were studied. There were 174 (75%) males and 58 (25%) females. Diabetes mellitus was the most common risk factor 57.32%) in patients followed by smoking (51.72%) and hypertension (43.53%). Inferior wall MI was the commonest type of MI accounting for 31.89% patients followed by anterior wall MI (28.87%).

The baseline demographic, risk factors and types of MI in both normoglycemic and hyperglycemic patients are summarized in Table 1.

Table 1: Baseline demographic, risk factors and types of MI		
Characteristics	**Normoglycemia n = 141 (60.8%)**	**Hyperglycemia n = 91 (39.2%)**
Age (Years)	51.53 ± 11.83	54.56 ± 10.16
Gender n (%)		
Male	114 (80.85)	60 (65.93)
Female	27 (19.14)	31 (34.06)
Risk Factors n (%)		
DM	75 (53.19)	58 (63.73)
HTN	17 (12.05)	84 (92.30)
Smoking	82 (58.15)	38 (41.75)
Positive FH	41 (29.07)	31 (34.06)
Prior MI	5 (3.54)	3 (3.29)
Prior PCI	2 (1.41)	1 (1.09)
Type of MI n (%)		
Anterior wall MI	45 (31.91)	22 (24.17)
Anteroseptal MI	7 (4.96)	7 (7.69)
Anterolateral MI	28 (19.85)	14 (15.38)
Inferior Wall MI	43 (30.49)	31 (34.06)
Inferolateral MI	2 (1.41)	3 (3.29)
Inferoposterior MI	3 (2.12)	4 (4.39)
Inferior wall+Right ventricular MI	10 (7.09)	8 (8.79)
High Lateral Wall MI	3 (2.12)	2 (2.19)

Results are expressed as mean ± standard deviation or frequency and percentage of patients. Males were more in both hyperglycemia and normoglycemia groups (p=0.010). Presence of arterial hypertension, hospital admission HbA1c, mean ST elevation pre PCI, mean left ventricular ejection fraction (LVEF) 24 hours after procedure and left ventricular dysfunction was significantly higher in hyperglycemic group. The other findings were similar in both groups.

LV dysfunction, defined as LVEF <40% on echocardiography, was significantly associated with admission hyperglycemia (p=0.002). Multivariable analysis of LV dysfunction was performed and it showed that in addition to hyperglycemia, hypertension was also significantly associated with left ventricular dysfunction (p=0.024).

In this study, hyperglycemia has no significant association with post PPCI coronary perfusion (p=0.492). Multivariate analysis showed that not a single factor studied during this study is statistically associated with poor coronary perfusion after PPCI.

Discussion

This is the first local study to assess the association of glycemic state upon hospital admission, based on HbA1c levels, with left ventricular function and coronary perfusion in patients with STEMI. In the current study, it was found that hyperglycemia upon hospital admission in patients with acute ST elevation MI who were treated with primary PCI was significantly associated with acute LV dysfunction. No statistically significant association was found between hyperglycemia and TIMI flow grade in these patients.

The Pathophysiology behind hyperglycemia in acute myocardial infarction is not identified. Previous studies have demonstrated that abnormal blood glucose level is very common in patients with acute myocardial infarction and around two-thirds of patients with unidentified DM could be classified as having newly diagnosed DM.[9, 10] This may be due to a greater rise in sheer-stress response and stress hormones as a result of more severe myocardial

Table II: Baseline clinical, angiographic & procedural characteristics according to glycemic state upon hospital admission			
Characteristics	**Normoglycemia n = 141 (60.8%)**	**Hyperglycemia n = 91 (39.2%)**	**p-Value**
Age, years	50.00 ± 15.00	55.00 ± 10.00	0.053[a]
Male	114 (80.85)	60 (65.93)	0.010[c]
Known DM	75 (53.19)	58 (63.73)	0.113[c]
Hypertension	17 (12.05)	84 (92.30)	0.000[c]
Symptom to Hospital Time, hours	3.00 ± 4.50	3.00 ± 3.50	0.867[a]
Symptom to Balloon Time, hours	5.50 ± 5.00	5.50 ± 5.50	0.787[a]
Hospital admission HbA1c, %	5.50 ± 0.90	8.80 ± 1.40	0.000[a]
Mean ST elevation pre PCI, mm	3.00 ± 3.00	4.00 ± 2.00	0.025[a]
Culprit Lesion			
LAD	83 (58.86)	45 (49.45)	0.159[c]
LCX	11 (7.80)	10 (10.98)	0.409[c]
RCA	45 (31.91)	35 (38.46)	0.306[c]
RI	2 (1.41)	1 (1.09)	1.000[b]
Multiple vessel disease	99 (70.21)	74 (81.31)	0.058[c]
TIMI flow grade pre-PCI			
0/1	122 (86.52)	83 (91.20)	
2	10 (7.09)	4 (4.39)	0.732[c]
3	9 (6.38)	4 (4.39)	
Thrombectomy	57 (40.42)	37 (40.65)	0.972[c]
Stent implantation	141 (100.00)	90 (98.90)	0.392[b]
TIMI flow grade 3 after procedure	132 (93.61)	83 (91.20)	0.492[c]
Mean ST elevation post PCI, mm	1.00 ± 1.00	1.00 ± 1.50	0.080[a]
Mean LVEF 24 hours after procedure, %	55.00 ± 19.00	45.00 ± 15.00	0.001[a]
LV dysfunction (LVEF ≤ 40%)	28 (19.85)	35 (38.46)	0.002[c]

Table III: Multivariate analysis of factors associated with left ventricular dysfunction

Variable	Odds Ratio (95% CI)	p Value
Age ≥ 60 years	1.065 (0.575-1.971)	0.842
Male	0.624 (0.328-1.185)	0.147
Time to recanalization > 2 hours	0.500 (0.202-1.235)	0.127
Multivessel disease	1.438 (0.716-2.891)	0.306
Slow/No reflow	0.814 (0.255-2.595)	0.727
Diabetes Mellitus	1.421 (0.783-2.579)	0.246
Hyperglycemia	2.522 (1.396-4.556)	0.002

Table IV: Multivariate analysis of factors associated with poor coronary perfusion after PPCI

Variable	Odds Ratio (95%CI)	p Value
Age ≥ 60 years	1.154 (0.410-3.249)	0.786
Male	2.642 (0.586-11.916)	0.190
Time to recanalization > 2 hours	0.769 (0.164-3.608)	0.739
Smoking	2.378 (0.810-6.981)	0.106
Multivessel disease	2.706 (0.600-12.201)	0.179
Diabetes Mellitus	0.494 (0.181-1.348)	0.162
Hyperglycemia	1.414 (0.525-3.809)	0.492

infarction, which can aggravate glycogenolysis and hyperglycemia. Increased blood sugar levels are associated with diminished coronary microcirculation.[11] Several mechanisms may explain the association between hyperglycemia and microvascular dysfunction. Persistent hyperglycemia may cause microvascular dysfunction through leukocyte capillary plugging, enhanced platelet activation, and accumulation of advanced glycation products, resulting in poor coronary perfusion.[12, 13] Kosuge et al. reported that although hyperglycemia is associated with impaired myocardial perfusion after recanalization, the effects of hyperglycemia on the microvascular circulation may depend on its severity and duration.[14] In the present study, there is lack of significant association between hyperglycemia and poor coronary perfusion (p=0.492). Multivariate analysis also showed no significant association between coronary perfusion and other variables. The underlying mechanism may include diminished microcirculation due to distal embolization of atheromatous plaque material, myocardial stunning in the infarct area and myocardial edema causing partial blockage of the coronary vasculature and poor coronary perfusion.

Acute hyperglycemia is independently associated with impaired LVEF, and with a larger infarct size due to an increased incidence of the no-reflow phenomenon. Many studies have demonstrated earlier the association between abnormal glucose levels and cardiac dysfunction in acute ischemic settings.[13, 15-17], but there is a lack of local data on the association between glycated hemoglobin, which shows long term glycemic status, and cardiac functions in acute myocardial infarction. Isihara et al. reported that acute hyperglycemia in acute anterior wall myocardial infarction is independently associated with an impaired left ventricular function (p=0.02) and poor prognosis.[18] Iwakura et al. reported that in patients with successful angioplasty, hyperglycemia is related to poor coronary perfusion on contrast echocardiography, resulting in myocardial dysfunction.[19] This study results correlate with the previous studies that hyperglycemia, defined as HbA1C >7%, is significantly associated with LV dysfunction in patients presented with acute STEMI (p=0.002).

Conclusion

The association between hyperglycemia (HbA1c >7%) upon hospital admission and left ventricular dysfunction in acute MI patients treated with PPCI is explained by lower left ventricular ejection fraction (≤ 40%) 24 hours after the procedure. But there is no statistically significant effect of hyperglycemia on post PCI coronary perfusion. Thus we conclude that persistent hyperglycemia influences the post PPCI left ventricular functions in STEMI patients.

Study limitations: Descriptive case series study was performed which cannot comment on the pre-PPCI cardiac functions. Another limitation is that plasma concentration of norepinephrine, cortisol, or angiotensin II, which might be helpful to show the association between glycemic status and cardiac functions. Magnetic resonance imaging should be performed to assess the infarct size pre and post-intervention to see the effect of hyperglycemia. Inflammatory markers such as neutrophil count and C-reactive protein levels were also not observed which could be causative of impaired coronary perfusion. Cardiac Further prospective studies should be conducted with more patients to confirm the association of hyperglycemia with coronary perfusion and cardiac dysfunction after primary interventions.

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