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The Relationship between Elevated Pre-procedural Random Blood Glucose Level and Periprocedural Myocardial Injury in Patients Undergoing Elective Percutaneous Coronary Intervention

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ABSTRACT
Background: In patients with coronary artery disease (CAD), regardless of their diabetes status, both hypoglycemia and hyperglycemia are unfavourably associated to cardiovascular events. According to the results of numerous research, both diabetic and non-diabetic patients with ST-elevation myocardial infarction (STEMI) frequently experience hyperglycemia, which is linked to a higher risk of in-hospital morbidity and mortality.
Objective: In patients undergoing elective percutaneous coronary intervention (PCI), the goal of this study is to evaluate the association between elevated pre-procedural random blood glucose levels and peri-procedural myocardial injury.
Patients and Methods: 110 patients with chronic coronary syndrome who underwent elective PCI at Ain Shams University Hospitals' Cardiology Department. made up this cohort study. They were split into two equal groups, 55 were hyperglycemic and the rest 55 were euglycemic. Prior to the procedure, cardiac troponin (I) and blood glucose levels were assessed. Blood samples for cardiac troponin were then collected 12 hours later
Results: Regarding the incidence of myocardial injury and infarction, there were statistically significant difference between the 2 groups, with the incidence of both conditions being greater in the hyperglycemic group (P-value = 0.001, 0.022 respectively). All five individuals with myocardial infarction had higher blood sugar levels. 23 patients belonging to the hyperglycemic group had myocardial injury. On the contrary only 7 patients with myocardial injury belonged to the euglycemic group. The cut-off point of blood glucose level at which myocardial infarction occurred was 166 mg/dl with 100% sensitivity and 72.4% specificity, and that at which myocardial injury occurred was 130 mg/dl with 76.7% sensitivity and 62.5% specificity.
Conclusion: We draw the conclusion that patients undergoing elective PCI are more likely to experience peri-procedural myocardial damage and infarction when their pre-procedural plasma glucose levels are excessively high, regardless of their diabetes status.
Keywords: Elective PCI, Myocardial infarction, Hyperglycemia.

INTRODUCTION

Regardless of a person's diabetes status, both hypoglycemia and hyperglycemia are unfavourably connected to cardiovascular events [(1)]. In STEMI patients receiving primary PCI, diabetes mellitus is independently associated with reduced myocardial reperfusion, a larger infarct size, the development of congestive heart failure, and a lower life expectancy [(2)].

Studies on human post-mortem tissues have shown that, at the level of the vascular wall, lesions from diabetic individuals have a larger macrophage content than lesions from people without diabetes. This difference correlates with glycated hemoglobin levels rather than lipid levels[(3)].

In individuals with acute myocardial infarction (MI), there is a strong association between hyperglycemia and major adverse cardiac events (MACE) within 30 days following PPCI [(4)]. Numerous studies have demonstrated that hyperglycemia is common in people with ST-elevation myocardial infarction (STEMI) who are diabetic or non-diabetic and is associated with an increased risk of death and hospital complications [(4,5)]. Data from human and animal studies support that high glucose has a direct pro-atherogenic effect on vascular cells since there is suggestive evidence that it is atherogenic, particularly at the level of the arterial endothelium.

Due to the lack of studies examining the relationship between blood glucose levels at the time of elective PCI and peri-procedural complications and the confusion around whether cardiac events are more likely to be associated to hyperglycemia than euglycemia. The goal of this study is to evaluate the association between elevated pre-procedural random blood glucose levels and peri-procedural myocardial damage.

PATIENTS AND METHODS

110 patients who underwent elective PCI and presented with chronic coronary syndrome to the Cardiology Department of Ain Shams University Hospitals made up this cohort study. They were split into two equal groups: 55 patients were the hyperglycemic group, and the rest were the euglycemic group.

Exclusion criteria: Patients with chronic kidney disease with estimated GFR below 60 mL/min., patients with any form of active infection, patients with recent cerebrovascular accident, patients with pre-existing left ventricular dysfunction, patients with anemia, patients with any type of different cardiomyopathies, patients with infiltrative cardiac diseases, patients with storage diseases, patients receiving chemotherapeutic drugs and

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patients with hypoglycemia with blood glucose level ≤ 70 mg/dl[6].

Methods:

History was taken from each participant in the study, including age and sex of the patient, cardiovascular risk factors, presence or absence of chronic kidney disease and prior history of myocardial revascularization either coronary artery bypass graft (CABG) or PCI.

A 12 leads ECG was done to all patients before and after the PCI procedure. Blood glucose level was measured prior to the procedure according which patients were classified into two groups: the first group included euglycemic patients with blood glucose level ranged from 81 to 125 mg/dL and the other group included hyperglycemic patients with blood glucose level ≥126 mg/dL [6].

Blood samples were obtained for cardiac troponin (I) before the procedure and repeated 12 hours after. Using troponin (I) level, whose normal reference ranged from (0.02-0.06 ng/L), patients were considered to have myocardial injury if blood levels of cardiac troponin (cTn) are increased above the 99th percentile upper reference limit (URL), and coronary procedure related myocardial infarction if an elevation of cTn values > 5 times 99th percentile URL in patients with normal baseline values [7]. Serum creatinine levels were obtained before the procedure from all patients. Patients with eGFR < 60 mL/min were excluded from the current study.

PCI was done to all patients and data obtained from angiographic films included: Intervention done to which coronary artery, whether PTCA was done or direct stenting strategy was adopted, number of stents deployed and any peri-procedural complications occurred including: coronary dissection, perforation, no reflow phenomenon and side branch occlusion.

Ethical consent:

This study was approved from Ain Shams University Academic and Ethical Committee, and every patient gave his consent to participate in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Frequencies and relative percentages were used to represent qualitative data. To determine the difference between two or more groups of qualitative variables, the chi square test was utilised. Continuous variables were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Demographic data and baseline characteristics of study population.

The mean age of the hyperglycemic group was significantly higher than euglycemic. Euglycemic group had significantly more males than females when compared to first group, there was no significant difference between 2 groups regarding smoking and hypertension, the mean blood glucose level in hyperglycemic group was significantly higher than in euglycemic group (Table 1)

Table (1): Demographic data and cardiovascular risk factors

		Hyperglycemic group No. = 55	Euglycemic group No. = 55	P-value	Sig.
Age (years)	Mean ± SD Range	60.87 ± 7.47 39 – 75	57.73 ± 7.12 42 – 72	0.026	S
Sex	Female Male	17 (30.9%) 38 (69.1%)	6 (10.9%) 49 (89.1%)	0.010	S
Smoking	No Yes	31 (56.4%) 24 (43.6%)	22 (40.0%) 33 (60.0%)	0.086	NS
Diabetic history	No Yes	12 (21.8%) 43 (78.2%)	32 (58.2%) 23 (41.8%)	<0.001	HS
Hypertensive history	No Yes	15 (27.3%) 40 (72.7%)	26 (47.3%) 29 (52.7 %)	0.030	S
Glucose level before PCI	Mean ± SD	200±46.17	111.13±10.61	<0.001	HS

Sig.: Significance, S: Significant, NS: Non-significant, HS: Highly significant

Angiographic and PCI data:

No significant difference was noted between the 2 groups regarding number of vessels affected, left main artery affection, and procedural complications, however, hyperglycemic group had significantly a greater number of patients who had 2 or 3 deployed stents (Table 2).

Table (2): Angiographic data between the two groups

		Hyperglycemic group		Euglycemic group		P-value	Sig.
		No.	%	No.	%		
Number of Stents	1DES	22	40.0%	36	65.5%	0.045	S
	2DES	21	38.2%	14	25.5%		
	3DES	11	20.0%	4	7.3%		
	4DES	1	1.8%	1	1.8%		
Number of Vessels affected	Single Vessel	34	61.8%	39	70.9%	0.313	NS
	Multi Vessel	21	38.2%	16	29.1%		
Left Main Artery	No	52	94.5%	54	98.2%	0.308	NS
	Yes	3	5.5%	1	1.8%		
Procedural Complications	Non complicated during intervention	53	96.3%	54	98.2%	0.39	NS
	No reflow	1	1.8%	0	0.0%		
	Dissection	0	0.0%	1	1.8%		
	Side branch occlusion	1	1.8%	0	0.0%		

Sig.: Significance, S: Significant, NS: Non-significant

The two groups differed statistically significantly from one another, with the incidence of both myocardial infarction and myocardial injury being greater in the hyperglycemic group (Table 3).

Table (3): Comparison of the incidence of myocardial infarction and injury between two groups

		Hyperglycemic group		Euglycemic group		P-value	Sig.
		No.	%	No.	%		
Myocardial Infarction	No	50	90.9%	55	100.0%	0.022	S
	Yes	5	9.1%	0	0.0%		
Myocardial Injury	No	32	58.2%	48	87.3%	<0.001	HS
	Yes	23	41.8%	7	12.7%		

Sig.: Significance, S: Significant, HS: Highly significant

There was highly significant relationship between hyperglycemia before PCI and incidence of myocardial infarction and myocardial injury (Table 4).

Table (4): The relationship between glucose level before PCI and incidence of myocardial infarction and injury

Glucose level Before PCI	No Myocardial Infarction	Myocardial Infarction	P-value	Sig.
Mean ± SD	147.70 ± 34.30	327.40 ± 74.36	<0.001	HS
Glucose level Before PCI	**No Myocardial Injury**	**Myocardial Injury**		
Mean ± SD	139.84 ± 31.79	198.60 ± 4.21	<0.001	HS

Sig.: Significance, HS: Highly significant

We calculated glucose level before PCI as a predictor of periprocedural myocardial infarction and myocardial injury using ROC curve and found that the cut-off point of blood glucose level at which myocardial infarction occurred was 166 mg/dl and that at which myocardial injury occurred was 130 mg/dl (Table 5 and Figure 1 and 2).

Table (5): ROC curve of Glucose level before PCI as a predictor of Myocardial Injury and infarction

Glucose level Before PCI	AUC	Cut-off Point	Sensitivity	Specificity	PPV	NPV
Myocardial Infarction	0.928	>166	100.0	72.38	14.7	100.0
Myocardial Injury	0.726	>130	76.67	62.50	43.4	87.7

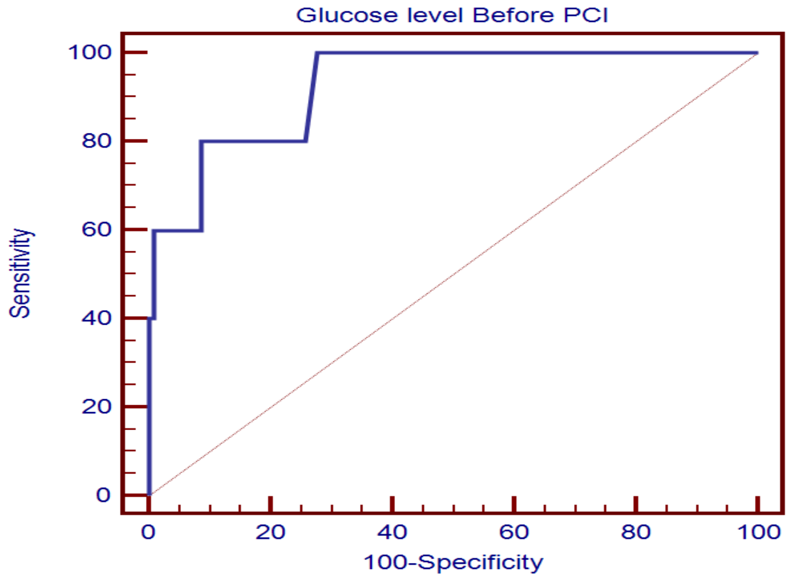

Fig. (1): ROC curve of preprocedural blood glucose level and incidence of myocardial infarction

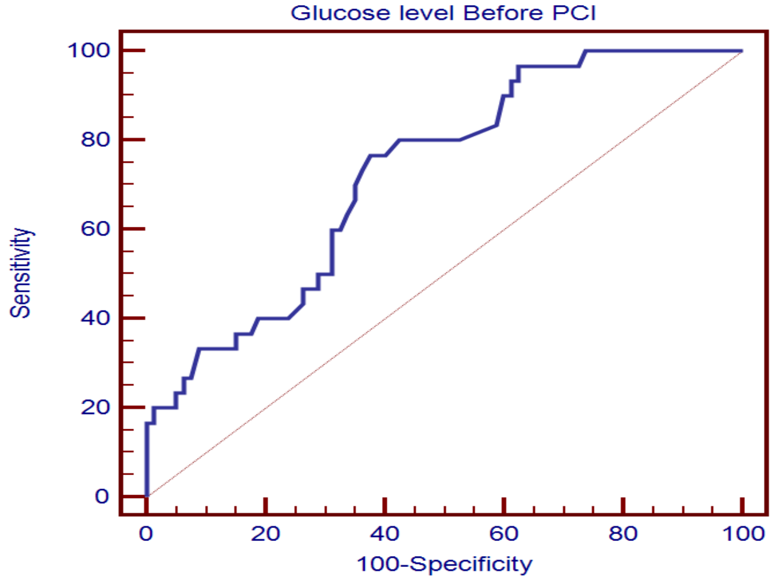

Fig. (2): ROC curve of preprocedural blood glucose level and incidence of myocardial injury

The relationship between demographic data and cardiovascular risk factors and incidence of both myocardial infarction and injury:

No significant relationship was found between age, sex, smoking history, and hypertension and incidence of myocardial infarction or myocardial injury, however diabetic patients had significantly higher incidence of periprocedural myocardial injury, with no significant increase in the incidence of myocardial infarction (tables 6 and 7).

Table (6): Relationship between demographic data and cardiovascular risk factors and incidence of myocardial infarction

		No Myocardial Infarction	Myocardial Infarction	P-value	Sig.
		No. = 105	No. = 5		
Age (years)	Mean ± SD Range	59.22 ± 7.53 39 – 75	61.00 ± 5.48 55 – 69	0.603	NS
Sex	Female Male	22 (21.0%) 83 (79.0%)	1 (20.0%) 4 (80.0%)	0.959	NS
Smoking	No Yes	52 (49.5%) 53 (50.5%)	1(20 %) 4(80 %)	0.197	NS
Diabetic history	No Yes	44(41.9%) 61 (58.1%)	0(0.0%) 5(100%)	0.062	NS
Hypertensive	No Yes	39 (37.1%) 66(62.9%)	2(40%) 3(60%)	0.897	NS

Sig.: Significance, NS: Non-significant

Table (7): Relationship between both age and sex and incidence of myocardial injury

		No Myocardial Injury	Myocardial Injury	P-value	Sig.
		No. = 80	No. = 30		
Age (years)	Mean ± SD Range	59.29 ± 7.43 39 – 75	59.33 ± 7.56 44 – 71	0.977	NS
Sex	Female Male	15 (18.8%) 65 (81.3%)	8 (26.7%) 22 (73.3%)	0.363	NS
Smoking	No Yes	39 (48.8%) 41(51.3%)	14 (46.7% 16 (53.3%)	0.846	NS
Diabetic	No Yes	37 (46.3%) 43(53.8%)	7 (23.3%) 23(76.7%	0.029	S
Hypertensive	No Yes	33 (41.3%) 47 (58.8%)	8(26.7%) 22(73.3%)	0.159	NS

Sig.: Significance, NS: Non-significant, S: Significant

There was no significant relationship between incidence of myocardial infarction and each of number of deployed stents and number of revascularized vessels (Table 8).

Table (8): Relation between angiographic findings and incidence of myocardial infarction

		No Myocardial Infarction		Myocardial Infarction		P-value	Sig.
		No.	%	No.	%		
Number of Stents	1DES 2DES 3DES 4DES	57 33 13 2	54.3% 31.4% 12.4% 1.9%	1 2 2 0	20.0% 40.0% 40.0% 0.0%	0.268	NS
Vessels affected	Single Vessel Multi Vessel	71 34	67.6% 32.4%	2 3	40.0% 60.0%	0.202	NS

Sig.: Significance, NS: Non-significant

DISCUSSION

We concluded in the current study that there was statistically significant relationship between preprocedural hyperglycemia and the incidence of both myocardial infarction and myocardial injury, both being higher among the hyperglycemic group, when compared to the euglycemic group in patients undergoing elective PCI.

All five individuals with myocardial infarction had higher blood sugar levels, 23 patients belonging to the hyperglycemic group had myocardial injury, on the contrary only 7 patients with myocardial injury belonged to the euglycemic group.

Regardless of whether a patient has diabetes, hyperglycemia is linked to unfavourable cardiovascular events in those with ischemic heart disease[1]. In addition to causing myocardial damage, hyperglycemia has also been shown by **Umpierrez and colleagues**[8] to have a poor prognostic impact on in-hospital mortality. They showed that patients with diagnosed hyperglycemia had considerably worse outcomes and a greater in-hospital mortality rate than those with euglycemia. Poor cardiac outcomes are a result of hyperglycemia in various mechanisms. Stress hyperglycemia, which is linked to greater inflammatory factor circulation in humans, is most likely a contributing component to the myocardial injury[9] and also by adrenaline and cortisol imbalance[4].

Several studies have discovered that both diabetic and non-diabetic STEMI patients oftenly experience hyperglycemia, which is associated with an increased risk of death and other in-hospital complications[5]. However, there are few studies dealing with the relationship between blood glucose levels at the time of elective PCI and peri-procedural complications. We conducted the current study to assess the association between pre-procedural blood glucose levels and both myocardial injury and infarction in patients who have undergone elective PCI because it is uncertain whether cardiac events are more likely to be linked with hyperglycemia than with euglycemia.

Our results were concordant with the results of the study conducted by **Mohsen and his colleagues** [10]. They examined the link between blood glucose measurements prior to PCI and myocardial damage in 1,012 consecutive patients who underwent elective PCI. The patients were classified into 4 glycemic groups (euglycemic, hypoglycemic, mildly hyperglycemic and hyperglycemic). Before the procedure, samples for troponin I and CK-MB fraction were obtained, and they were then repeated at intervals of 8, 16, and 24 hours. They discovered that the hyperglycemic group had significantly higher postprocedural troponin I levels (P=0.027). Additionally, they discovered that pre-procedural hypoglycemia and a recent smoking are linked to an increased incidence of peri-procedural myocardial damage in individuals undergoing elective PCI for coronary angioplasty[10].

In a prospectively assembled cohort of 1612 patients divided into four groups in 2003, **Muhlestein and his colleagues**[11] investigated the impact of fasting glucose levels on mortality rates in patients with and without diabetes mellitus (DM) and CAD undergoing PCI. First group included patients with clinical diagnosis of DM (CDM), second group included those with no clinical diagnosis of DM but with elevated fasting glucose levels ≥ 126, third group included those with impaired fasting glucose (IFG) 110-125 mg/dL, and last group with normal blood glucose levels (NFG) <110 mg/dL. Survival was assessed for 2.8 ± 1.2 years.

Higher death rates were seen in the CDM (44/394 [11.2%], P 0.0001), ADA-DM (27/283 [9.5%], P 0.001), and IFG (20/305 [6.6%], P = 0.04) groups than in the NFG group (12/630 [1.9%]). They found that FG 109 mg/dL, (sensitivity: 81%; specificity: 51%) was the optimum cut-off for increased risk, indicating that individuals with CAD who are undergoing PCI have a prognostically significant abnormalities of FG (61%) than expected [11]. In our study, with the random blood sugar (RBS) cut-off values for myocardial injury and infarction were 130 mg/dl and 166 mg/dl, respectively. This difference in cut-off values may be due to the different clinical groups in the two studies and the different study designs.

Shen and his colleagues[12] discovered in 2006 that decreased microvascular flow measured by using thrombolysis in myocardial infarction (TIMI) myocardial perfusion grade and corrected TIMI frame count is independently correlated with elevated glucose levels in ST-segment elevation myocardial infarction patients treated with primary PCI. Patients were divided into 3 groups based on their admission glucose levels: group 1< 7.8 mmol/L; group 2, <7.8 - 11.0) mmol/L; and group 3, > 11.0 mmol/L. Groups 2 and 3 outperformed group 1 in terms of corrected TIMI frame counts (CTFC). 30.9% of patients with hyperglycemia had TIMI myocardial perfusion grade 0–1. Of note the previous study included patients with STEMI, while the current study included patients undergoing elective PCI [12], we studied the effect of hyperglycemia on myocardium, by using troponin level and found that there is detrimental effect of elevated blood glucose levels on myocardium**.**

Nusca and his colleagues[1] had four groups according to pre procedural blood glucose levels; hypoglycemia ≤ 80 mg/dl; euglycemia 81-109 mg/dl; mild hyperglycemia 110-125 mg/dl; hyperglycemia ≥ 126 mg/dl. The incidence of peri-procedural MI was the main end point, while the occurrence of major adverse cardiac events during follow-up served as the secondary end point.

They found that 51% of those with hypoglycemia experienced peri-procedural MI, compared to 30% of those with euglycemia, 29% of those with mild hyperglycemia, and 37% of those with hyperglycemia. The incidence of MACE was 38% in the hypoglycemic group, 12% in the euglycemic group, 14% in the mild hyperglycemic group, and 22% in the hyperglycemic group after a mean follow-up of 15± 8 months [1].

Li and his colleague[13] carried out another trial in 2014 in individuals with type 2 DM to examine the association between myocardial injury and hemoglobin A1c (HbA1c) following elective PCI. A cohort of 994 diabetic individuals with CAD who were undergoing elective PCI was investigated. Analysis of troponin I (cTnI) was used to assess periprocedural myocardial damage. It was assessed whether there was a correlation between pre-procedural HbA1c levels and the peak cTnI values within 24 hours following PCI. They discovered that in diabetic patients undergoing elective PCI, there was a decreased risk of myocardial injury with higher preprocedural HbA1c levels. This is discordant with our study and all the previous mentioned studies, and this may be attributed to using different methodology using HbA1c instead of measuring pre-procedural blood glucose level, reflecting stress hyperglycemia, which may be linked to greater inflammatory circulation, and also by adrenaline and cortisol imbalance.

Limitations: This was a one center study involving a relatively small sample size. Only in-hospital follow-up was done with no long-term follow-up.

CONCLUSION

We draw the conclusion that patients undergoing elective PCI are more likely to experience peri-procedural myocardial injury and infarction when their pre-procedural plasma glucose levels are excessively high, the cut-off point of blood glucose level at which myocardial infarction occurred was 166 mg/dl, and that myocardial injury occurred was 130 mg/dl.

RECOMMENDATIONS

Adequate pre-procedural blood glucose level control for patients undergoing elective percutaneous coronary intervention is recommended in order to decrease the incidence of both peri-procedural myocardial injury and myocardial infarction.

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Conflict of interest: Nil.

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