Journal of Cardiovascular Diseases & Diagnosis

Suresh V Patted et al., J Cardiovasc Dis Diagn 2019, 7:3

Research Article Open Access

Association between Admission Serum Blood Glucose Levels and 30-Day Mortality in Patients Presenting with ST Elevation Myocardial Infarction

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Received: May 04, 2019; **Accepted:** May 09, 2019; **Published:** May 16, 2019

Abstract

Objectives: The aim of the study was to evaluate the association between stress hyperglycaemia and in hospital and 30-day mortality in patients with acute ST elevation myocardial infarction (STEMI).

Materials and methods: This one-year hospital based cross sectional study was performed in the Department of Cardiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2017 to December 2018. A total of 465 patients with STEMI were evaluated for ad-mission blood glucose levels and outcome.

Results: Out of 465 patients, 255 (54.84%) patients had elevated admission blood sugar levels (≥ 140 mg/dL). A total of 47 patients (10.10%) died out of which 34 died during hospitalization. Those who presented with serum blood glucose levels of more than 140 mg/dL had an advanced Killip class and a poorer outcome. Mortality was significantly higher in patients with admission blood glucose levels of >200 mg/dL (15.28% *vs.* 8.11% with 140 to 200 mg/dL and 7.62% with <140 mg/dL; p=0.046) irrespective of the diabetic status and the mean blood sugar level in patients who expired was significantly higher (227.09 ± 131.53 *vs.* 178.83 ± 96.02 g/dL; p=0.018). Also, non survivors had a greater degree of left ventricular dysfunction (40.11 ± 5.56 *vs.* 43.70 ± 4.61%; p<0.001) and lower mean systolic blood pressure (96.36 ± 30.75 *vs.* 123.17 ± 27.56 mm Hg; p<0.001) in comparison to survivors.

Conclusion: Based on univariate analysis stress hyperglycaemia on admission is a predictor of mortality and could be used in stratification of risk in patients with Acute STEMI.

Keywords: Diabetes mellitus; STEMI; Stress hyperglycaemia

Introduction

In recent years, much attention has been given to the evidence that the concomitant occurrence of hyperglycaemia in patients admitted to the intensive care units with an acute myocardial infarction enhances the risk of mortality and morbidity whether the patient has diabetes or not [1]. Subjects with diabetes mellitus have a substantially increased risk of death after myocardial infarction, as compared with non-diabetic age matched controls. The high prevalence of undiscovered abnormal glucose metabolism among patients with AMI, may in part explain the association between glucose levels and mortality, especially in individuals who are not diagnosed as having diabetes at the time of the AMI. Although the diagnosis of diabetes may not be made on the basis of a single blood glucose value, casual blood glucose levels of >200 mg/dl (11.1 mmol/l) or more suggest the existence of diabetes, and as a consequence, the risk of mortality after AMI in this group may be disproportionately high and should be evaluated separately [2].

High blood glucose levels after Acute Myocardial Infarction may be the result of high levels of circulating stress hormones but may also be an indicator of incipient pancreatic beta cell failure that becomes unmasked under stressful conditions. Although hyperglycaemia may itself be detrimental for the ischemic myocardium, in many patients it may rather represent a marker of metabolic abnormalities clustered in the insulin resistance syndrome, which is associated with high risk of cardiovascular disease. Alternatively, it has been proposed that blood glucose constitutes a risk factor for cardiovascular disease over a wide array of values, even in the normoglycemic range [2]. However, even though a positive association between hyperglycaemia at the time of event and subsequent mortality from MI has been reported, its prognostic impact in non-diabetic and diabetic individuals has not been very well understood [2-4].

Considering the lack of data on Prognostic Impact of Hyperglycemia in Nondiabetic and Diabetic patients with ST-Elevation Myocardial Infarction, the present study was under-taken with special emphasis on in hospital and 30-day mortality.

Research Methodology

Study population

This hospital based prospective observational study was undertaken in the Department of Cardiology of a tertiary care teaching hospital situated in north Karnataka, India from January 2017 to December 2018. Considering the availability of cases, feasibility, a total of 465 patients aged more than 18 years, diagnosed to have Acute ST myocardial infarction (STEMI) based on electrocardiogram (ECG) were included. Patients with renal failure requiring renal replacement therapy, conditions that affect blood glucose per se, such as pregnancy, drug therapy – e.g. steroid and concomitant acute infections were excluded from the study. The ethical clearance was obtained from the Institutional Ethics committee prior to the commencement.

Patients who were eligible were briefed about the nature of the study and interventions to be done and a written informed consent was obtained. They were interviewed and demographic data like gender and age were noted. Also, history of diabetes mellitus, hyper-tension, smoking, and alcohol consumption were obtained. A thorough physical examination was conducted to assess the vital parameters.

Electrocardiographic and enzymatic analysis

The included patients were subjected for ECG in order to diagnose the type of myocardial infarction, followed by systemic examination. A standard 12-lead ECG with maximal ST-segment elevation was chosen for measurements. The ECG was recorded at a paper speed of 25 mm/sec at a calibration of 1 mV=10 mm. STEMI was diagnosed according to the ESC and ACC criteria [5,6] as constrictive chest pain lasting longer than 30 min and an increased CK (MB fraction >200 U/l) and/or increased cardiac TI more than 2 microgram\L and/ or new ST elevation at the J point in two contiguous leads >0.2 mv leads v2-v3 or >0.1 mv in other leads) [6].

Echocardiography

All included patients were assessed with echocardiography at the time of index hospitalization. The left ventricular end-diastolic diameter was measured from the long axis of the left ventricle, and the left ventricular ejection fraction was calculated using single -plane Simpson's method using two-dimensional echocardiography (ECHO).

Glucose Measurements

Under all aseptic precautions, blood samples were collected by venipuncture and collected in vacutainer. The sample was collected at the time of admission to investigate HbA1c and blood sugar levels. HbA1c was calculated by high performance liquid chromatography.

Study End Points

Endpoint event was in hospital cardiac death and 30-day mortality. Each patient/reliable relative was telephonically contacted after 30 days of admission to assess their clinical state/survival status.

Statistical Analysis

The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test or Fisher's exact test. The continuous data was expressed as mean ± standard deviation (SD) and comparison was done using independent sample t test. At 95% CI a prob-ability value (p value) of less than or equal to 0.05 was considered as statistically significant.

Results

The baseline characteristics of the study population are depicted in Table 1. The mean age of patients was 58.24 ± 11.53 years and 76.13% of the study population were males.

Parameters	Findings	Distribution (n=465) Number	Percentage
Admission blood sugar levels (mg/dL)	< 140	210	45.16
	140 to 200	144	30.97
	> 200	111	23.87
Mean blood sugar levels (Mean ± SD)	184.90 ± 90.75 mg/dL	--	--
Median blood sugar levels (Range)	154 mg/dL (65-663 mg/dL)	--	--
HbA1c levels (%)	< 6.5	111	23.87
	≥ 6.5	199	42.8
	Not done	155	33.33
Mean HbA1c (%)	7.93 ± 2.31	--	--
Median HbA1c (Range) (%)	7.35 (4.40 to 15.90)	--	--
History of diabetes mellitus	Positive history of DM	168	36.13
	Newly detected diabetic	55	11.83
	Non diabetic	242	52.04
Risk factors	Hypertension	206	44.3
	Smoking/Tobacco consumption	48	10.32
	Alcohol consumption	9	1.94
Gender	Male	354	76.13
	Female	111	23.87
Age group (years)	21 to 30	8	1.72
	31 to 40	26	5.59
	41 to 50	75	16.13
	51 to 60	162	34.84
	61 to 70	141	30.32
	71 to 80	41	8.82
	81 to 90	11	2.37
	> 90	1	0.22
Mean age (Mean ±SD) (years)	58.24 ± 11.53	--	--

Median age (Range) (years)	59 (24 to 92)	--	--
Time from onset of symptom to admission (hours)	> 6	218	46.88
	≤ 6	247	53.12
Type of MI	AWMI	252	54.19
	HLMI	2	0.43
	IWMI	207	44.52
	PWMI	4	0.86
Coronary angiography findings	Not Done	61	13.12
	Single vessel disease	214	46.02
	Double vessel disease	125	26.88
	Triple vessel disease	53	11.4
	Recanalized	12	2.58
Mode of treatment	Conservative	46	9.89
	Primary angioplasty in myocardial infarction	147	31.61
	Plan old balloon angioplasty	1	0.22
	Reteplase	10	2.15
	Streptokinase	255	54.84
	Streptokinase/Tenecteplase	1	0.22
	Tirofiban	1	0.22
	Thrombus aspiration	1	0.22
	Tenecteplase	2	0.43
	Urokinase	1	0.22
Killips Class	I	252	54.19
	II	145	31.18
	III	38	8.17
	IV	30	6.45
Left ventricular ejection fraction	30 to 39	42	9.03
	40 to 49	336	72.26
	50 to 60	87	18.71
Mean LVEF (Mean ±SD) (%)	43.33 ± 4.83	--	--
Median (Range) (%)	45 (30 to 55)	--	--
Outcome	Alive	418	89.89
	In hospital mortality	34	7.31
	Mortality within 30 days	13	2.8

Table 1: Baseline characteristics of the patients.

Anterior STEMI was present in 252 (54.19%) of the patients and a history of Diabetes Mellitus as a Cardiovascular risk factor was present in 168 (36.13%) patients. Among the 465 patients included in the study, 147 (31.61%) patients underwent primary PCI, whereas 269 patients (57.84%) received fibrinolytic therapy, while 47 patients were treated conservatively (8.34%) and one patient (21%) was treated with POBA and thrombus aspiration. History of hypertension was obtained in 206 (44.30%) patients and 10.32% of the individuals gave a history of smoking/tobacco consumption (Table 1).

Value of glycemia on admission was higher in patients with Diabetes Mellitus in comparison to non-diabetics. Glycemia of >140 mg/dL was present in 78.02% of the diabetic patients and only 17.40% of the non-diabetic patients. In hospital mortality was comparable in patients with or without DM (4.73% *vs.* 2.58%) (Table 2).

Serum RBS at admission	Outcome				Total	
	Survivor		Non survivor*			
	No	%	No	%	No	%
< 140	194	92.4	16	7.62	210	100
140 to 200	102	91.9	9	8.11	111	100
> 200	122	84.7	22	15.3	144	100
Total	418	90.5	47	9.55	465	100

Note: p=0.046; *Non survivors include in hospital as well as mortality within 30 days

Table 2: Association of Admission blood glucose levels with outcome.

In-Hospital Events

Irrespective of the diabetic status, mortality in patients with glycemia of >140 mg/dL on admission was significantly higher in comparison to patients with glycemia of <140 mg/dL (6.6% *vs.* 3.4%; p=0.046) (Table 2).

Parameters	Survivors		Non survivors*		p value
	Mean	SD	Mean	SD	
Age (Years)	57.58	11.51	64.06	10.15	<0.001
Pulse rate (/Minute)	85.29	18.07	83.45	33.06	0.708
SBP (mm Hg)	123.17	27.56	96.36	30.75	<0.001
DBP (mm Hg)	74.13	20.23	52.3	31.46	<0.001
LVEF (%)	43.7	4.61	40.11	5.56	<0.001
Serum RBS at admission (mg/dL)	178.83	96.02	227.09	131.53	0.018
HbA1c (%) **	7.85	2.27	8.74	2.54	0.073

Note: *Non survivors include in hospital as well as mortality within 30 days
**n=310 patients after excluding the patients who did not undergo investigation for HbA1c (n=17 non survivors; n=138 survivors; total n=155).

Table 3: Clinical characteristics and outcome.

The mean RBS on admission in non survivors (227.09 ± 131.53 mg/dL) was higher in comparison to survivors (178.83 ± 96.02 mg/dL) (p=0.018). The mean systolic blood pressure among non survivors (96.36 ± 30.75 mm Hg) was lower in comparison to survivors (123.17 ± 27.56 mm Hg) (p<0.001) and non survivors exhibited greater degree of Left ventricular dysfunction (p<0.001) which suggests the possibility of a larger infarct size in non-survivors (Table 3).

A total of 30 (6.4%) patients presented in Killip class IV out of which 23 patients had their admission serum blood glucose levels more than 140 mg/dL. A similar finding was observed in patients who presented in Killip class III, where 25 out of the 38 patients had their admission glucose levels >140 mg/dL, indicating that glycemia of >140 mg/dL may be associated with a poorer Killip class (Table 4).

Killip class	Outcome				Total	
	Survivors		Non survivors			
	No	%	No	%	No	%
I	242	96.03	10	3.97	252	100
II	132	91.03	13	8.97	145	100
III	26	68.42	12	31.58	38	100
IV	18	60	12	40	30	100
Total	418	89.89	47	10.11	465	100
Note: p<0.001; *Non survivors include in hospital as well as mortality within 30 days						

Table 4: Association of Killips class with outcome.

Of the 34 patients who had an in-hospital mortality, 18 patients presented in Killip class III and above and the mean blood sugar level in these patients was 270 ± 127.3 mg/dL. Also, the mean blood sugar level of patients that expired in hospital was more than that of patients that experienced out of hospital mortality (253.32 ± 143.27 *vs.* 158.46 ± 53.11). Mortality was found to be significantly higher when the admission glucose levels were more than 200 mg/dL (Table 5).

Killip class	n	Survivors (n=418)		n	Non-Survivors (n=47)	
		Mean	SD	Mean	SD	
I	242	175.46	89.03	10	178.6	161.07
II	132	171.99	90.77	13	237.77	125.51
III	26	235.92	161.52	12	223.33	94.41
IV	18	191.78	79.28	12	259.67	146.91
Note: n= Number of patients						

Table 5: Killips class mean RBS among survivors and non survivors.

Discussion

Stress hyperglycaemia refers to phenomenon of high blood glucose level, insulin resistance, or impaired glucose tolerance due to altered glucose metabolism in response to stress of serious illness or trauma. Several studies have shown that hyperglycaemia is common among patients with AMI with or without a history of diabetes [7]. The present study, based on a non-selected cohort of patients with STEMI, highlights the relevance of stress hyperglycemia on admission to accurately identify a group of patients at high risk for short term outcomes. This relationship was unaffected by the diabetic status.

The relationship between admission hyperglycemia and short-term mortality in sub-jects without known DM after AMI has been very well documented [8]. Increased glucose levels on admission (ranging from 110 to 144 mg/dL (6.1-8 mmol/L) confers an almost 4-fold risk of death in patients without known DM after an AMI [9]. An increase of 18 mg/dL (1 mmol/L) in glucose levels was associated with a 4% increase of mortality in non-diabetic patients in a retrospective study [2]. In the present study, our findings highlight an increase in mortality risk with hyperglycaemia after STEMI, as an additive to clinical parameters. Also, the preliminary observations from the present study demonstrate direct association between admission blood glucose levels and 30-day mortality in patients presenting with STEMI. Moreover, it is interesting to note that the probability of mortality was not modified when DM was added to the model, indicating the predictive influence of DM was marginal [8].

It is difficult to explain why DM did not play a significant role in the outcomes of these patients. The definition of stress hyperglycaemia is intrinsically difficult in patients with DM as these patients are more likely to receive insulin or oral anti-diabetic drugs for hyper-glycaemia before experiencing an AMI, which might not reflect the true state of hyperglycemia [8].

In our study the overall mean random blood sugar levels were 184.90 ± 90.75 mg/dL and median levels were noted as 154.00 mg/dL. However, the admission blood sugars were more than ≥ 200 mg/dL in 23.87% of the study population. Furthermore, out of 47 patients that expired, 22 patients had admission blood sugar levels of ≥ 200 mg/dL compared to nine patients who had admission blood sugar levels between 140 to 199 mg/dL and 16 patients who had admission blood sugar levels <140 mg/dL respectively. This difference was statistically significant (p=0.046) and clearly indicates that mortality risk increases substantially with hyperglycaemia in the setting of STEMI. Also as stated earlier, the mean admission glucose levels were significantly high among non survivors (227.09 ±131.53 mg/dL) in comparison to survivors (178.83 ± 96.02 mg/dL) (p=0.018). These observations suggest strong association between admission blood glucose levels and 30-day mortality.

The strong association observed between admission blood glucose levels and 30-day mortality was reflected on HbA1c quantitatively (p=0.021) but not qualitatively (p=0.073). Also, history of diabetes mellitus failed to demonstrate an association with 30-day mortality (p=0.155). However, there was a strong association between diabetic history and elevated admission blood sugar levels (p<0.001).

The pathophysiologic mechanism underlying the association between hyperglycaemia and mortality in patients is not completely understood. Twenty-five years ago, Oswald et al. [10] observed that the concentration of cortisol, epinephrine and nor epinephrine were the main determinants of plasma glucose levels measured in non-diabetic patients with AMI. Recently, Kadry et al. [11] observed a strong association between blood glucose concentration and presence of left ventricular failure on admission. There is strong experimental and clinical evidence that hyperglycaemia per say may be detrimental. Acute hyperglycemia attenuates endothelium-dependent vasodilatation in humans in vivo, abolishes the effect of ischemic

preconditioning, and induces oxidative stress affecting platelet function, coagulation and fibrinolysis [12-14]. All these factors lead to an increase in mortality which may in part be explained by resistance to intrinsic fibrinolysis secondary to the hyperglycemic state. Finally, many of the non-diabetic patients who develop stress hyperglycaemia are likely to be dysglycemic when not stressed. Norhammar et al. [15] found that 65% of the non-diabetic patients with glycemia >11 mmol/L had undiagnosed DM or impaired glucose tolerance. However, a diagnosis of DM cannot be confirmed in > 50% of patients who present with severe increase of blood glucose level (>200 mg/dL) at the time of AMI, further strengthening the notion that STEMI induces systemic changes that lead to transient impairment of glucose tolerance [16].

A high blood glucose level on admission is often attributed to 'stress' and might reflect an acute response to the hyperadrenergic state. The impact of admission blood glucose level, as an indicator of glucometabolic state, has been less well studied in the setting of acute coronary syndromes but appears to be a marker of adverse outcome after STEMI [17,18].

Conclusion

Hyperglycemia on admission is a strong predictor of mortality in patients with STEMI and could be used in risk stratification of these patients.

Conflicts of Interest

There are no conflicts of interest for the present study.

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