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BLOOD GLUCOSE LEVELS ON ADMISSION AS POTENTIAL INDICATOR FOR MORTALITY DURING HOSPITAL STAY IN NON-DIABETIC PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION

Cardiology

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ABSTRACT

Background and Objectives: Hyperglycaemia is common among patients with acute myocardial infarction (AMI) and is associated with high risk of mortality and morbidity. However, the relationship between admission plasma glucose (APG) levels and mortality in diabetic and non diabetic patients with AMI need further investigation. This study aims at exploring the association between APG and hospital stay mortality in non diabetic patients presenting with AMI.

Methods: The study was conducted over the period of 24 months on 300 non diabetic patients presenting with AMI admitted in ICCU at Al-Ameen Medical College Hospital, Bijapur. The cases were divided into group I to IV based on admission plasma glucose levels. There were 90 patients in group I (admission RBS < 120mg %), 50 patients in group II (admission RBS 120- 139mg %), 100 patients in group III (admission RBS 140- 167mg %) and 60 patients in group IV (admission RBS > 167mg %). All cases were subjected to investigations, and in-hospital complications were noted. Each patient was then followed up till discharge from hospital. In hospital complications and hospital stay mortality was analyzed using appropriate statistical methods across the groups (I- IV).

Results: Of the 300 cases, all had ST segment elevation myocardial infarction. Age and sex were comparable between the groups. Patients with admission plasma glucose levels >167mg% (Groups IV) were found to have lower systolic blood pressure (P= 0.002), diastolic blood pressure (P=<0.001) and lower left ventricular ejection fraction (LVEF) on admission and had greater chances of development of cardiogenic shock (P=0.01). The incidence of hospital stay mortality was more in group IV (P=0.01).

Conclusion: In our study in-hospital complications were more common in subjects with high admission plasma glucose levels. There was a positive linear correlation between admission plasma glucose levels and hospital stay mortality.

KEYWORDS:

Acute Myocardial Infarction; Diabetes Mellitus; Hyperglycaemia.

INTRODUCTION

The mortality and morbidity of the diabetic patient sustaining a myocardial infarction is poor, compared with that of non-diabetic patients.[1] Much attention has been given to the evidence that the concomitant occurrence of hyperglycaemia in patients admitted to intensive care units with an acute myocardial infarction (AMI) enhances the mortality and morbidity, whether the patient has diabetes or not.2 Elevated admission glucose levels in non diabetic patients with acute myocardial infarction are independently associated with large infarct sizes and a higher mortality rate when compared with patients with normal glucose levels.3 A positive association between hyperglycaemia at the time of the event and subsequent mortality from AMI has frequently been reported.4,5,6,7 A strong correlation between glycaemia and shock or development of heart failure has also been reported.8,9 Consequently, understan ding the possible mechanisms through which hyper glycaemia worsens the prognosis of AMI, as well the effectiveness of its control during AMI, seems to be of great relevance.

Ischemic heart disease (IHD) causes more death and disability and incurs greater economic burden than any other illness. With rapid urbanization and sedentary lifestyles the incidence of IHD is on an increase in India. By 2020 IHD is going to be the most common cause of death the world over.

The pathological mechanism of hyperglycaemia induced by AMI is not explained yet, although several explanations have been suggested. Stress during the myocardial infarction is a possible reason.10 Excessive secretion of catecholamine during the first hours of an acute infarction augments hepatic glycogenolysis, which contributes to increase plasma glucose level. Moreover, the stress induced secretion of catecholamine leads to partial inhibition of pancreatic β-cell release of insulin with increase cortisol and glucagon levels, leading to impaired glucose tolerance and elevated glucose levels.[11,12]

Acute hyperglycaemia in healthy subjects and in patients with impaired glucose tolerance or overt diabetes produces a rise in inflammatory markers. Following this line of thought, it might be speculated that the detrimental effect of stress hyperglycaemia in acute MI might also stem from its ability to increase inflammation.

Determination of blood sugar is a simple procedure, requires no expertise, is inexpensive and importantly, it is a correctable factor, having a bearing on morbidity and mortality. Based on conflicting literature and because of lack of similar studies conducted in the region, this study aims at exploring the association between the admission glycemic status and hospital stay mortality in acute myocardial infarction in non diabetic patients.

Aim of this research to analyze the impact of admission glycaemia on hospital stay mortality in non diabetic patients with acute myocardial infarction.

METHODOLOGY

We conducted prospective study over period of 24 months. Data collected in Al Ameen Medical College Hospital, Bijapur, India. Institutional ethical committee approval was taken. Study included

all 300 non-diabetic patients admitted in ICCU with raised serum cardiac enzymes, any or all of the symptoms suggestive of myocardial infarction for at least 30 minutes, ECG changes on at least two contiguous leads with ST elevation(>0.1mV) in limb leads or ST elevation (>0.2mV) in chest leads. The time for beginning of symptoms to admission to ICCU has to be less than 48 hours. All patients' blood glucose level was measured on admission by glucometer and patients who had no history or treatment for diabetes mellitus at entry were included.

Inclusion criteria included patients with acute myocardial infarction proven by cardiac enzymes, ECG and symptoms suggestive of acute myocardial infarction who had no previous history of diabetes. Exclusion criteria included known case of diabetes, had received dextrose containing intravenous fluids before admission, post surgical or post traumatic (up to one month),patients receiving drugs elevating blood glucose levels (e.g.: corticosteroids), time from the beginning of symptoms to admission to the ICCU more than 48 hours.

The patient's cardiovascular history, their medication at the time of admission, their risk factors, their clinical course, including Killip's class and initial diagnostic and therapeutic management was recorded. ECG of all the patients were read (territory of infarction, STEMI, NSTEMI, Rhythm disturbances) and recorded. Patients were followed up during hospital stay. The end point of study was till hospital discharge or till death during hospitalization. Patients were subjected to routine investigations as per protocol of the study.

Investigations and interventions conducted on the patients: Routine blood investigations, Random Blood Sugar at admission, Electrocardiogram, Cardiac Enzymes (CK MB), Echocardiography.

Patients were grouped in to FOUR categories according to their admission blood glucose levels, Group I: If their blood glucose level is ≤ 120 mg%, Group II: If their blood glucose level is 121- 139 mg%, Group III: If their blood glucose level is 140- 167 mg% and Group IV: If their blood glucose level is > 167 mg%.

We then compared the mortality data according to their admission blood glucose levels. Groups were compared by pre-tested and pre-designed Performa and the data thus collected was analyzed. Chi-square test and one way ANOVA with post hoc test were used to identify differences between 4 groups. Bivariate correlation using Pearson's method was used to identify different correlates of death as outcome.

RESULTS Table 1: Distribution of Patients (N=300) across the groups depending on admission RBS:

Variable	Group I	Group II	Group III	Group IV
Admission RBS	< 120mg%	120-140 mg%	140-167 mg%	>167 mg%
Number of patients	90	50	100	60
% group distribution of the patients	30%	17%	33%	20%

Table 2: Distribution of the patients (n=300) across the groups depending on age:

Variable	Group I N= 90	Group II N= 50	Group III N= 100	Group IV N= 60	P value
Mean age	61.11±8.61	57.6±8.14	58.9±6.89	62.33±17.81	0.857
Age ≥ 60yrs	68±9.09 (n=40)	63.3±2.88 (n=30)	63.5±3.78 (n=60)	73±8.53 (n=40)	0.158

Table 3: Distribution of the patients (n=300) across the groups depending on sex:

Variable	Group I N= 90	Group II N= 50	Group III N= 100	Group IV N= 60	P value
Male	50	40	60	40	0.823
Female	40	10	40	20	

Table 4: Personal history details:

Variable	Group I N= 90		Group II N= 50		Group III N= 100		Group IV N= 60		P
	Yes	No	Yes	No	Yes	No	Yes	No	
Hypertension	30	60	10	40	30	70	0	60	0.456
Smoking	20	70	30	20	30	70	20	40	0.542
Alcohol	20	70	30	20	20	80	20	40	0.406

Table 5: General physical examination:

Variable	Group I N= 90	Group II N= 50	Group III N= 100	Group IV N= 60	P value
Pulse rate (beat/min)	77.33±8.72	80.2±4.49	76.3±9.36	63.74±17.04	0.056
SBP (mmHg)	132.22±20.5	122±16.4	133±22.6	85±30.2	0.002
DBP (mmHg)	81.1±12.7	79.2±5.8	81.2±11.2	38.3±36.0	<0.001

SBP; systolic blood pressure, DBP; diastolic blood pressure.

Table 6: Blood investigations

Variable	Group I N= 90	Group II N= 50	Group III N= 100	Group IV N= 60	P value
Admission RBS (mg %)	100.8±8.9	128.8±4.6	151±6.5	316±34.9	<0.001
CK-MB	41.56±12.9	46.8±20.86	48±12.3	45.67±11.4	0.836
HbA1c	5.43±0.5	5.86±0.46	5.7±0.83	5.6±0.54	0.651

Table 7 : Development of cardiogenic shock:

Variable	Group I N= 90		Group II N= 50		Group III N= 100		Group IV N= 60		P
	Yes	no	Yes	no	Yes	no	Yes	no	
Cardiogenic shock	0	90	0	50	0	100	30	30	0.01

Table 8: Left ventricular ejection fraction:

Variable	Group I N= 90	Group II N= 50	Group III N= 100	Group IV N= 60	P value
LVEF (%)	47.22±6.67	48±7.58	46.9±6.9	35±3.69	0.004

Table 9: Hospital stay mortality:

Variable	Group I N= 90		Group II N= 50		Group III N= 100		Group IV N= 60		P value
	Yes	no	Yes	no	Yes	no	Yes	No	
Death	0	90	0	50	0	100	30	30	0.01

Table 10: Correlations of hospital stay mortality, death as an outcome:

Variable	N	r (pearson correlation)	P
Age	300	0.189	0.37
Age >60yrs	130	0.554	0.049
Sex	300	0.208	0.271
History of smoking	300	0.000	1.00
History of alcohol	300	0.024	0.899
History of hypertension	300	-0.184	0.331
Admission RBS	300	0.646	<0.001
Systolic BP	300	-0.724	<0.001
Diastolic BP	300	-0.901	<0.001
Heart rate	300	-0.743	<0.001
CK-MB	300	-0.091	0.632
HbA1c	300	-0.088	0.646
LVEF%	300	-0.534	0.002
Cardiogenic shock	300	1.00	

DISCUSSION

The mean age were compared between the groups, which were statistically not significant. The number of patient > 60 years of age

was also compared between the groups which was not statistically significant. However previous studies have shown that as age advances there is higher admission glycemic status, which is in accordance with the known fact that there is impaired glucose tolerance with advancing age.[5,13]

The number of males and females between the groups were comparable which was not significant (P= 0.823). But in a previous study by Kadri et al women had higher admission RBS compared to males of similar age.[13] There was no statistically significant difference in number of smokers, alcohol consumption and prevalence of hypertension between the groups. There was a statistically significant (P= 0.002) drop in the mean systolic BP as we move from Group I to Group IV. There was statistically significant (P= <0.001) in the mean diastolic BP as we move from Group I to Group IV. Probable explanation for this systolic and diastolic drop of BP is that patients in the higher admission blood glucose groups had a lower LV ejection fraction and poorer LV function. There occurred no statistically significant difference in the mean heart rate at admission across the groups. Previous studies [13, 14] have reported similar results with respect to mean systolic BP, but their observation was that a higher heart rate was associated with higher admission RBS values. This was probably due to raised sympathetic tone.

There was no statistical significant difference (P= 0.651) in the HbA1c levels across the groups, which implies a similar glycemic status in all the study subjects prior to acute myocardial infarction. All our study subjects had HbA1c within normal range and were comparable. Thus glucose values at admission were probably the result of acute stress. CK-MB levels across the groups were raised suggestive of AMI. Distribution of CK-MB level across the groups was statistically not significant. Earlier studies[14, 15] have an observation of higher level of enzymes correlated with higher admission RBS values. In-hospital complications were more common in patients with raised admission glycemia. 50% of the patients in group IV had cardiogenic shock. The occurrence of cardiogenic shock when compared between the groups was statistically significant (P=0.004). Incidence of hospital stay mortality was highest in group IV, and it was statistically significant (P=0.01).

In our study, when we carried out Pearson's correlation on death as outcome with different variables, the results revealed that admission RBS had statistically significant positive correlation with death. Systolic BP, diastolic BP and, heart rate and LV ejection fraction had negative correlation with death. Finally the raised admission RBS is an important correlate of hospital stay mortality in our study. However we observed that it is not an independent predictor of death in our study. These results are in accordance with Foo et al[16] who studied a cohort of 2127 patients presenting with acute coronary syndromes. They observed that admission glycemia was related to in hospital mortality by univariate analysis. Its prognostic significance disappeared when left ventricular failure was included in the statistical models of their study. However Kadri et al[13] reported admission glycemia as an independent and powerful predictor of in hospital and late mortality in the presence or absence of left ventricular failure. In our study admission RBS was potential indicator of hospital stay mortality but it was not the independent predictor of hospital stay mortality. Probable explanation as to why higher admission glycemia was not an independent predictor of mortality, though it was a positive correlate of death in our study is, smaller sample size (N=300).

Several hypotheses have been put forward to explain the relation between stress hyperglycemia and poor outcome. Stress hyperg lycemia may be a marker of extensive myocardial damage, reflecting a surge of stress hormones such as catecholamines and cortisol that produce or augment an insulin-resistant state.[17, 18] Relative insulin deficiency and excess catecholamines reduce glucose uptake by the ischemic myocardium and promote lipolysis and increased circulating free fatty acids. The latter inhibit glucose oxidation (the "glucose–fatty acid cycle") and are toxic to ischemic myocardium, resulting in increased membrane damage, arrhythmias, and reduced contractility.[19-22] Alternatively, elevated blood glucose levels per se adversely affect outcome through the cumulative effects of several mechanisms, including induction of endothelial dysfunction,[23] oxidative stress,[8] hypercoagulability, and impaired fibrinolysis.[24] admission hyperglycemia may not be only the cause of more severe myocardial damage, but also its consequence. Large infarcts are more likely to cause catecholamine release, which affect fatty acid and glucose homeostasis. In a study by Oswald et al[17] concentrations of cortisol, epinephrine and norepinephrine were the main determinants of plasma glucose concentration measured in non diabetic patients with acute myocardial infarction.

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KEY TO MASTER CHART

ASMI	Antero septal Myocardial Infarction
AWMI	Anterior wall Myocardial Infarction
Car shock	Cardiogenic shock
CK-MB	MB Isoenzyme of Creatine Phosphokinase
D- BP	Diastolic Blood Pressure
F	Female
HbA1c	Glycosylated Hemoglobin
h/o	History of
HR	Heart Rate
HTN	Hypertension
IP No	Inpatient number
IWMI	Inferior wall Myocardial Infarction
LVEF	Left Ventricular Ejection Fraction
M	Male
RBS @ adm	Random Blood Sugar at admission
S – BP	Systolic Blood Pressure
TOI	Territory of Infarct

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Declaration: