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### Prevalence and prognostic implication of stress hyperglycemia in patients of acute ST elevation myocardial infarction in a tertiary care centre in Eastern India

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### ABSTRACT

This observational study was carried out in non-diabetic patients admitted with ST elevation MI within 24 hrs of onset of chest pain with the aim of investigating the association and prognostic implications between stress hyperglycemia and STEMI The study population comprised of 58 patients, aged 30-70 years], presenting with acute ST elevated myocardial infarction (MI) within 24 hours of chest pain admitted in the Department .Patients who were admitted more than 24 hrs from the onset of symptoms, known diabetics, and those with renal failure (creatinine>1.5), inflammatory disorders, infection and malignancy were excluded. logistic regression analysis admission sugar levels were found to be a significant predictor of MPI, WMS, WMSI, CRP.

In conclusion, an association among admission blood glucose level, left ventricular EF, WMS, WMSI, MPI, CRP and CPKMB were observed in ST elevation AMI patients in our study.

**Keywords:** stress hyperglycemia, acute STEMI, cardiac enzymes, inflammatory markers, prognosis, echocardiographic parameters.

### Introduction

Acute myocardial infarction associated with ST elevation (STEMI) is frequently accompanied by hyperglycemia at the time of hospital admission. There is an ongoing debate as to whether this hyperglycemia is a transient elevation of blood glucose (stress hyperglycemia) as a result of acute coronary syndrome or a manifestation of latent diabetes. Recent observational studies have showed that stress hyperglycaemia is an important prognostic indicator in acute myocardial infarction (AMI)<sup>(1)</sup> and may be a reflection of the severity of

the underlying condition and not a cause of it. It is well known that while type 2 diabetics have a threefold elevated risk of major cardiovascular disease, pre-diabetics have a twofold increased risk of the same (in the absence of persistent hyperglycemia).<sup>(2)</sup> Therefore, knowledge about the prevalence and prognostic implication of hyperglycemia in AMI patients along with other morbidity and mortality predictors may help to generate predictive models that can aid clinician decision making, in particular in identifying patients who are at high risk or low risk of death. Such risk assessment methods may help in effective utilization of health resources and in that way may reduce the economic burden of our country.

In this study, we tried to investigate the interrelationship between blood glucose level at the time of admission (henceforth referred to as admission plasma glucose or APG) and the relevant biochemical parameters in ST elevation myocardial infarction (STEMI) patients in a tertiary care centre in Eastern India. We also carried out a review of the available literature data prognostic implication of stress on the hyperglycemia in acute STEMI patients and compared it with our findings.

#### **Aims and Objectives**

The aims of the study are- to assess the prevalence of stress hyperglycaemia in patients with STEMI, to analyze the available literature data on prognostic implication of admission hyperglycaemia in patients with STEMI and to investigate the association between stress hyperglycaemia, inflammatory markers and echocardiographic parameters of functional outcome.

### **Materials and Methods**

This observational and cross sectional study was conducted in the Department of Cardiology, R.G.Kar Medical College, Kolkata, a tertiary care centre of Cardiology from April 2014 to April 2015.The study population comprised of 58 patients, aged 30-70 years ,presenting with acute ST elevated myocardial infarction (MI) within 24 hours of chest pain admitted in the Department . A written informed consent to participate in the study was taken from them. Patients who were admitted more than 24 hrs from the onset of symptoms, known diabetics, and those with renal failure (creatinine>1.5), inflammatory disorders, infection and malignancy were excluded.

STEMI was defined based on the criteria established by current guidelines as persistent (>30mins) retrosternal pain associated to ST segment elevation >0.1 mv in two or more limb leads or >0.2 mv in two or more precordial leads or acute left bundle branch block (LBBB).All relevant demographic data were obtained from all patients according to proforma. Their clinical history and physical examination were noted.

Hyperglycaemia has been defined as an admission plasma glucose of >140 mg/dl (7.8 mmol/l) (11). DM has been defined as prior history of diabetes obtained from previous records or when patients report receiving pharmacologic treatment for DM or HbA1c values >6.5%.

All patients received recommended standard management for STEMI. All diabetic or nondiabetic patients with hyperglycaemia in acute phase of STEMI received subcutaneous short acting insulin according to digital glycaemic test. Measurement of brachial blood pressure, BMI, plasma glucose level, HbA1C, Troponin T, CPK MB, CRP and other routine blood tests are obtained on admission. All biochemical parameters were estimated in a clinical laboratory following quality control.

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.Baseline	Stress	Normoglycaemia
characteristics of	hyperglycaemia	
patients		
Patients (n)	21	18
Sex(m/f)	14/7	12/6
BMI(kg/msq)	26±0.5	25±0.3
SBP(mmHg)	128±10	120±12
DBP(mmHg)	83±5	80±7
Mean age(yrs)	63.10±5.59	60.11±7.36
EF	39.21±6.73	43.05±3.79
Wall Motion Score	30.67±4.97	23.89±2.47
(WMS)		
Wall motion score	1.788±0.364	1.417±0.120
index (WMSI)		
CPK MB(iu/ml)	207.71±70.54	166.67±47.029
CRP(mg/dl)	13.05±1.8	10.44±1.68
Admission blood	228±38.26	97.67±16.29
glucose		
level(mg/dl)		
Myocardial	$0.\overline{6048 \pm 0.061}$	0.5222±0.484
Performance Index		
(MPI)		

Table1: table showing a comparison of the

relavant parameters in 2 groups of patients.



Figure 1 showing CPK MB Level

Of the 58 patients, 19 (33%) patients were excluded from the study as they were categorized as diabetic as per definition followed in the study. The stress hyperglycaemia group consisted of 21 (36%) with no prior history of diabetes , who were found to have on APG >140mg/dl and HbA1c level<6.5%. The rest 18 (31%) patients comprised the normoglycaemic group. Table1 depicts the baseline characteristics of the study group. There were no differences in the sex distribution, smoking habits, level of plasma cholesterol and triglyceride level or creatinine level in both the

groups. The mean age is little higher in stress hyperglycaemia group but it is not statistically significant (63.10±5.6 vs 60.11±7.4).Blood pressure and heart rate were slightly higher in stress hyperglycaemia group. Patients in stress hyperglycaemia group had significantly higher APG level compared to normoglycaemia group (p<0.0001). The APG in stress hyperglycaemia group was 228±38.26mg/dl whereas it was 97.67±16.29mg/dl in normoglycaemia group. CPK Mb level was significantly higher in stress hyperglycaemia (207.71±70.54 group vs 166.67±47.03) as compared to normoglycaemia group and it was statistically significant (p<0.001). Moreover plasma CRP levels were higher in stress hyperglycaemia group than in normoglycaemia group (p<0.043).

Echocardiographic analysis was presented in table1 . Stress hyperglycaemia group patients had higher Wall Motion Score (WMS) (p<0.0001) and Wall Motion Score Index (WMSI) (p<0.0001), but lower Ejection Fraction (EF) (p<0.09) than normoglycaemic patients. Moreover they had an increased Myocardial Performance Index (MPI) (p<0.0001).

In logistic regression analysis admission sugar levels were found to be a significant predictor of MPI, WMS, WMSI, CRP.

#### Discussion

The prevalence of stress hyperglycaemia in our study was around 36% as against 25-50 % in other studies.<sup>(3,4,5)</sup>. In our study, hyperglycaemia was associated with higher CPK MB level, infarct size, WMS and WMSI and negatively correlated with EF. The increase in MPI, which measures both systolic and diastolic parameters of ventricular function <sup>(6,7)</sup>, indicates a worse functional outcome of the STEMI in stress hyperglycaemia patients. Hyperglycaemic patients had also had higher circulatory levels of CRP compared to normoglycaemics. The positive correlation that we found between blood glucose level and CRP also suggests that the increased inflammatory process may be a link between hyperglycemia and

poor functional cardiac outcome in hyperglycemic patients during AMI.

Stress hyperglycaemia represents increased blood glucose level that is result of neurohormonal process in organism exposed to stress. Increased glucose level during stress is result of sympathetic nervous system activation and raised production of catecholamines (adrenaline and noradrenaline) and cortisol that stimulate process of gluconeogenesis, glycogenolysis and lipolysis. These hormones are responsible for insulin resistance, on both receptor and post receptor level, thus leading to simultaneous hyperglycaemia, hyperinsulinemia and insulin resistance <sup>(8)</sup>.

Increased APG is associated with an elevated risk of in-hospital mortality as well as long term mortality (9,10) irrespective of previous diabetic status. Hyperglycemia may lead to fatal arrhythmias, significant QT prolongation,<sup>(11)</sup> impaired left ventricular function <sup>(12)</sup>, and a larger infarct size due to an increased incidence of the no-reflow phenomenon.<sup>(13)</sup> Animal studies have demonstrated that acute hyperglycaemia may abolish ischaemic pre-conditioning.<sup>(14)</sup>. Finally, a myocardial performance has worse been demonstrated patients with in acute MI(myocardial infarction) and concomitant hyperglycaemia.<sup>(15)</sup> The association of MI with increased thrombophilia is an old finding.<sup>(16,17)</sup> It has been reported that increased platelet activation after an MI is correlated with hyperglycaemia in non-diabetic patients.<sup>(18)</sup> The possible role of hyperglycaemia in the activation of blood coagulation has been previously reviewed.<sup>(19)</sup> It emerges that acute glycaemic variations are accompanied with a series of alterations in coagulation that are likely to cause a thrombosis. Acute hyperglycaemia induces a shortening of the fibrinogen half-life, (20) increases in fibrinopeptide A,<sup>(21)</sup> fragments of pro-thrombin,<sup>(22)</sup> factor VII,<sup>(23)</sup> and in platelet aggregation,<sup>(24)</sup> which are all phenomena suggesting increased activation of thrombosis.

However, our study has got certain limitations. Firstly, due to observational nature and small sample size of this study, the possibility of selection bias and/or residual confounding factors from unknown or unmeasured covariates cannot be excluded. Secondly, this is a single centre observational study, so we should be cautious in hypothesizing about the mechanism involved and the generalizability of our conclusions to other population.

#### Conclusion

Hyperglycaemia on admission is a common occurrence in patients with STEMI. It is not simply a manifestation of stress; rather it is an important prognostic indicator of functional cardiac outcome and is mainly a reflection of severity of underlying condition and not a cause of it. It can be used in risk stratification of these patients. In conclusion, an association among admission blood glucose level, left ventricular EF, WMS, WMSI, MPI, CRP and CPKMB were observed in ST elevation AMI patients in our study.

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