



## PROGNOSTIC IMPLICATIONS OF STRESS HYPERGLYCEMIA IN ACUTE MYOCARDIAL INFARCTION – A PROSPECTIVE OBSERVATIONAL COMPARATIVE EVALUATION BETWEEN DIABETICS AND NON-DIABETICS

### Cardiology

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### ABSTRACT

Stress hyperglycemia occurs in 25-50% of the patients with acute myocardial infarction. It often worsens the prognosis due to associated risk of intrahospital complications such as mortality, heart failure and cardiogenic shock. There is lack of evidence in Indian patients, particularly taking into consideration contemporary management of acute myocardial infarction. Thus, we aim to assess the incidence and prognostic implication of stress hyperglycemia in diabetic and non-diabetic patients.

**Method** This prospective observational study enrolled patients with acute myocardial infarction who presented to the Department of Cardiology, Osmania Government General Hospital, Hyderabad, India from 2011 to 2012. Data regarding random blood sugar, admission blood glucose and HbA1c levels, 2D echo, serial ECGs and oral glucose tolerance test were measured and collected. The prognosis was based on resolution of chest pain and ST segment changes, wall motion score index, ejection fraction and in-hospital development of complications like arrhythmias, cardiogenic shock, re-infarction and death.

**Results** Normoglycemics (class I) with admission blood glucose (ABG) < 140 were 20, non-diabetics with stress hyperglycemia (class II) with ABG > 140 and HbA1c < 6.6 were 40 and diabetics (class III) with ABG > 140 and HbA1c > 6.6 were 40. Mean blood glucose in class I, II and III was 93.5 mg/dL, 161.0 mg/dL and 262.1 mg/dL, respectively. Incidence of stress hyperglycemia among non-diabetics was found to be 40 (66.6%). Mean age of the patients was 48 years, 51 years and 58 years in class I, II and III respectively. In our study males were predominantly affected (75%). Mean HbA1c of class I was 5.32 mmol/mol, class II was 5.37 mmol/mol and class III was 6.77 mmol/mol. The most common site of infarction was anterior wall myocardial infarction. Patients with class II and III class have moderate to severe left ventricular dysfunction with more number in class II. Mean ejection fraction in class I was 60%, class II was 51% and class III was 53%. ST segment reduction was found to be 71.8%, 51.6% and 60.8% in three classes respectively. Complications were more in class II constituting about 28 (46.6%) and class III constituted 10 (25%). Left ventricular failure was common in class II 12 (30%), while in class III it was 6 (15%). Recurrent angina was commonly found to be 3 (7.5%) in class II. Mortality was found to be 0 (0%), 8 (20%) and 6 (17.45%) in class I, II and III respectively. Mean of oral glucose tolerance test in class I and II after 2 hours was within normal range, 84.4 and 123.2, while in class III it was 181.7, which is above the normal range.

**Conclusion** Stress hyperglycemia is associated with poorer prognosis than chronic diabetes.

### KEYWORDS:

Diabetes, complications, stress, hyperglycemia

### Introduction

Acute myocardial infarction (AMI) is one of the leading causes of morbidity and mortality throughout the world. Just like adding fuel to the fire, stress hyperglycemia, which is defined as admission plasma glucose >140 mg/d, is associated with increased risk of in-hospital mortality in patients with myocardial infarction (1). Stress hyperglycemia is estimated to be present in 25% to 50% of the patients presented with acute coronary syndrome (2). It is often found to worsen the prognosis due to associated risk of intrahospital complications such as mortality, heart failure and cardiogenic shock (3-5).

There has been much debate about the plausible reasons behind the occurrence of hyperglycemia at the time of admission and seems to be multifactorial. While many studies evidenced that it is due to "stress" of the acute cardiac event or neuroendocrine changes of the early phase of AMI, others believe that it is due to undiagnosed diabetes. It is a known generalizable fact that administering insulin to decrease glucose levels decreases mortality in diabetic patients. This clearly indicates that it is not simply an epiphenomenon of stress response (6). Thus, it can be modified and controlled to improve outcomes in MI patients with stress hyperglycemia.

To gain better insight and consequently attain favorable outcomes, several studies were undertaken. They evaluated the prognostic significance of stress hyperglycemia in diabetic and non-diabetic patients with stress hyperglycemia. But most of the studies, including the study in Indian patients were conducted in the pre-thrombolytic era. Thus, we aim to assess the incidence and prognostic implication of stress hyperglycemia in diabetic and non-diabetic patients in this contemporary era.

### Methodology

This prospective observational study enrolled patients with acute myocardial infarction who presented to the Department of Cardiology, Osmania Government General Hospital, from 2011 to 2012. The study was conducted in accordance with the principles of Good Clinical Practice and Declaration of Helsinki. The institutional ethics committee approval was obtained and the informed consent was obtained from all the patients enrolled in the study.

### Inclusion criteria

Following patients were included: 1) With typical chest pain 2) With ECG showing ST elevation > 1mm in limb leads or > 2 mm in chest leads 3) Window period < 12 hours 4) With first time detected MI 5) Diabetics 6) Not known diabetics

### Exclusion criteria

Patients were excluded if: 1) Contraindicated to thrombolytic therapy 2) They were given 5% dextrose or 25% dextrose before admission 3) Hemoglobinopathies 4) Administering sympathomimetic or sympatholytic drugs 5) Co-morbid illnesses like cerebrovascular accidents, sepsis, fever, psychological stress

### Study parameters and endpoints

Acute myocardial infarction was defined according to criteria of world health organization (7). Parameters such as heart rate, blood pressure were measured and Killip class was determined. Thrombolytics and standard care of treatment were given according to the guidelines. Random blood sugar, admission blood glucose and HbA1c levels were measured. 2D echo was done on day 2 after admission. Serial ECGs were taken daily for 1 week and oral glucose tolerance test was done at the time of discharge. The prognosis was based on resolution of chest

pain and ST segment changes, wall motion score index and ejection fraction and development of complications like arrhythmias, cardiogenic shock, re-infarction and death.

**Statistical evaluation**

Statistical evaluation was done using Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15. Continuous variables are presented as mean ± standard deviation and compared using student's t-test, while categorical variables are presented as counts and percentages and compared using chi-square test. A p value <0.05 was considered as statistical significant.

**Result**

Normoglycemics (class I) with admission blood glucose (ABG) < 140 were 20, non-diabetics with stress hyperglycemia (class II) with ABG > 140 and HbA1c < 6.6 were 40 and diabetics (class III) with ABG > 140 and HbA1c > 6.6 were 40. Mean blood glucose in class I, II and III was 93.5 mg/dL, 161.0 mg/dL and 262.1 mg/dL respectively. Incidence of stress hyperglycemia among non-diabetics was found to be 40 (66.6%). Mean age of the patients was 48 years, 51 years and 58 years in class I, II and III respectively. In our study males were predominantly affected (75%). Mean HbA1c of class I was 5.32 mmol/mol, class II was 5.37 mmol/mol and class III was 6.77 mmol/mol. The most common site of infarction was anterior wall myocardial infarction. Patients with class II and III class have moderate to severe left ventricular dysfunction with more number in class II. Mean ejection fraction in class I was 60%, class II was 51% and class III was 53% (p < 0.05). ST segment reduction was found to be 71.8%, 51.6% and 60.8% in three classes respectively.

Complications were more in class II constituting about 28 (46.6%) and class III constituted 10 (25%). Left ventricular failure was common in class II 12 (30%), while in class III it was 6 (15%). Recurrent angina was commonly found to be 3 (7.5%) in class II. Mortality was found to be 0 (0%), 8 (20%) and 6 (17.45%) in class I, II and III respectively. Mean of oral glucose tolerance test in class I and II after 2 hours was within normal range, 84.4 and 123.2, while in class III it was 181.7, which is above the normal range.

**Discussion**

The study assesses the incidence and prognostic significance of stress hyperglycemia by a comparative evaluation between diabetic and non-diabetic patient with acute myocardial infarction. The incidence of stress hyperglycemia was found to be 66.6%. It quite coincides with the previously published studies in which it ranges from 36% to 71% (8-10).

Some of the studies have clearly demonstrated that appropriate treatment have earned better and improved outcomes in patients with stress hyperglycemia. Especially, in case of AMI, it is a potentially modifiable risk factor. Yet, there is no mention of specific glucose targets in AMI guidelines (11, 12). This means that there is still a facet of relationship between glucose levels and AMI mortality which needs to be evaluated.

Some studies have demonstrated that higher admission glucose levels have impaired outcomes in patients with AMI who do not have antecedent diabetes than patients with diabetes (6, 13, 14), while other showed that there is no predilection and both the groups are equally affected (15, 16). These conflicting results and lack of complete evidence clearly justifies the aim of the current study being carried out. Though inconclusive, it is thought to believe that transient hyperglycemia is a marker of extensive myocardial damage (17). In a study by Marfella and associates, stress hyperglycemia was positively correlated with wall motion score index (18). Contrastingly, in our study there was no significant difference in WMSI between the groups. However, a diminished ejection fraction, as evidenced in our study, gives an idea that stress hyperglycemia may influence cardiac synchronization during MI. Moreover, moderate to severe left ventricular dysfunction occurred in majority of the patients with stress hyperglycemia, accounting for about 87.5%.

Stress hyperglycemia was also associated with an increased risk of mortality in patients with diabetes who had myocardial infarction, but the effect was smaller than that in patients without diabetes (6). There are several possible reasons. First, the threshold values that defined hyperglycemia may have been too low to distinguish between patients with diabetes who did and did not have stress hyperglycemia. Moreover, the definition of stress hyperglycemia is intrinsically difficult in patients with diabetes because the unstressed baseline

concentration of glucose is not known. The observation in patients with diabetes that higher mean glucose concentrations were associated with higher mortality strongly supports this possibility. Undiagnosed diabetics have a chronic rise in blood glucose levels with relative insulin deficiency. These patients are accustomed to the high glucose levels and probably the acute further rise in blood glucose may not have that much adverse effect as that of non-diabetics with stress hyperglycemia(19).

A study by Hadjadj S. et al emphasizes acute rather than chronic glycometabolic state for prognosis after myocardial infarction. It established a positive correlation between peak creatine kinase and admission plasma glucose in their patients. Admission plasma glucose may influence endothelial dysfunction and it is one of the reasons for increased complications in acute myocardial infarction (20).

Moreover, patients with diabetes are more likely to receive insulin for hyperglycemia during myocardial infarction. This treatment may lessen the rise in free fatty acid during myocardial infarction, promote myocardial uptake of glucose for anaerobic metabolism and decrease coagulability because of reduced production of thromboxane A and PAII activity.

**Conclusion**

The increased complication and mortality in patients with stress hyperglycemia as compared to diabetic patients leads us to the conclusion that stress hyperglycemia is associated with poorer prognosis than chronic diabetes.

**Study limitations**

Stress hyperglycemia is intrinsically difficult in patients with diabetes because the unstressed baseline concentration of glucose is not known and also we are not able to differentiate whether the raised blood glucose levels are due to uncontrolled diabetes as such or due to stressful condition.

**Table 1: Classification of patients based on blood glucose levels**

Admission blood glucose	Patients n (%)	Blood glucose levels (mean ± SD)
Class I	20 (20%)	93.5 ± 22.027
Class II	40 (40%)	161.025 ± 22.62
Class III	40 (40%)	262.125 ± 43.1

**Table 2: Baseline demographic characteristics between groups**

Characteristics	Class I	Class II	Class III
<b>Age</b>			
<55 years	15 (75%)	22 (55%)	11 (27.55%)
>55 years	5 (25%)	18 (45%)	29 (72.5%)
<b>Gender</b>			
Male	15 (75%)	30 (75%)	30 (75%)
Female	5 (25%)	10 (25%)	10 (25%)
<b>HbA1c (mean ± SD)</b>	5.32 ± 0.219	5.37 ± 0.189	6.77 ± 0.202
<b>Site of infarction</b>			
Anterior wall	12 (60%)	25 (62.5)	23 (57.5%)
Interior wall	8 (40%)	13 (32.5%)	15 (37.5%)
Others	0	2 (5%)	2 (5%)
<b>Killip class</b>			
I	16(80%)	12(30%)	20(50%)
II	3 (15%)	21 (52.5%)	14 (35%)
III	0 (0%)	5 (12.5%)	4 (10%)
IV	1 (5%)	2 (5%)	2 (5%)
<b>LV function</b>			
Good	18 (90%)	5 (12.5%)	15 (37.5%)
Moderate	1 (5%)	25 (62.5%)	20 (50%)
Severe	1 (5%)	10 (25%)	5 (12.5%)
<b>Ejection fraction</b>	60 ± 0.03	51 ± 0.05	53 ± 0.07

**Table 3: Mortality and complications between groups**

Complication / Mortality	Class I	Class II	Class III
Ventricular fibrillation, n (%)	0 (0%)	3 (7.5%)	2 (5%)
Cardiogenic shock, n (%)	1 (4%)	6 (15%)	3 (7.5%)
Complete heart block, n (%)	0 (0%)	2 (5%)	1 (2.5%)
Left ventricular failure, n (%)	1 (4%)	12 (30%)	6 (15%)
Recurrent angina, n (%)	0 (0%)	3 (7.5%)	1 (2.5%)
Mortality, n (%)	0 (0%)	8(20%)	6(15%)

**Table 4: Oral glucose tolerance test values between groups**

Admission Blood Glucose	Class I	Class II	Class III
<b>Mean OGTT</b>			
1 <sup>st</sup> hour	83.28	84.4	140.5
2 <sup>nd</sup> hour	116.8	123.2	181.7

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