Impact of Acute and Chronic Hyperglycemia on in-Hospital Outcomes of Patients with Acute Myocardial Infarction

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ABSTRACT

Introduction: Acute myocardial infarction remains a leading cause of morbidity and mortality worldwide. It has been reported that hyperglycemia causes oxidative stress, enhances inflammation, induces apoptosis and activates coagulation, which deteriorate myocardial damage in the setting of ischemia.

Material and Methods: This cross sectional time bound study consisted of 120 patients. Acute hyperglycemia was defined as admission plasma glucose ≥200mg/dl and chronic hyperglycemia as hemoglobin A1c≥6.5%. 120 patients were divided into those with acute hyperglycemia and those without acute hyperglycemia, those with chronic hyperglycemia and those without chronic hyperglycemia and were analysed between them. All those patients with sepsis, trauma, stroke, Patients with chronic kidney disease: defined by glomerular filtration rate <30ml/min/1.73 m^2 and those who did not give consent were excluded from the study. In all the subjects, detailed history was taken and thorough physical examination and appropriate laboratory investigations were done.

Results: Acute hyperglycemia was associated with higher mortality (46.51% vs 9.09% *P* <0.001), higher levels of creatine phosphokinase MB (91.82±81.26 vs 18.11±14.78 *P* <0.001), troponin I (17.68±10.36 vs 4.10±2.68 *P* <0.001) and decreased left ventricular ejection fraction (48.72±5.99 vs 59.09±3.32 *P* <0.001), while no significant association was found with chronic hyperglycemia.

Conclusions: Acute hyperglycemia was associated with higher in-hospital mortality, higher levels of cardiac biomarkers and decreased in left ventricular ejection fraction thereby suggesting larger infarct size as compared to chronic hyperglycemia.

Keywords: Acute Myocardial Infarction, Acute Hyperglycemia, Chronic Hyperglycemia.

INTRODUCTION

Acute myocardial infarction (AMI) remains a leading cause of morbidity and mortality worldwide. Myocardial infarction occurs when myocardial ischemia, a diminished blood supply to the heart, exceeds a critical threshold and overwhelms myocardial cellular repair mechanisms designed to maintain normal operating function and homeostasis. Ischemia at this cfritical threshold level for an extended period results in irreversible myocardial cell damage or death.

It is a well established fact that hyperglycemia (HG) causes oxidative stress, enhances inflammation, induces apoptosis, and activates coagulation, which deteriorate myocardial damage in the setting of ischemia.[1-3] In the clinical practice, admission plasma glucose is used as a measure of acute-HG and hemoglobin A1c (HbA1c) for chronic-HG. However, it remains unclear how acute-HG and chronic-HG affect short-term outcomes in patients with AMI. Therefore, the purpose of the present study is find out the impact of acute-HG and chronic-HG on short-term outcome after AMI.

The purpose of the present study was to find out the impact of acute and chronic hyperglycemia on in-hospital outcomes of patients with acute myocardial infarction (AMI).

MATERIAL AND METHODS

This cross sectional study was done on 120 patients during the period of 1 year. Out of 300 patients admitted to department of cardiology SRN Hospital MLN Medical college, Allahabad, with acute myocardial infarction, 180 patients were excluded as they either were in exclusion criteria groups or did not give consent for the study due to various reasons such as financial constraint, apprehension etc. While 120 patients who gave informed consent and falls in the inclusion criteria were included in this study. Ethical clearance was taken before the study from the local ethical clearance committee. An informed consent was taken from the study subjects. In this study AMI was defind by a combination of two of the following three:

1. Chest pain longer than 30 minutes
2. Electrocardiographic signs and
3. Elevation of serum creatine phosphokinase MB more than twice the upper normal limit /troponin I (>0.06ng/ml indicates AMI).

All these patients were evaluated for the outcome by the following ways such as levels of cardiac biomarkers (creatine phosphokinase MB and troponin I), 2D ECHO study to assess the impact on LV systolic function and mortality. On admission, age, gender and co-morbidities such as hypertension, diabetes were recorded. Random blood sugar (RBS) was obtained on admission while other investigations such as HbA1c, 2D ECHO, creatine phosphokinase MB and troponin I level were obtained during hospitalization. Acute hyperglycemia (HG) was defined as admission RBS ≥200mg/dl.[4] Chronic HG was defined as HbA1c ≥6.5%.[5]

Inclusion criteria

All age group with AMI admitted in the department of cardiology SRN Hospital MLN Medical college Allahabad.

Exclusion criteria

Sepsis
Trauma

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Parameters	Acute HG	Without acute HG	*P* value
Mortality (%)	20 (46.51%)	7 (9.09%)	0.00
CPKMB (ng/dl)	91.82±81.26	18.11±14.78	0.00
Trop I (ng/dl)	17.68±10.36	4.10±2.68	0.00
LVEF (%)	48.72±5.99	59.09±3.32	0.00

Table-1: Comparison of different parameters between acute HG and without acute HG

Parameters	Chronic HG	Without chronic HG	*P* value
Mortality (%)	4 (14.81%)	25 (26.88%)	0.15
CPKMB	35.61±27.87	47.11±67.64	0.22
Trop I	9.47±8.78	8.82±9.40	0.74
LVEF (%)	55.19±5.46	55.43±7.01	0.86

Table-2: Comparisons of different parameters between chronic HG and without chronic HG

Stroke

Patients with chronic kidney disease: defined by GFR<30ml/min/1.73 square metre.

Patients who refused to give consent.

STATISTICAL ANALYSIS

The databases were analyzed and assessed with appropriate statistical methods within different groups using Graph Pad software version 6.0. Given statistical tools were employed to analyze the result obtained: - Mean, Standard deviation, 't' test and chi squared test were used.

RESULTS

This study consisted of 120 patients, out of these 43 patients had acute HG, table 1 lists the baseline characteristic of patients with and without acute HG. While 27 patients had chronic HG, table 2 lists the baseline characteristic of patients with and without chronic HG.

Mortality among the acute HG group was 20 (46.51%) while that of without acute HG was 7 (9.09%) which was statistically significant (*P* value 0.00). Mortality among the chronic HG group was 4 (14.81%) while that of without chronic HG was 25 (26.88%) which was statistically insignificant (*P* value 0.15).

Mean CPKMB among acute HG group was 91.82±81.26 while that of without acute HG was 18.11±14.78 which was statistically significant (*P* value 0.00). Mean CPKMB among chronic HG group was 35.61±27.87 while that of without chronic HG was 47.11±67.64 which was statistically insignificant (*P* value 0.22).

Mean Trop I among acute HG group was 17.68±10.36 while that of without acute HG was 4.10±2.68 which was statistically significant (*P* value 0.00). Mean Trop I among chronic HG group was 9.47±8.78 while that of without chronic HG was 8.82±9.40 which was statistically insignificant (*P* value 0.74).

Mean LVEF among acute HG group was 48.72±5.99 while that of without acute HG was 59.09±3.32 which was statistically significant (*P* value 0.00). Mean LVEF among chronic HG group was 55.19±5.46 while that of without chronic HG was 55.43±7.01 which was statistically insignificant (*P* value 0.86).

DISCUSSION

The present cross sectional study consisted of 120 patients with AMI and the impact of acute HG and chronic HG were analysed.

Mortality among the acute HG group was 46.51% while that of without acute HG was 9.09% which was statistically significant (*P* value 0.001) suggesting that acute HG was associated with higher mortality in patient with AMI which was supported by study done by Fujino M et al[6] where the mortality was found in 9.8% with acute HG and 1.6% in patients without acute HG (*P* value <0.001).

Mortality among the chronic HG group was found in 14.81% while that of without chronic HG was 26.88% which was statistically insignificant (*P* value 0.15) suggesting that chronic HG was not associated with higher mortality in patient with AMI, which was supported by study done by Fujino M et al[6] where the mortality was found in 3.3% with chronic HG and 3.7% in patients without chronic HG (*P* value 0.79).

Mean CPKMB among acute HG group was 91.82±81.26 while that of without acute HG was 18.11±14.78 which was statistically significant (*P* value 0.00) suggesting that acute hyperglycemia was associated with higher levels of CPKMB in patients with AMI, it was supported by study done by Fujino M et al[6] where acute HG was associated with higher peak creatine kinase MB (4094±4594) against (2526±2227) in patients without acute HG (*P* value <0.001).

Mean CPKMB among acute HG group was 35.61±27.87 while that of without acute HG was 47.11±67.64 which was statistically insignificant (*P* value 0.22) suggesting that chronic hyperglycemia was not associated with higher levels of CPKMB in patients with AMI, it was supported by study done by Fujino M et al[6] where creatine kinase MB level in chronic HG (4094±4594) against (2526±2227) in patients without chronic HG (*P* value <0.59).

In additions to CPKMB, we also measured the value of Troponin I where the mean was found to be 17.68±10.36 among acute HG while that of without acute HG was 4.10±2.68 which was statistically significant (*P* value 0.001) suggesting that acute hyperglycemia was associated with higher levels of Trop I in patients with AMI. Chronic HG was not found to be associated with higher level of Trop I.

We also found statistically significant decreased in LVEF in patients with acute HG (48.72±5.99 vs 59.09±3.32, *P* value<0.001).

The present study found that acute HG was associated with higher in-hospital mortality, higher levels of cardiac biomarkers (Trop I and CPKMB) and statistically significant decreased in left ventricular ejection fraction thereby suggesting larger infarct size as compared to chronic HG, while chronic HG was not asssoiated with either higher mortality or larger infarct size. As previous studies have reported.[7-11] the present study showed that acute HG is associated with larger infarct size and higher in-hospital mortality in patients with AMI. Although there has been a debate as to whether acute HG is casually related to poor outcome after AMI or is simply an epiphenomenon of the severe disease conditions, most recent studies have demonstrated that acute HG is casually associated with further deterioration of myocardial damage and poor outcomes after reperfusion.

Acute HG is observed not only in diabetic but also in nondiabetic patients with AMI. Although earlier studies classified nondiabetics patients with acute HG as preexisting undiagnosed diabetes, recent studies have shown that acute HG in nondiabetic

patients does not represent preexisting undiagnosed diabetes.[12] In the thrombolysis era, it has been reported that diabetes and chronic glucose dysregulation, as assessed by HbA1c levels, are prognostic factors for in-hospital mortality in patients with AMI.[13] However, Briton KA et al and Timmer JR et al in their studies have shown that diabetes or HbA1c is not associated with short term outcomes after AMI.[14,15] In the present study too, it was found that chronic HG was not associated with larger infarct size and higher in-hospital mortality.

Several clinical and experimental studies have shown that acute increase in glucose causes several unfavourable effects, including oxidative stress, inflammation, apoptosis, endothelial dysfunction, and hypercoagulation, that may contribute to the poor outcomes in patients with AMI.

Esposito et al[16] reported that plasma cytokine levels increased as the plasma glucose level increased during consecutive pulses of intravenous glucose but immediately returned to normal as the plasma glucose level returned to normal. Of note, when the first elevation in the blood glucose level was maintained by subsequent continuous intravenous glucose infusion, plasma cytokine concentrations gradually returned to normal levels, despite sustained high plasma glucose level. apoptosis is also enhanced by intermittent, rather than constant, high glucose concentration[2]

In the patients with AMI, Iwakura et al[17] have shown that no-reflow phenomenon assessed by contrast echocardiography was predicted by acute HG but not by a history of diabetes or by HbA1c. Recently, Teraguchi et al[18] reported, using continuous glucose measurement and cardiac magnetic resonance imaging, that there was a significant negative relation between glucose fluctuation and myocardial salvage index. Ishihara M et al[19] reported in their study concluded that acute HG abolishes ischemic preconditioning that has potent endogenous cardioprotective effect against myocardial ischemia, these findings which were in line present study findings suggest that acute elevation of plasma glucose but not constant high glucose concentration deteriorates myocardial damage and outcomes after AMI.

Results of the previous studies that have investigated whether continous insulin infusion to normalize the glucose level will improve the outcome of patients with AMI are inconsistent.[20,21] Most of these studies consisted of patients with diabetes and/or acute HG. Because impact of acute HG is more pronounced in patients without chronic HG, glucose control to correct acute HG may be more beneficial for patients without chronic HG or diabetes. Further studies should be warranted into the appropriate management in patients with AMI and acute HG in the contemporary intervention era.

Limitations of the study

1 The study was time bound.
2 The sample size was small.
3 Cardiac biomarkers could not be measured serially due to patients financial constraints.

CONCLUSION

Acute HG was associated with higher in-hospital mortality in patients with AMI. Acute HG was also associated with higher levels of cardiac biomarkers namely Trop I and CPKMB and significant decreased in LVEF resulting from larger infarct size. While chronic HG was neither associated with higher mortality nor larger infarct size in patients with AMI.

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