

In Hospital Outcome of Myocardial Infarction in Nondiabetic Patients with High on Admission Blood Glucose Level

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Abstract

Keywords:

STEMI, NSTEMI, Blood glucose.

Background: Patients without a history of diabetes often develop hyperglycemia during an acute coronary syndrome (ACS). Our aim was to evaluate the impact of admission hyperglycemia on in hospital outcome of non-diabetic patients admitted for acute coronary syndromes.

Methods: The retrospective study was conducted in National Institute of Cardiovascular Diseases among the patients with acute myocardial infarction without history of diabetes. 50 patients with ST elevation MI (STEMI) with complications, 50 patients with STEMI without complications, 50 patients with non-ST elevation MI (NSTEMI) with complications and 50 patients without complications were included in the study. Every patient got the treatment as per protocol of the institute. On admission blood glucose of the patients was recorded. Level of blood glucose was correlated with the frequency of complications.

Results : Average on admission blood sugar level was higher in patients who developed complications with STEMI (11.4 vs 8.78 mmol/L). On admission blood sugar level was also significantly higher in patients with NSTEMI with complications (10.6 vs 8.6 mmol/L). The frequency of individual complications had no significant relation with the blood sugar level.

Conclusion : Higher level of admission blood glucose is related to poor in hospital outcome in both STEMI & NSTEMI even in nondiabetic patients. It may be used as a predictor of poor outcome of patients with myocardial infarction.

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Introduction:

The reported prevalence of hyperglycaemia among those with acute coronary syndrome (ACS) varies widely. An early series reported 20% of patients with acute myocardial infarction (AMI) presenting with plasma glucose >11.0 mmol/l.¹ Hyperglycaemia remains common even after excluding diabetic individuals. Of 38 864 nondiabetic patients with troponin-positive ACS admitted to hospitals in England and Wales, 9.9% presented with blood glucose >11.1 mmol/l,² and of 1604 non-diabetic patients admitted to French hospitals, 16.4% presented with blood glucose 7.9–9.3 mmol/l and 16.7% presented with blood glucose >9.3 mmol/l.³

In a systematic review of 15 studies (1966–1998) on AMI, the association of hyperglycaemia with increased in-hospital mortality was stronger in non-diabetic patients than in diabetic patients.⁴ Hyperglycaemia at presentation, while often

reflecting undiagnosed and persisting abnormalities of glucose handling, may also represent a transient stress response mediated through the autonomic nervous system with release of catecholamines and adrenal corticosteroids.⁵

This catecholamine response occurs early, is restricted to the first five days and is proportional to the size of infarction—being associated with faster heart rate, poorer Killip class and lower ejection fraction on discharge.^{6,7} Hyperglycaemia has been labeled an “epiphenomenon”—a marker of larger infarction and poorer left ventricular function—being associated with larger infarcts,^{8,9} heart failure on admission⁵ and elevated brain natriuretic peptide.¹⁰

On the other hand whatever the cause of hyperglycaemia in acute myocardial infarction, it has got a detrimental effect on myocardium itself. Effects of hyperglycaemia include the promotion

of oxidative stress, impairment of endothelial function, promotion of coagulation, non-enzymatic glycation of platelet glycoproteins with abrupt changes in aggregability, amplification of inflammation (with adverse effects most marked in those with coexisting raised inflammatory markers¹¹), suppression of immunity and direct toxicity to myocytes and promotion of apoptosis. Acute hyperglycaemia has been shown to impair ischaemic preconditioning, attenuate the protective effect of pre-infarction angina on microvascular function¹² and reduce the effectiveness of collateral blood supply into ischaemic zones.¹³⁻¹⁶

Study population:

The study was conducted in the National Institute of Cardiovascular Diseases, Dhaka, from June 2010 to August 2010. Two sets of patients who were not previously diagnosed as diabetic were included-STEMI and NSTEMI. In STEMI group two subsets of patients were included, 50 patients without any in-hospital complications like i) post MI angina, ii) heart failure iii) arrhythmia iv) hypotension v) cardiogenic shock vi) death; and another 50 patients with such complications. All patients were admitted within 12 hours of onset of chest pain and all the patients received thrombolytics. Similarly in NSTEMI group two subsets were selected; 50 patients without above mentioned in-hospital complications and 50 patients with such complications. All the patients received treatment as per protocol of the Hospital. On admission blood glucose level of all the patients were collected. On admission blood glucose level of the patients were correlated with the frequency of in hospital outcome of MI in both the groups separately. Whether high admission blood glucose level has an impact on in hospital outcome of STEMI &

NSTEMI differently was also evaluated.

Results:

This study was done in the cardiology department of National Institute of Cardiovascular diseases. The study was done to correlate the association of on admission blood glucose level with different complications in patients with no history of diabetes mellitus. The study was conducted in patients with both STEMI and NSTEMI. Smoking, hypertension, diabetes, family history of premature coronary artery disease and dyslipidaemia was present in 66%, 44%, 8% and 2% patients with STEMI with complications. The prevalence of these risk factors was 62%, 50%, 16% and 6% respectively in patients with STEMI without complications. There was no significant difference in the frequency of these risk factors among the patients with STEMI in relation to incidence of complications. Similarly in patients with NSTEMI the prevalence of the risk factors was 72%, 56%, 16%, 8% in patients with complications; and 60%, 52%, 12%, 08% in patients without complications. So the distribution of risk factors was almost similar in patients with or without complications.

The average age of the patients with STEMI was 56.6 yrs in patients with complications and 54.9 yrs in patients without any complications. It was 60.7 in patients with NSTEMI with complication and 58.5 in patients without complications. 84% of patients with STEMI & complication was male and 78% of uncomplicated patients with STEMI was female. 70% of complicated patients with STEMI was male and 78% of uncomplicated patients with NSTEMI was male. Patients with STEMI who developed complications appeared later in the hospital in relation to those who didn't develop complication (9.3 hrs vs 6.8); but it was not

Table-I
Correlation of risk factors with complications of STEMI & NSTEMI

Parameters	STEMI with complication	STEMI without complication	p-value	NSTEMI with complication	NSTEMI without complication	p-value
HTN	22	25	.689	28	26	.562
Smoking	30	31	.500	36	30	.086
Dyslipidaemia	01	03	.617	06	04	.715
Family history	04	08	.357	08	06	.356

statistically significant. Similarly patients with NSTEMI who presented later in the hospital had complications (11.2 vs 9.4 hrs), but it was not also statistically significant. Serum creatinine and serum sodium level was similar in all the groups.

Patients were received drugs as per protocol of the institute. Nitrate, calcium channel blocker, ACE inhibitor and angiotensin receptor blocker had no effect on the incidence of complications. But

betablocker significantly reduced the complication rate both in STEMI and NSTEMI.

Average on admission blood sugar level was higher in patients who developed complications with STEMI (11.4 vs 8.78 mmol/L). On admission blood sugar level was also significantly higher in patients with NSTEMI with complications (10.6 vs 8.6 mmol/L). The frequency of individual complications had no significant relation with the blood sugar level.

Table-II

Correlation of age, sex and renal function with complications of STEMI & NSTEMI

Parameters	STEMI with complication	STEMI without complication	p-value	NSTEMI with complication	NSTEMI without complication	p-value
Age (years)	56.6	54.9	.463	60.7	58.5	.634
Sex (M/F)	42 08	39 11	.611	35 15	39 11	.495
Duration of chest pain(hours)	9.3	6.8	.150	11.2	9.4	.080

Table-III

Correlation of drugs used with complications of STEMI & NSTEMI

Parameters	STEMI with complication	STEMI without complication	p-value	NSTEMI with complication	NSTEMI without complication	p-value
Aspirin	50	50	-	50	50	-
Clopidogrel	50	50	-	48	49	1.0
Nitrate	42	32	.039	42	45	.06
CCB	10	00	.360	1	4	.36
ACE inhibitor	17	10	.063	10	12	0.8
ARB	02	02	1.00	0	1	1.0
Beta blocker	21	41	.0003	22	33	.016
Serum creatinine (mg/dl)	1.5	1.2	.128	1.15	1.08	.078
Serum sodium level (mmol/L)	135	136	.331	135.3	136.2	.532

Table-IV

Correlation of RBS with complications of STEMI & NSTEMI

Parameters	STEMI with complication	STEMI without complication	p-value	NSTEMI with complication	NSTEMI without complication	p-value
Random blood sugar (mmol/L)	11.4	8.78	0.05	10.6	8.6	.004

Discussion:

This study evaluated the effect of on admission hyperglycaemia in patients with both NSTEMI & STEMI. The average age of the patients with STEMI was 56.6 yrs and 54.9 yrs in patients with and without complications respectively. Similarly the average age of the patients with NSTEMI with and without complications was 60.7 & 58.5 respectively. This is consistent with the other studies involving the MI patients in our institute.¹⁷ The age distribution of the patients in different groups was similar. In all the groups male patients were predominant. This was because of the more male patient number admitted in the hospital.

The frequency of different risk factors in study population was also comparable with other studies conducted in recent times. The risk factor distribution was almost similar in different groups.¹⁸ Smoking was the most prevalent one followed by hypertension, dyslipidaemia and family history of coronary heart disease. These risk factors had no significant relation with the rate of complications. Probably a larger number of study population may had a different result. Patients who presented later had more complications in the setting of both STEMI and NSTEMI. But it was not statistically significant. It happened such as the patients who presented more than 12 hours after onset of chest pain were excluded from the study.

All the patients were treated with the drugs as per protocol of the institute. Beta-blocker was used more frequently in the patients with STEMI and NSTEMI patients who had no complications. There was no correlation of other drugs with the frequency of complications.

Complications like post MI angina, heart failure, arrhythmia, hypotension, shock and death was recorded in the study. The patients who had NSTEMI and had any one of these complications were with higher on admission blood glucose level. Similarly patients STEMI and complications had higher on admission blood glucose level. But the blood glucose had no specific relation with any of the specific complication. Artur et al demonstrated that in hospital mortality was higher in patients with NSTEMI treated conservatively.¹⁹ Belen Cid-Alvarez et al also showed that patients with ACS who are not known to suffer from diabetes,

admission and fasting blood glucose are both strong predictors of mortality. They also mentioned that the predictive values of admission and fasting blood glucose are similar for forecast times of up to about 1 year, but the better predictor of long term mortality is fasting blood glucose level.²⁰

Our study results are similar to the meta-analysis made by Angeli F et al.²¹ They concluded that in patients without a prior diagnosis of diabetes who are admitted to hospital for ACS, NH increases the risk of both short and long-term mortality.

In one study Carpentier et al²² on admission blood glucose level as a risk factor in the evaluation of chest pain in the emergency department. They concluded that a blood glucose level > 140 mg/dl in patients admitted to an emergency department for chest pain is associated with non-ST elevation ACS. In another study J Sala et al²³ defined the blood glucose level increasing the risk is 6.67 mmol/L. Higher 28 day mortality was observed among MI patients with glycaemia on admission >6.67 mmol/l compared with patients with lower levels, independently of major confounding variables and, particularly, previous diagnosis of diabetes.

Our study results are consistent with findings of other similar studies which have shown that in STEMI, admission hyperglycaemia independently is associated with incomplete resolution of ST-segment elevation,²⁴ persisting occlusion of the infarct-related artery after thrombolytic treatment²⁵ and (unlike HbA1c or previous diagnosis of diabetes) predicts poor flow in this artery before,²⁶ and poorer myocardial perfusion and ST-segment resolution after, successful primary PCI.²⁷⁻²⁹

In the Hellenic Heart Failure Study Serum glucose level at hospital admission correlates with left ventricular systolic dysfunction in nondiabetic, acute coronary patients. Study revealed that a 10 mg/dl difference in glucose levels was independently associated with 8% (95% confidence interval 2%-14%) higher likelihood of left ventricular systolic dysfunction.³⁰

Whether hyperglycemia is a mediator or marker of adverse outcomes remains unclear. In any patient, diabetic or not, elevated glucose during AMI could in part reflect the severity of illness resulting from a high catecholamine state and

increased circulating concentrations of other factors, such as cortisol. On the other hand, Higher glucose levels in patients with AMI have been associated with higher free fatty acid concentrations, insulin resistance, and impaired myocardial glucose use, thus increasing the consumption of oxygen and potentially worsening ischemia.^{31,32}

Another possible explanation is that these patients are truly diabetic. As a few small reports have suggested that between 25% and 70% of these patients may in fact have undiagnosed diabetes.^{33,34,35} Another explanation is that substantial proportion of hyperglycemic patients without a history of diabetes had at least an underlying insulin resistance, which may have conferred higher risk of mortality, as suggested by others.³⁶

Our findings highlight an important potential opportunity to improve care and outcomes for hyperglycemic AMI patients without known diabetes. Experience in other patient populations³⁷ indicates that tight glycemic control with insulin therapy during hospitalization may be at least as important for these patients as in diabetics.³⁸ Large-scale randomized clinical trials are needed to definitively establish the utility of target-driven aggressive glucose control in this patient group. Our results suggest that these trials should use a target glucose of 110 mg/dL and are in agreement with the recent statements by the American Diabetes Association and American College of Endocrinology on in-hospital glucose management.^{39,40}

Conclusion:

Higher level of admission blood glucose is related to poor in hospital outcome in both STEMI & NSTEMI even in nondiabetic patients. It may be used as a predictor of poor outcome of patients with myocardial infarction. This early, simple, and inexpensive marker of bad prognosis after MI should prompt the application of more aggressive treatment of MI and risk factors and, probably of hyperglycaemia during admission.

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