Influence of admission blood glucose and hemoglobin A1c on outcome of acute myocardial infarction

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Introduction
Patients either with or without a prior history of diabetes mellitus may present with hyperglycemia during acute myocardial infarction (AMI); it is uncertain whether hyperglycemia upon admission, irrespective of the diagnosis of diabetes, remains an independent predictor of in-hospital morbidity and mortality.

Aim of the study
We aimed in this study to assess the impact of admission blood glucose level on the hospital course and outcome in patients presenting with AMI in ICU.

Patients and methods
We included 50 patients with AMI divided into two groups: group I included 30 patients with admission blood glucose level less than 180 mg/dl and group II included 20 patients with admission blood glucose level 180 mg/dl or more. Group I was subdivided into group IA including 16 patients with HbA1c less than 6% and group IB including 14 patients with HbA1c of 6% or more. All patients were subjected to complete history taking and complete clinical examination; 12-lead ECG was performed for every patient and routine laboratory investigations including cardiac enzymes, admission blood glucose level, and HbA1c were estimated at the time of admission of the patients.

Results
There was significant correlation between admission blood glucose level and history of diabetes mellitus and history of smoking (P = 0.000 and 0.008, respectively). There was also significant correlation between admission blood glucose level and complications of myocardial infarction including sinus tachycardia, arrhythmia, and ICU length of stay (P = 0.008, 0.002, and 0.000, respectively). However, HbA1c level was not found to be correlated with any of the previous parameters.

Conclusion
We concluded that elevated admission glucose level is a strong predictor of short-term adverse outcome in patients with AMIs. However, the prognostic value of diabetic control (i.e. hemoglobin A1c levels) in patients with AMI is still undefined.

Keywords:
acute myocardial infarction, glucose level, HbA1c

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Introduction

Patients either with or without a prior history of diabetes mellitus may present with hyperglycemia during acute myocardial infarction (AMI). Among patients with no prior history of diabetes, hyperglycemia may reflect previously undiagnosed diabetes, pre-existing carbohydrate intolerance, stress-related carbohydrate intolerance, or a combination of these [1]. Several studies have reported an association between elevated blood glucose upon admission and subsequent increased adverse events, including congestive heart failure (CHF), cardiogenic shock, and death [2,3]. However, an overview of these reports [1] was critical of the varying definitions for hyperglycemia [blood sugar ranged from 119 mg/dl (6.6 mmol/l) to 200 mg/dl (11.1 mmol/l)] and of the sketchy assessment of patient variables, previous medical therapy, and in-hospital interventions. Furthermore, many of the studies were conducted in the prethrombolytic era.

Given that the management of diabetes mellitus, other cardiac risk factors, and AMI has evolved significantly since the publication of these reports, it is uncertain whether hyperglycemia upon admission, irrespective of the diagnosis of diabetes, remains an independent predictor of in-hospital morbidity and mortality. The objective of this study was to determine whether the level of blood glucose upon admission remains associated with adverse in-hospital clinical outcomes after AMI in the contemporary era, considering recent advances in treatment, and we sought to take a population-based approach toward examining this question.

Aim of the study

We aimed at studying a population of unknown diabetes mellitus with AMI to evaluate the effect of their admission blood glucose and glycated hemoglobin on their prognosis.

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Materials and methods

Patients

Fifty patients with myocardial infarction were included in this randomized clinical trial. Patients were collected from Critical Care Department of Kasr Al-Ainy University Hospital and New Kasr Al-Ainy Teaching Hospital over a period of 6 months. The patients included were 41 men and nine women.

Inclusion criteria

Adult patients admitted to ICU with AMI ST segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI) were included.

Patients were diagnosed as having STEMI when they had new or presumed new ST segment elevation of 1 mm or more seen in any location or new left bundle-branch block with at least one positive cardiac biochemical marker of necrosis (including creatine kinase MB, creatine phosphokinase, or troponin). In cases of NSTEMI, at least one positive cardiac biochemical marker of necrosis without new ST segment elevation seen on the index or subsequent electrocardiogram had to be present.

Exclusion criteria

Patients with noncardiovascular causes for the clinical presentation, such as trauma, major surgery aortic aneurysm, CHF, renal insufficiency, hepatic insufficiency, and extensive comorbidities were excluded.

Patients were enrolled into the study after approval from the ethical committee and informed consents were obtained. The duration of the study was 6 months.

Study design

(1) Randomized clinical trial.
(2) The study duration was 6 months.
(3) Follow-up evaluation was performed everyday during the study period until patient's discharge.
(4) Fifty patients with AMI (STEMI and NSTEMI) were divided into group I including 30 patients with admission blood glucose level less than 180 mg/dl and group II including 20 patients with admission blood glucose level 180 mg/dl or more. Group I was subdivided into group IA including 16 patients with HbA1c less than 6% and group IB including 14 patients with HbA1c 6% or more.

All patients were subjected to the following:

Complete history taking and complete clinical examination to detect the type of myocardial infarction, hemodynamic instability, and incidence of complications.

Investigations

(1) Serial electrocardiogram.
(2) Echocardiography with its findings about regional wall motion abnormalities and global systolic function.
(3) Serial cardiac enzyme (CK total and CK-MB).
(4) Biochemical tests including kidney function tests, liver function tests, lipid profile, admission blood glucose level, and glycosylated hemoglobin.

Blood samples were taken at the time of admission for HbA1c, blood glucose level on admission, and routine measurements. Samples for FPG level were taken after 8 h fast. HbA1c was assessed quantitatively using colorimetric technique by glycohemoglobin reagent set.

Statistical analysis and data management

Data were statistically described in terms of mean±SD, median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was carried out using the Mann–Whitney *U*-test for independent samples. *P* values less than 0.05 were considered statistically significant. All statistical calculations were performed using computer program SPSS (statistical package for the social science; SPSS Inc., Chicago, Illinois, USA), version 15 for Microsoft Windows.

P value greater than 0.05 was considered insignificant, *P* value less than 0.05 was considered significant, and *P* value less than 0.01 was considered highly significant.

Results

Demographic data

Our study comprised 50 patients with a mean age of 53 years (range from 31 to 86 years). Forty-one patients (82%) were men and the remaining nine patients (18%) were women.

This study included 50 patients with AMI (STEMI and NSTEMI) for whom random blood glucose level and HbA1c were determined on admission. According to the blood glucose level on admission (GOA), they were classified into two groups: group I included 30 patients with admission blood glucose level less than 180 mg/dl and group II included 20 patients with admission blood glucose level 180 mg/dl or more. Group I was subdivided according to HbA1c level

into group IA including 16 patients with HbA1c less than 6% and group IB including 14 patients with HbA1c 6% or more (Fig. 1).

Clinical data

Twenty-two patients were hypertensive (44%) with a mean systolic pressure of 140 mmHg and diastolic arterial blood pressure of 90 mmHg; all patients were on antihypertensive drugs, 21 were patients with diabetes (42%), nine were dyslipidemic (64%), 29 patients were smokers (58%), and 11 had history of ischemic heart disease (22%) (Fig. 2).

Correlation between history of diabetes mellitus and GOA groups

There was a significant correlation between elevated GOA and patients with history of diabetes mellitus (P = 0.000; Table 1 and Fig. 3).

Correlation between history of diabetes mellitus and HbA1c groups

There was nonsignificant correlation between HbA1c level and patients with history of diabetes mellitus (P = 0.276).

Correlation between dyslipidemia and GOA level

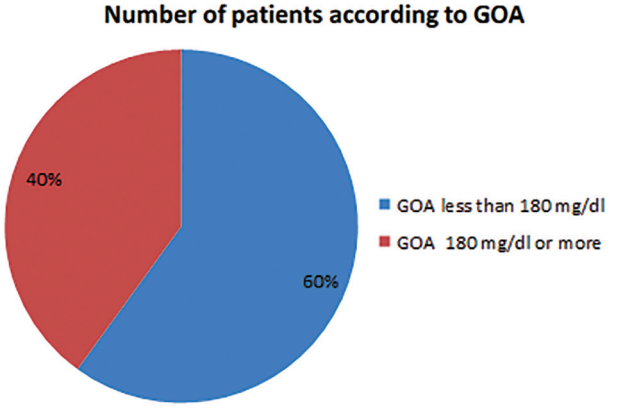
In group I, 20 (66%) patients of the 30 had dyslipidemia and in group II 12 (60%) patients of the 20 had dyslipidemia; it was of nonsignificant value in our study. This explains that most of the patients with AMI are dyslipidemic.

Table 1 Correlation between history of DM and elevated GOA

Variables	GOA<180 mg/dl (group I) (n = 30)	GOA ≥ 180 mg/dl (group II) (n = 20)	P value
Not DM	28	1	0.000
DM	2	19	

DM, diabetes mellitus; GOA, glucose level on admission.

Figure 1



Patients distribution according to glucose level on admission (GOA) in the study.

Correlation between type of myocardial infarction (STEMI and NSTEMI) and GOA

There were five patients of the 30 in group I who developed NSTEMI, whereas rest of the patients developed STEMI. However, there were four patients of the 20 in group II who developed NSTEMI and rest of them developed STEMI. There was nonsignificant correlation (P = 0.523).

There was also nonsignificant correlation between the types of myocardial infarction and HbA1c level (P = 0.567).

Correlation between new ischemia and GOA level

In group I, two patients of the 30 had new ischemia, but in group II three patients of the 20 had new ischemia; it was of nonsignificant correlation (P = 0.310).

Correlation between smoking and GOA level

In group I, 22 patients were smokers and in group II seven patients gave history of smoking, resulting in significant correlation between smoking and elevated glucose level (P = 0.008) (Fig. 4).

However, there was nonsignificant correlation between smoking and HbA1c level (P = 0.154).

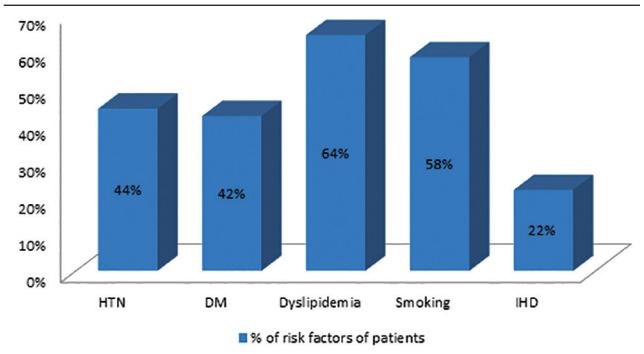
Correlation between heart rate and GOA level

There was significant correlation between elevated GOA and heart rate (P = 0.008; Table 2).

Correlation between arrhythmia and GOA level

In group I, only one patient had arrhythmia but in group II eight patients were complicated by arrhythmia giving significant correlation between elevated GOA and development of arrhythmia (P = 0.002; Fig. 5).

Figure 2



Risk factors of myocardial infarction. DM, diabetes mellitus, HTN, hypertension; IHD, ischemic heart disease.

However, there was nonsignificant correlation between arrhythmia and HbA1c level (P = 0.533); only one patient developed arrhythmia of the 16 patients with HbA1c 6% or more.

Correlation between heart failure and GOA level

In group I, only three patients developed heart failure but in group II 16 patients had heart failure, which was of significant correlation (P = 0.000) (Fig. 6).

However, there was nonsignificant correlation between HbA1c level and heart failure (P = 0.552).

Correlation between ICU length of stay and GOA level

There was significant correlation between ICU length of stay and GOA level (P = 0.000; Table 3).

However, there was nonsignificant correlation between HbA1c levels and ICU length of stay (P = 0.199).

Correlation between mortality and GOA level

In group II, only one patient died of the 20 patients and no mortality occurred in group I. This was of nonsignificant correlation (P = 0.400).

In addition, there was nonsignificant correlation between HbA1c level and mortality.

Discussion

Diabetes mellitus is an established major cardiovascular risk factor associated with increased prevalence of coronary artery disease (CAD) [4]. Patients with diabetes often have numerous concomitant cardiac risk factors with a higher incidence of AMI and CHF. Poor glycemic control and insulin resistance are

Table 2 Correlation between heart rate and GOA level

Variables	Minimum	Maximum	Mean	SD	*P* value
HR in group I	60	103	84.63	10.85	0.008
HR in group II	80	130	95.30	16.40	

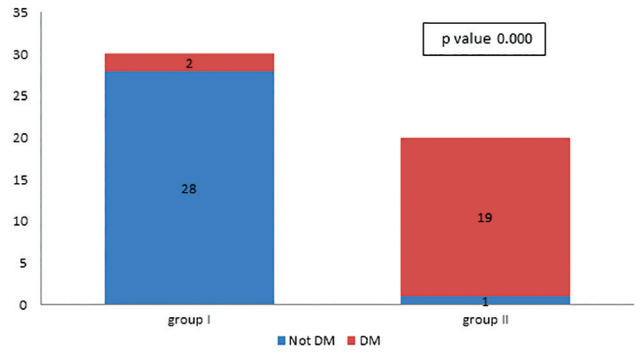
HR, heart rate; GOA, glucose level on admission.

Table 3 Correlation between ICU length of stay and elevated GOA

ICU length of sstay (days)	Minimum	Maximum	Mean	SD	*P* value
Group I	2	9	4.70	1.466	0.000
Group II	3	10	6.55	1.932	

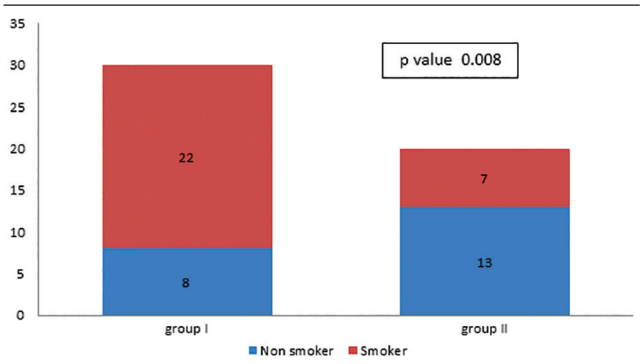
GOA, glucose level on admission.

Figure 3



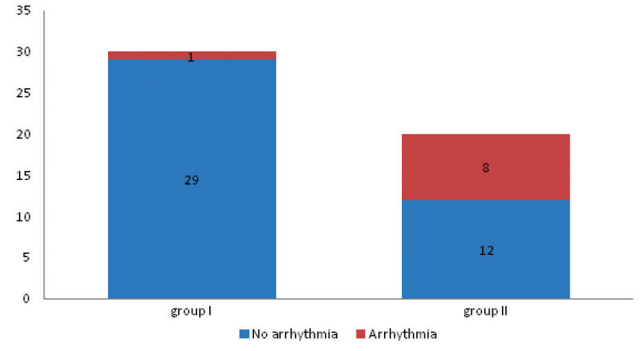
Correlation between history of DM and elevated GOA. DM, diabetes mellitus; GOA, glucose level on admission.

Figure 4



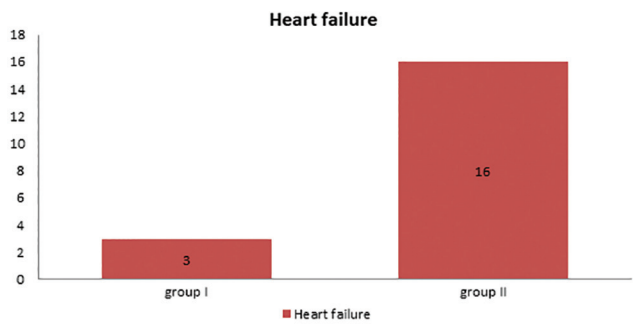
Correlation between smoking and glucose level on admission (GOA).

Figure 5



Correlation between arrhythmia and glucose level on admission (GOA).

Figure 6



Correlation between heart failure and glucose level on admission.

associated with significant endothelial cell dysfunction, procoagulability, and diffuse multivessel CAD.

A high blood glucose level on admission is often attributed to 'stress hyperglycemia' and might reflect an acute response to the hyperadrenergic state. The impact of admission blood glucose level, as an indicator of glucometabolic state, has been less well studied in the setting of acute coronary syndromes but appears to be a marker of adverse outcome after STEMI [5,6].

Interventional studies have established that cardiovascular complications are mainly or partly dependent on sustained chronic hyperglycemia [7,8]. This glycemic disorder can be estimated as a whole from the determination of HbA1c level, which integrates both basal and postprandial hyperglycemia [9,10].

HbA1c reflects the average blood glucose concentrations over the preceding 2–3 months. There are advantages of HbA1c testing compared with plasma glucose. The measurement of HbA1c is well standardized, and the biologic variability is less and does not require fasting. In addition, it is relatively unaffected by acute changes in glucose levels.

Hence, we aimed in this study to assess the impact of admission blood glucose level and HbA1c on the hospital course and outcome in patients presenting with AMI in ICU.

In our study, we included 50 patients with AMI, 41 patients were men and nine were women, divided into two groups: group I included 30 patients with admission blood glucose level less than 180 mg/dl and group II included 20 patients with admission blood glucose level 180 mg/dl or more (the level 180 was chosen according to the NICE-SHUGAR study investigators) [11]. Group I was subdivided into group IA including 16 patients with HbA1c less than 6% and group IB including 14 patients with HbA1c 6% or more.

All patients were subjected to complete history taking and complete clinical examination; 12-lead ECG was performed for every patients and routine laboratory investigations were performed, including cardiac enzymes, which were important for diagnosis of AMI. Admission blood glucose level and HbA1c were estimated at the time of admission of the patients.

Our study substantially expands the current understanding of the relationship between admission glucose values and adverse outcomes in patients with AMI.

We tried to find this correlation between GOA and HbA1c with the adverse outcome of these patients who were admitted to the critical care unit with AMI.

With respect to age and sex, there was no significant correlation with elevated GOA or HbA1 in these patients; this is in agreement with the study conducted by Cakmak *et al*. [12], who studied 100 patients with elevated GOA and HbA1c and could not detect any significant correlation between sex and clinical results.

There was a significant correlation between history of both smoking and diabetes mellitus and elevated GOA. (P = 0.008 and 0.000, respectively) and these results are in agreement with the results of Pres *et al*. [13] who also detected the highest significant correlation between history of both smoking and diabetes mellitus and elevated GOA (P = 0.000 and 0.018, respectively).

In contrast, there was no significant correlation between history of hypercholesterolemia or hypertension among our study.

We detected an increased incidence of developing heart failure (detected by low ejection fraction) in patients with AMI and elevated GOA level, with high significant correlation between them (P = 0.000). These results are in agreement with the study by Gasior *et al*. [14] in which of the 3166 consecutive patients with STEMI 258 had heart failure.

In agreement with our study, Kosiborod and McGuire [15] also found that higher blood GOA in patients with AMI was associated with higher Killip classification and lower ejection fraction %.

We could not assess the proper correlation between elevated GOA or HbA1c and mortality as only one patient from group II died (P = 0.400).

This is not in agreement with the study by Kosiborod and McGuire [15], who studied 141 680 patients hospitalized with AMI over 2-year study duration; they concluded that higher glucose levels were associated with greater 30-day mortality (P < 0.001).

The difference between our results and the results of these studies may be because of difference in sample size as their studies were conducted on a very high number of patients.

With respect to HbA1c, we did not find any significant correlation between its level and outcome of patients with AMI, and this is in agreement with the study conducted by Timmer [16] who concluded that elevated HbA1c was not significantly associated with increased mortality or adverse outcome in their study, which was previously described.

Similarly, study by Chan *et al.* [17] suggested that HbA1c level before admission is not associated with short-term cardiovascular outcome in diabetic patients subsequently admitted with acute coronary syndrome.

In contrast to our study was a systematic review by Liu *et al.* [18] to quantify the association between elevated HbA1c level and all-cause mortality among patients hospitalized with CAD. A systematic search of electronic databases for studies published from 1970 to May 2011 was performed. Cohort, case–control studies, and randomized controlled trials that examined the effect of HbA1c on all-cause mortality in patients with acute coronary syndrome were included.

Finally, our discussion concluded that elevated admission blood glucose level in patients with AMI appears more important than prior long-term abnormal glucose metabolism (detected by elevated HbA1c) in predicting outcome in patients with AMI, and this may be because a stress response accompanied by high levels of catecholamines and cortisol; these hormones increase glycogenolysis and lipolysis and reduce insulin sensitivity, resulting in elevated glucose levels [12]. Therefore, patients with elevated glucose levels may represent patients with an increased stress response, for example, due to more severe hemodynamic compromise or more extensive myocardial damage [19,20]. Stress hyperglycemia increases mortality, CHF, and cardiogenic shock after AMI [21]. Elevated cytokine, particularly tumor necrosis factor-α (TNF-α), also increases glucose levels. TNF-α is released in AMI and directly decreases myocardial contractility, probably by inducing myocardial apoptosis [22]. TNF-α also causes impaired endothelial function [23]. This, in turn, may be responsible for impaired myocardial perfusion.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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