Association of Hyperglycemia with In-Hospital Mortality and Morbidity in Libyan Patients with Diabetes and Acute Coronary Syndromes

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ABSTRACT

Objective: Hyperglycemia on admission and during hospital stay is a well-established predictor of short-term and long-term mortality in patients with acute myocardial infarction. Our study investigated the impact of blood glucose levels on admission and in-hospital hyperglycemia on the morbidity and mortality of Libyan patients admitted with acute coronary syndromes (acute myocardial infarction and unstable angina). *Methods:* In this retrospective study, the records of patients admitted with acute coronary syndrome to The 7th Of October Hospital, Benghazi, Libya, between January 2011 and December 2011 were reviewed. The level of blood glucose on admission, and the average blood glucose during the hospital stay were recorded to determine their effects on in-hospital complications (e.g. cardiogenic shock, acute heart failure, arrhythmias, and/or heart block) and mortality.   *Results:* During the study period, 121 patients with diabetes were admitted with acute coronary syndrome. The mortality rate in patients with diabetes and acute coronary syndrome was 12.4%. Patients with a mean glucose level greater than 200mg/dL had a higher in-hospital mortality and a higher rate of complications than those with a mean glucose level ≤200mg/dL (27.5% vs. 2.6%, *p*<0.001 and 19.7% vs. 45.5%, *p*=0.004, respectively). There was no difference in in-hospital mortality between patients with a glucose level at admission ≤140mg/dL and those admitted with a glucose level >140mg/dL (6.9% vs. 14.3%; *p*=0.295), but the rate of complications was higher in the latter group (13.8% vs. 34.1%; *p*=0.036). Patients with admission glucose levels >140mg/dL also had a higher rate of complications at presentation (26.4% vs. 6.9%; *p*=0.027).   *Conclusion:* In patients with diabetes and acute coronary syndrome, hyperglycemia during hospitalization predicted a worse outcome in terms of the rates of in-hospital complications and in-hospital mortality. Hyperglycemia at the time of admission was also associated with higher rate of complications particularly at the time of presentation.

Cardiovascular disease is the leading cause of death worldwide.[1] In 2008, 17.3 million people died from this disease; 7.3 million of those deaths were due to acute myocardial infarction (AMI).[1] Diabetes mellitus (DM) is a well-known risk factor for coronary artery disease.[2] Poor glycemic control can lead to endothelial injury, and to coronary artery disease and myocardial infarction.[2] In both diabetic and non-diabetic patients, hyperglycemia is a common concomitant finding in patients with AMI. Epidemiological studies showed that over half of patients with AMI had hyperglycemia at the time of hospital admission.[3] Studies from different populations demonstrated that hyperglycemia at admission and during hospital stay was associated with poorer outcomes in both diabetics and non-diabetics.[4,5] Hyperglycemia has been linked to increased morbidity, congestive heart failure (CHF) and cardiogenic shock, and mortality.[6-14] However, evidence of a direct correlation between elevated blood glucose and outcomes, including AMI, is lacking.[9,10,12-14] We retrospectively examined the relationship between hyperglycemia at the time of hospital admission and during hospital stay with morbidity and mortality in patients with acute coronary syndrome (ACS) and diabetes.

METHODS

The medical records of patients admitted with (ACS) to The 7th Of October Hospital, Benghazi,

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Libya, between January 2011 and December 2011 were reviewed retrospectively. Demographic data and data on the presence or absence of diabetes, hypertension, tobacco smoking, and history of previous myocardial infarction were collected from the patients' medical records. Details of treatment, particularly thrombolytic and antiplatelet therapies, were noted.

The level of blood glucose at admission and the average blood glucose during hospital stay were recorded to determine their effect on in-hospital mortality and complications. The mean in-hospital blood glucose was only calculated for those patients with at least three blood glucose measurements available.

Patients were categorized into two groups according to their glucose levels on admission; those ≤140mg/dl and those >140mg/dL. Similarly, patients were also categorized into those whose mean blood glucose was ≤200mg/dL and those with mean blood glucose of >200mg/dL.

The difference in mortality and rates of complications were determined between each set of groups. Recorded complications included cardiogenic shock, acute heart failure, arrhythmias, and/or heart block.

Data were analyzed using the SPSS Statistics (SPSS Inc., Chicago, US) version 17.0. Discrete variables were expressed as numbers and percentages, and continuous variables as the mean and standard deviation (SD).

Differences between categorical values were analyzed using the chi-square test while the Student's *t*-test was used for continuous values. A *p*-value less than 0.050 was considered statistically significant.

RESULTS

During the study period, a total of 121 patients with diabetes, four with type I DM and 117 with type II DM, were admitted with ACS. AMI was the reason for admission in 71 (58.7%) patients, and unstable angina (UA) in the remaining 50 patients.

The overall in-hospital mortality rate was 12.4%. Mortality was higher in those with AMI than in those with UA, but the difference was not significant (16.9% vs. 6%; *p*=0.070). Complications (cardiogenic shock, acute heart failure, arrhythmias, and/or heart blocks) occurred in 35 (28.9%) patients during their hospitalization.

Table 1: Characteristics of patients with diabetes and acute coronary syndrome according to their blood glucose level at admission.

Patients' characteristice	Admission glucose		*p*-value
	≤140mg/dL	>140mg/dL	
Total patients	29 (24.2)	91 (75.8)	
Men	17 (58.6)	49 (53.8)	0.653
Age*(years)	59±9	61±11	0.408
Hypertension	23 (79.3)	51 (56.0)	0.025
Smoking	5 (17.2)	19 (20.9)	0.670
History of MI	8 (27.6)	11 (12.1)	0.046
History of CAD	11 (37.9)	40 (44.0)	0.568
Mean systolic BP*	150±31	145±34	0.501
Mean diastolic BP*	86±16	86±19	0.978
MI	15 (51.7)	55 (60.4)	0.407
Thrombolysis	10 (34.5)	29 (31.9)	0.793
Antiplatelets	29 (100.0)	88 (96.7)	0.322

Data presented as n (%).
*mean±SD.
BP: blood pressure, CAD: coronary artery disease, MI: myocardial infarction.

Blood glucose levels on admission were noted in the records of 120 patients out of the 121 patients admitted with ACS.

Table 1 shows the background characteristics of the 120 study patients categorized according to their blood glucose level at admission. There was no difference in in-hospital mortality between patients with an admission glucose level ≤140mg/dL and those with an admission glucose level >140mg/dL (6.9% vs. 14.3%; *p*=0.295). Patients with an admission glucose level >140mg/dL have higher rate of complications at time of their presentation (26.4% vs. 6.9%; *p*=0.027) as well as higher rate of overall complications occurring during their hospital stay (34.1% vs. 13.8%; *p*=0.036).

Table 2 shows the background characteristics of the 116 patients with respect to their average blood glucose level.

Data from at least three measurements of blood glucose were available for 116 patients. Seventy-six (65.5%) of these patients had an average blood glucose of ≤200mg/dL, and the remaining 40 (34.5%) had an average blood glucose of >200mg/dL. Those with a mean glycemia >200 mg/dL had a higher in-hospital mortality (27.5% vs. 2.6%; *p*<0.001) and a higher overall rate of in-hospital complications (19.7% vs. 45.5%; *p*=0.004) than those with a mean glycemia ≤200mg/dL.

Table 2: Characteristics of the patients with diabetes and acute coronary syndrome according to the mean glycemia level.

Patients' characteristice	Mean glycemia		p-value
	≤200mg/dL	>200mg/dL	
Total patients	76 (65.5)	40 (34.5)	
Men	48 (63.2)	16 (40)	0.017
Age* (years)	59±10	62±11	0.128
Hypertension	49 (64.5)	25 (62.5)	0.833
Smoking	17 (22.4)	5 (12.5)	0.198
History of MI	17 (22.4)	2 (5)	0.016
History of CAD	34 (44.7)	15 (37.5)	0.453
Mean systolic BP*	143±45	151±29	0.223
Mean diastolic BP*	85±21	90±13	0.171
MI	33 (43.4)	17 (42.5)	0.924
Thrombolysis	24 (31.6)	14 (35)	0.709
Anti-platelets	76 (100.0)	37 (92.5)	0.016

Data presented as n (%).
mean ±SD.
BP: blood pressure; CAD: coronary artery disease; MI: myocardial infarction.

DISCUSSION

Several studies have shown that blood glucose levels predict the outcome of patients with diabetes and ACS.[7-14] Most of these studies relied on the blood glucose level at first admission as a predictor of outcome,[1,7,8,15] whereas others used fasting blood glucose[15-17] or average glucose levels during the admission period.[18,19] However, there is no well-accepted definition of hyperglycemia as different studies used different glucose levels to define hyperglycemia in this setting.

Several studies have suggested that blood glucose levels between 110mg/dL and ≥200mg/dL are associated with adverse outcomes.[6] In the American Heart Association Scientific Statement on Hyperglycemia and Acute Coronary Syndrome, hyperglycemia was defined as a blood glucose level >140mg/dL at any time during hospitalization.[20] However, the relationship between glycemic status and the outcome may vary depending on the diabetic status of the patient. In non-diabetic patients, the mortality rate increases when blood glucose >120mg/dL, while in diabetic patients, a blood glucose >200 mg/dL is associated with a poor outcome.[6,20]

A large cohort study evaluated the relationship between blood glucose at admission, classified in five different groups (≤110, >110–140, >140–170, >170–240, >240mg/dL), and patients with AMI.[6] They found that both short- and long-term mortality increased linearly with elevated admission glucose level. In patients with established DM, 30-day mortality increased from 10% to 39% and one-year mortality from 22% to 55% as the blood glucose level at admission increased within a range of 110–240mg/dL.[6] However, their measurements consisted of only a single value at admission rather than hyperglycemia during the entire period of hospitalization.

In a large multicenter study from Oman, severe admission hyperglycemia, defined as blood glucose levels ≥200mg/dL, was associated with increased in-hospital mortality among those without previously diagnosed diabetes but not among those with established diabetes.[21]

Despite the differences in blood glucose cut-off points used by different studies, most studies consistently reported a high mortality rate and a high rate of cardiac complications, including CHF, malignant arrhythmia, and cardiogenic shock.[6-14]

Glycosylated hemoglobin (HbA_{1c}) levels have also been studied as a possible predictor of outcome in patients with ACS. Unlike blood glucose levels, studies of HbA_{1c} yielded conflicting results. A study by Chan et al,[22] in patients with diabetes and ACS suggested that HbA_{1c} levels are not associated in short-term (up to six months) outcomes.

In our study, we assessed both the first admission blood glucose level as well as the mean glycemia during hospitalization using the cut-offs of 140mg/dL and 200mg/dL, respectively.

We found no statistically significant difference in the mortality rate between those with an admission blood glucose level of less than 140mg/dL and those with admission blood glucose greater than 140mg/dL. However, mortality rates were higher among those with higher average blood glucose during hospitalization (>200mg/dL).

There are many explanations for the lack of an effect of admission blood glucose on mortality in our study. First, other studies concluded similar results and suggested that it is the fasting blood glucose and not the random blood glucose taken at the time of admission that predicts the mortality in patients with ACS.[19,23]

Because of the retrospective nature of our study, we cannot verify the fasting status of our patients

at the time of admission. Second, this lack of effect could also be attributed to the smaller number of those presenting with a blood glucose of less than 140mg/dL (n=29) compared to those with levels greater than 140mg/dL (n=91). However, both admission blood glucose and average blood glucose during hospitalization were associated with higher rate of complications both at the time of admission as well as during hospitalization.

There are several mechanisms by which hyperglycemia may exacerbate myocardial damage and worsen the prognosis in patients with ACS. First, hyperglycemia induces oxidative stress by producing free radicals, which leads to myocardial cellular injury.[24] Hyperglycemia has also been shown to affect cardiac contractility and reduce both end-diastolic volume and stroke volume by promoting osmotic diuresis and lowering the circulating volume.[25,26]

Our patient population is slightly different from those in previously published studies, reflecting the type of patients treated in an under-resourced setting. First, there is no cardiac catheterization service in our hospital meaning that all patients were treated either with thrombolytic therapy or anticoagulants. Second, all our patients were treated by subcutaneous insulin sliding scale protocols instead of intravenous insulin infusion. However, most patients (65%) achieved good control of blood glucose (<200mg/dL) during their hospitalization.

CONCLUSION

Our study showed that a worse outcome accompanies hyperglycemia during hospital stay in terms of in-hospital mortality and rate of in-hospital complications in patients with diabetes and ACS. Hyperglycemia at admission was also associated with a higher rate of complications, particularly at the time of presentation.

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