Impact of Admission Hyperglycemia on Outcomes of Patients With Acute ST-Elevation Myocardial Infarction

Kenan Ali*

(Received 6 / 11 / 2019. Accepted 17 / 12 / 2019)

□ ABSTRACT □

Objective: the present study aims to evaluate the impact of admission hyperglycemia on short-term outcomes in patients admitted with ST- elevation myocardial infarction (STEMI).

Methods and Patients: Consecutive patients with STEMI admitted to our Coronary Care Unit (CCU) between February 2018 and January 2019 were enrolled in the study. Patients were divided into two groups based on admission glucose level, Group1 (n=60) patients with hyperglycemia ≥200 mg/dl, Group2 (n=88) patients without admission hyperglycemia <200 mg/dl, and their short-term outcomes were compared.

*Results***:** A total of 148 patients were included **,** Mean age was 60.14 ± 12.68 years in (Group 1) versus 54.92 ± 11.4 years in (Group2), P=0.01 and 107(72.29%) were male, hyperglycemia was detected in 60(40.5%) of the patients .

In Univariate analysis, patients Group1 were more likely to experience acute heart failure (38.3% vs. 7.9%, P<0.001), Cardiogenic shock (28.3% vs. 1.1%, P<0.001), and mortality (26.6% vs. 1.1% P<0.001). In Multivariate regression analysis hyperglycemic remains prognostic factor for mortality (OR : 2.7, 95% CI : 2-6.3 , p=0.04) and acute heart failure (OR:7.2,CI95%:2.8-18.2,p=0.0001).

Conclusion: Hyperglycemia at admission is a bad prognostic factor for mortality and acute heart failure in patients with STEMI.

Keywords: ST-segment elevation myocardial infarction; hyperglycemia; mortality

*Master- Faculty of Medecin- Tishreen University- Lattakia- Syria

تاثير ارتفاع سكر الدم عند القبول على مرضى احتشاء العضلة القلبية العابر للجدار

كنان علي*

(تاريخ الإيداع 6 / 11 / 2019. قُبِل للنشر في 17 / 12 /2019)

□ ملخّص □

الهدف: تهدف الدراسة الحالية الى تقييم تاثير فرط سكر الدم عند القبول لدى المرضى المقبولين بقصة احتشاء عضلة قلبية حاد عابر للجدار

الطرق والرضى: تم دراسة جميع المرضى المقبقولين في وحدة العناية المشددة بقصة احتشاء عابرللجدار بين شباط2018 وكانون الثاني 2019

تم تقسيم المرضى الى مجموعتين بناء على قيمة سكر الدم عند القبول،المجموعة الاولى(60مريض) وهي مجموعة فرط سكرالدم عند القبول (<200ملغ/دل)والمجموعة الثانية(88مريض)وهي المجموعة بغياب فرط سكرالدم عند القبول(>200ملغ/دل) تم متابعة المرضى خلال فترة الاستشفاء والمقارنة بينهما ا

النتائج:تبين في التحليل احادي البيانات ان مرضى فرط سكر الدم عند القبول كان لديهم معدل وفيات اعلى بالمقارنة مع مرضى سكر الدم غير المرتفع عند القبول(26%vs.1.1%0.000.1>p

التحليل متعدد البيانات اظهر ان سكر الدم المرتفع عند القبول كان عامل خطرمستقل للوفيات عند مرضى الاحتشاء العابر للجدار(or:95,2:7% ci:2-6,3،p=0,04)

الخلاصة: فرط سكر الدم عند القبول عامل خطر مستقل للوفيات عند مرضى احتشاء العضلة القلبية الحاد العابرللجدار

الكلمات المفتاحية: الاحتشاء العابر للجدار،فرط سكر الدم،الوفيات

* **ماجستير-كلية الطب البشري-جامعة تشرين- اللاذقية-سورية**

Introduction:

Acute myocardial infarction is the leading cause of death worldwide with increasing incidence(1). The identification of risk predictors of mortality is important for tailoring more aggressive therapies that can improve survival in these patients.

Hyperglycemia is common during acute myocardial infarction with reported incidence up to 50% in patients presented with ST- elevation myocardial infarction (STEMI) regardless history of diabetes mellitus.

It is associated with increased risk of mortality and major cardiovascular complications[2]. Several mechanisms have been proposed for the harmful effects of hyperglycemia in STEMI patients. However, it remains unclear whether elevated blood glucose levels are a marker of greater illness severity attributable to more extensive cardiac damage or a risk factor with a direct causal relationship to the observed adverse clinical outcomes[3]. This study will evaluate the impact of hyperglycemia on the outcomes in patients admitted with acute STEMI.

Materials and Methods

study design

In this prospective cohort study, all patients with ST elevation myocardial infarction (STEMI) admitted in CCU between February 2018 and January 2019 were enrolled. Patients baseline characteristics as gender, age, cardiovascular risk factors (smoking, hypertension, diabetes mellitus…etc.) are reported.

Definitions

ST –elevation Myocardial Infarction (STEMI) was defined according to the following criteria:

1-Presence of persistent chest discomfort or pain (>20 min).
2-ST- elevation at the J-point in at least two contiguous leads of ≥ 2.5mm in men < 40 years, ≥2mm in men > 40 years, or ≥ 1.5mm in women in leads V2–V3 and/or ≥ 1mm in the other leads.
3-Detection of a rise and/or fall of serum cardiac biomarkers (CK-MB and cT I or T) [4].

Admission hyperglycemia was defined as glucose level ≥ 200 mg/d(11.0 mmol/L) according to NICE guidelines [5]. Patients were divided into two groups, one with hyperglycemia (glucose ≥200mg/d), and the other group without (admission glucose < 200mg/d) and followed up during the hospital stay.

The primary endpoints of this study were defined as mortality and complications. Outcomes of mortality were all causes of death (cardiogenic and non-cardiogenic). Outcomes of complications included:
Acute heart failure on-admission defined as KILLIP III according to ESC 2017.
Cardiogenic shock defined as KILLIP IV class according to ESC 2017.
Life threatening bleeding (intracranial hemorrhage or decreased Hb≥ 5 g/dL)[6].

Statistical analysis

Differences of distribution examined using the chi-square test or Fisher exact test if it was needed. Initially, univariate analysis is done and p-value less than 0.05 was considered statistically significant. Then, factors with statically significance are put into covariate and multivariate analysis. Odd ratio (OR) more than 2considered significant.

Results

Patients' Baseline characteristics

A total of148 patients admitted with ST-elevation myocardial infarction (STEMI) were enrolled in the study. The Baseline characteristics of patients according to admission blood glucose are listed in Table 1.

Table 1. Baseline characteristics of the study population

Patients	Group1 With hyperglycemia (n= 60)	Group2 Without hyperglycemia n=88	p-value
Gender (male %)	34 (56.6%)	69 (78.4%)	0.005
Age (year)	60.14 ± 12.68	54.92 ± 11.4	0.01
Prognostic factors			
Diabetes	41 (68.3%)	19 (21.6%)	0.0001
Hypertension	38 (63.3 %)	41 (46.6 %)	0.04
Dyslipidemia	22 (36.6 %)	26 (29.5%)	0.4
Obesity (BMI ≥30 kg/m2)	15 (25%)	21 (23.9%)	0.9
Tobacco use	34 (56.6%)	74 (84.1%)	0.0001
Previous CAD	11 (18.3%)	14(15.9%)	0.6
Previous PAD	5 (8.3%)	5 (5.7%)	0.4
Family history	22 (36.6%)	32 (36.4%)	0.7
Lab values			
ABG	318.6±95.4	138±32.2	0.0001

ABG : Admission Blood Glucose

Mean age of the study population was 60.14 ± 12.68 years in Group1 patients versus 54.92 ± 11.4 years in Group2 patients (P=0.01) and 107(72.29%) were male. The mean admission blood glucose was 318.6±95.4 in Group1 patients versus 138±32.2 in Group 2 patients (P<0.001).

Group1 Patients had higher prevalence of prognostic factors: diabetes mellitus and hypertension (P<0.001), whereas Tobacco use was more prevalent in Group2 patients.

Clinical outcomes

The clinical outcomes of patients are listed in Table2.

Table 2. Outcomes during the follow-up period among groups

	Group 1 n (60)	Group 2 n (88)	p-value
Cardiogenic shock	17 (28.3%)	1 (1.1%)	0.0001
Acute heart failure	23 (38.3%)	7 (7.9%)	0.0001
Bleeding	1 (1.6%)	2 (2.3%)	0.7
Mortality	16 (26.6%)	1 (1.1%)	0.0001
Duration of hospitalization	6.36±2.8	4.32±1.1	0.03

In Univariate analysis, mortality, cardiogenic shock, and acute heart failure was more prevalent in Group1 patients (p=0.0001). In addition, group1 patients experienced longer duration of hospitalization (P=0.03).

Admission hyperglycemia as prognostic factor of mortality and complications in STEMI patients is shown in Table3.

Table 3. Multivariate logistic regression analysis of hyperglycemia as a prognostic factor for mortality and complications in STEMI patients

Variable	OR	Confidence interval (95%)	P-value
In-hospital mortality	2.7	[2-6.3]	0.04
Bleeding	0.7	[0.06-4.2]	0.1
Acute heart failure	7.2	[2.8-18.2]	0.0001
Cardiogenic shock	1.6	[1.1-2.3]	0.02

In Multivariate analysis, admission hyperglycemia was independently associated with mortality (OR: 2.7, 95% CI: 2-6.3, p=0.04) and acute heart failure (OR: 7.2, 95% CI 2.8-18.2, p=0.0001). However, admission hyperglycemia was not prognostic factor for Cardiogenic shock and Bleeding, (Odd ratio<2).

Discussion

The incidence of hyperglycemia on admission was 40.5%. Group1 patients had higher prevalence of prognostic factors: a history of hypertension and diabetes mellitus. Higher prevalence of (mortality, cardiogenic shock, acute heart failure and long duration of hospitalization) has been reported in patients Group1. Hyperglycemia is prognostic factor for mortality and acute heart failure.

There are numerous potential pathophysiological mechanisms by which hyperglycemia may impact toxicity during myocardial ischemia.

First, stress hyperglycemia is the result of sympathetic nervous system activation and the hypothalamic-pituitary axis with consequent raised production of catecholamines and cortisol that stimulate processes of gluconeogenesis, glycogenolysis, lipolysis, and free fatty acid formulation [8].

Secondly, hyperglycemia reduces the bioavailability of nitric oxide (NO) because superoxide radical combines with NO to form the strongest toxic ion peroxynitrite, which inactivate function of free radicals scavengers, and these observed in acute hyperglycemia not in sustained elevation of the blood glucose level [9].

Furthermore, admission hyperglycemia increases the release of inflammatory and vasoconstrictive factors, which impair coronary endothelial function, and increases expression of adhesion molecules [9].

In addition, the abnormal metabolic state that accompanies hyperglycemia alters the functional properties of platelets causing changes in their structure, altered Ca homeostasis, increased expression of activation dependent adhesion molecules GPIIb/IIIa and P2Y12, elevated plasminogen activator inhibitor1(PAI-1) levels, elevated clotting factors, and decrease of fibrinolysis and susceptibility to coagulation[10,11]

Admission hyperglycemia may have a role in the attenuation of coronary collateral blood flow, increasing infarct size and producing a significant lengthening of the QT interval, which is a well-known risk factor for sudden death[12].

Finally, hyperglycemia induces apoptosis and decreases ischemic preconditioning [13].

Although the association between admission hyperglycemia and increased mortality and in-hospital complications in patients with STEMI has been confirmed in different studies,

others not revealed this importance of admission hyperglycemia as a prognostic factor for STEMI.

Capes *et al*.2000, showed that patients of ST –elevation myocardial infarction with hyperglycemia are at increased risk of in hospital mortality, heart failure and cardiogenic shock, whereas in our study hyperglycemia was not prognostic factor of Cardiogenic shock [14].

Oswald *et al*. showed that mortality increased significantly in patients of acute myocardial infarction with increasing plasma glucose concentration [15].

This study also consisted with Walid Jomaa *et al* .2018 which found that admission hyperglycemia in STEMI patients independently associated with mortality [16].

Other studies revealed importance of admission hyperglycemia as a prognostic factor for STEMI according to gender, in Julio et al (2012) study mortality was related to admission glucose in men but not in women [17].

Conclusion

Admission hyperglycemia was independently associated with increased mortality and had an additional poor prognostic value in STEMI patients.

Recommendation:

This study suggests that blood glucose should be monitored in patients with STEMI to predict mortality and cardiovascular complications.

Disclosure

The author declared no conflicts of interest. No funding was received for this study.

References

1- W. H. O. Mendis, S., Puska, P., Norrving, B., "Global Atlas on cardiovascular disease prevention and control," vol.30 Geneva. World Health Organization, 2011.

2- G. F. Viana MV, Moraes RB, Fabbrin AR, Santos MF, "Assessment and treatment of hyperglycemia in critically ill patients," vol. 26, no. 1, pp. 71–76, 2014.

3- M. A. Williams, S. B., Goldfine, A. B., Timimi, F. K., Ting, H. H., Roddy, M. A., Simonson, D. C., & Creager, "Acute hyperglycemia attenuates endothelium-dependent vasodilation in humans in vivo," *Ciculation*, vol. 97, no. 17, pp. 1695–1701, 1998.

4-G. H. Germany, A. K. Germany, M. J. Lenzen, E. P. Denmark, and P. Vranckx, "2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST - segment elevation The Task Force for the management of acute myocardial infarction," pp. 1–66, 2017.

5-A. Senthinathan, V. Kelly, and M. Dzingina, "Hyperglycaemia in acute coronary syndromes : summary of NICE guidance," pp. 8–10, 2011.

6-C. Prevention *et al.*, "2016 European Guidelines on cardiovascular disease prevention in clinical practice The Sixth Joint Task Force of the European Society of Cardiology," 2016.

7-Marfella R, Siniscalchi M, Esposito K et al: Effects of stress hyperglycemia on acute myocardial infarction: role of inflammatory immune process in functional cardiac outcome. Diabetes Care, 2003; 26: 3129–35.

8-K.C. Mccowen ,A. Malhorta, and B.R. Bistrian, STRESS-INDUCED, vol.17,no.1,2001.

9- Monnier *et al*,Louis, Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 Diabetes, Jama , vol.14,pp.1681-1687,2006.

10-R.Article,(Platelet activation in type 2 diabetes mellitus , no .March,pp.1282-1291,2004.

11-P.J.Grant et al., ESC GUIDELINES ESC Guidelines on diabetes,pre-diabetes,and cardiovascular disease developed in collaboration with the EASD the European Society of Cardiology (ESC) and developed in collaboration ,pp.3035-30872013.
12-M.D.Amico *et al*. High glucose induces ventricular instability and increases vasomotor tone in rats,pp.464-470,2001.
13-J.R.Kersten *et al.*, Acute hyperglycemia abolishes ischemic preconditioning in vivo ,Am.Physiol.Soc,no.18,pp.721-725,1998.
14-Capes SE,Hunt D,Malmberg K.Stress hyperglycemia and increased risk of death after myocardial infarction in patients with or without diabetes: a systematic overview.Lancet 2000;355:773.
15- Oswald GA, Corcoran S .Prevalence and risks of hyperglycemia and undiagnosed diabetes in patients with acute myocardial infarction .Lancet 1984:1;1264-7.
16- Walid Jomaa,Sana EL Mhamdi,Imen Ben Ali,Faouzi Maatouk.Prognostic value of hyperglycemia on admission in diabetes versus non-diabetes patients presenting with ST- elevation myocardial infarction in Tunisia.Indian Heart Journal 2018:772-776.
17-Julio Yoshio Takada,Roqerio Bicudo Romos,Larissa Cardoso Roza.In-hospital death in acute coronary syndrome was related to admission glucose in men but not in women.Cardiovascular Diabetology 2012.