e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(8); 281-286

Original Research Article

A Hospital-Based Assessment of the Implications of Admission Hyperglycemia in Non-Diabetic Acute Myocardial Infarction Patients

Munindra Kumar[1], Ravi Shankar Singh[2], Manoj Kumar[3]

[1]Assistant Professor, Department of General Medicine, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India

[2]Assistant Professor, Department of General Medicine, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India

[3]Assistant Professor, Department of General Medicine, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India

Received: 20-06-2023 / Revised: 29-07-2023 / Accepted: 12-08-2023
Corresponding Author: Dr. Ravi Shankar Singh
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess the prognostic implications of admission hyperglycemia in non-diabetic acute myocardial infarction patients.

Methods: The study was conducted on 200 non diabetic STEMI patients admitted at department of General Medicine for the period of one year. There were 100 patients in group I and 100 patients in group II.

Results: There was total 127 males and 73 females in the study. Group I had 35 females and 65 males. Group II had 38 females and 62 males. There was no significant difference between the number of males and females in two groups (p= 0.812). The mean age of patients in Group I and Group II were 61.48 ± 11.29 and 64.16 ± 12.38 respectively. There was no significant difference in patients' mean age in between the groups (p= 0.634). There were total 45 (22.5%) smokers in the study of which 25 were in group I and 20 in group II. There was no significant difference in number of smokers in between the two groups (p= 0.314). There were total of 62 patients with history of alcohol consumption in the study. There was no significant difference in number of patients with history of alcohol consumption between the two groups. The history of hypertension was present in 58 patients out of which 26 patients were in Group I and 32 patients in Group II. There was no statistically significant difference in number of hypertensives between the two groups. Mean heart rate, systolic blood pressure and diastolic blood pressure between the two groups. There was a statistically significant difference in heart rate, SBP and DBP between the two groups.

Conclusion: Therefore, hyperglycemia has different effects on the prognosis of patients with diabetes or undiagnosed diabetes. Hyperglycemia is more predictive of adverse events in patients with undiagnosed diabetes compared to those with diagnosed diabetes. Although the pathophysiological mechanism underlying this phenomenon is unknown, there are several explanations. Some undiagnosed diabetic patients, especially those with severe hyperglycemia, may be at high risk because they have never been treated for diabetes.

Keywords: hyperglycemia, non-diabetic, acute myocardial infarction patients, prognosis

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Acute coronary syndromes (ACS) are a leading cause of death worldwide. Although declining, short and long term mortality rates in patients presenting for ST-elevation myocardial infarction (STEMI) remain highly preoccupying. [1] Compared to non-diabetic patients, diabetic ones are known to carry worse early and late outcomes. [2] On the other hand, and depending on the definition used, prevalence of hyperglycemia in different epidemiological studies ranges from 3% to 71% of patients hospitalized for ACS. [3] In patients presenting for STEMI, hyperglycemia on-admission has already been identified as a powerful predictor of adverse outcomes regardless to the implementation of a reperfusion therapeutic either by thrombolysis or primary percutaneous coronary intervention (pPCI). [4,5] Nevertheless, controversy remains as for a possible interaction between diabetic status and the prognostic value of hyperglycemia in patients presenting for STEMI. In patients presenting for STEMI, hyperglycemia on-admission has already been identified as a powerful predictor of adverse outcomes regardless to the implementation of a reperfusion therapeutic either

by thrombolysis or primary percutaneous coronary intervention (pPCI). [6,7] Nevertheless, controversy remains as for a possible interaction between diabetic status and the prognostic value of hyperglycemia in patients presenting for STEMI.

Data are lacking on diabetes status differences in absolute measures of mortality risk associated with admission hyperglycemia. Therefore, there is a critical need to take patients' diabetes status into account to avoid incorrect estimation of the real prevalence of admission hyperglycemia. Previous epidemiological studies showed that 25–50% of ACS patients had elevated blood glucose (BG) level at admission. Recent studies suggest that the effects of hyperglycemia on the prognosis of ACS differ between diagnosed and undiagnosed diabetes. Hyperglycemia is a stronger predictor of adverse events in ACS patients without known diabetes than those with history of diabetes. [8,9]

Acute hyperglycaemia in healthy subjects and in patients with impaired glucose tolerance or overt diabetes produces a rise in inflammatory markers. Following this line of thought, it might be speculated that the detrimental effect of stress hyperglycaemia in acute MI might also stem from its ability to increase inflammation.

The aim of the present study was to assess the prognostic implications of admission hyperglycemia in non-diabetic acute myocardial infarction patients.

Materials and Methods

The study was conducted on 200 non diabetic STEMI patients admitted at department of General Medicine, Lord Buddha Koshi Medical College and Hospital, Saharsa , Bihar, India for the period of one year. There were 100 patients in group I and 100 patients in group II.

Inclusion Criteria:

> Patients with acute myocardial infarction proven by
> ECG (ST segment elevation > 0.1mV in at least 2 contiguous leads)
> Cardiac enzymes (Positive Troponin I or CPK-MB)
> Symptoms suggestive of acute myocardial infarction who have no previous history of diabetes.
> Patients with HbA1c <6.5

Exclusion Criteria:

> Patients who present with Non-ST Elevation MI (NSTEMI)
> Patients with a previous history of diabetes mellitus.
> Patients receiving drugs that are known to elevate blood sugar levels (eg. Corticosteroids)
> Patients who received dextrose containing intravenous fluids before admission.
> Time from the beginning of symptoms to admission to Critical Care Unit more than 48 hrs.

A complete history of all patients was noted. All patients' blood sample was collected on admission for estimating plasma glucose level. Complete general and systemic examination of the patients was done. ECG of all the patients were read and recorded. Patients were examined for complications of AMI including arrhythmias, cardiogenic shock, conduction abnormalities.

Patients were grouped in to TWO categories according to their admission blood glucose levels,

Group I: Blood glucose level ≤ 140 mg%, Group II: If their blood glucose level is > 140 mg%.

The groups were compared to demonstrate correlation between stress hyperglycemia and cardiovascular outcomes of arrhythmias, cardiogenic shock, AV block and death. Normality of data was tested by Kolmogorov- Smirnov test. If the normality was rejected then non parametric test was used. Quantitative variables were compared using Independent t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups. Qualitative variables were correlated using Chi-Square test/Fisher's Exact test. Univariate and multivariate logistic regression was used to assess the significant risk factors of RBS>140. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results

Table 1: Patient details

Parameters	Group I	Group II	P Value
Gender			
Male	65	62	0.812
Female	35	38	
Mean age	61.48 ± 11.29	64.16 ± 12.38	0.634

There were total 127 males and 73 females in the study. Group I had 35 females and 65 males. Group II had 38 females and 62 males. There was no significant difference between the number of males and females in two groups (p= 0.812). The mean age of patients in Group I and Group II were 61.48 ± 11.29 and 64.16 ± 12.38 respectively. There was no significant difference in patients' mean age in between the groups (p= 0.634).

Table 2: Personal and past history

Parameters	Group I	Group II	P Value
Smoking			
Yes	25	20	0.314
No	75	80	
Alcohol			
Yes	32	30	0.710
No	68	70	
Hypertension			
Yes	26	32	0.530
No	74	68	

There were total 45 (22.5%) smokers in the study of which 25 were in group I and 20 in group II. There was no significant difference in number of smokers in between the two groups (p= 0.314). There were total of 62 patients with history of alcohol consumption in the study. There was no significant difference in number of patients with history of alcohol consumption between the two groups. The history of hypertension was present in 58 patients out of which 26 patients were in Group I and 32 patients in Group II. There was no statistically significant difference in number of hypertensives between the two groups.

Table 3: General physical examination

Parameters	Group I	Group II	P Value
Mean heart rate (beats/min)	75.85 ± 12.58	81.83 ± 12.58	0.022
Mean SBP (mmHg)	124.46 ±23.77	113.57 ±24.26	0.001
Mean DBP (mmHg)	78.02 ± 13.67	73.47 ± 15.17	<0.001

Mean heart rate, systolic blood pressure and diastolic blood pressure between the two groups. There was a statistically significant difference in heart rate, SBP and DBP between the two groups.

Table 4: Complications

Complications	Group I	Group II	P Value
Cardiogenic shock	10	20	0.025
Arrhythmias	10	40	0.028
AV Block	6	14	0.045

Total 30 patients developed cardiogenic shock. 10 patients in group I and 20 patients in group II developed cardiogenic shock. There was statistically significant (p= 0.025) increase in number of patients developing cardiogenic shock in group II. A total of 40 patients developed arrhythmias of which 10 patients were in group I and 40 patients in group II. There was a statistically significant increase in number of patients with arrhythmias in group II (p= 0.028). Total 20 patients in the study developed an AV block of ≥2nd degree. 6 patients in group I developed AV block (≥2nd degree) and 14 patients in group II developed AV block. There was a statistically significant (p=0.045) increase in patients developing AV block in group II.

Discussion

Diabetes is an important independent risk factor for coronary atherosclerosis. Many previous studies have confirmed that hyperglycemia at admission is common in patients with acute coronary syndrome (ACS), and it is a risk factor for in hospital death and complications. [10-13] Previous epidemiological studies showed that 25–50% of ACS patients had elevated blood glucose (BG) level at admission. Recent studies suggest that the effects of hyperglycemia on the prognosis of ACS differ between diagnosed and undiagnosed diabetes. Hyperglycemia is a stronger predictor of adverse events in ACS patients without known diabetes than those with history of diabetes. [14,15]

There were total 127 males and 73 females in the study. Group I had 35 females and 65 males. Group II had 38 females and 62 males. There was no significant difference between the number of males and females in two groups (p= 0.812). The mean age of patients in Group I and Group II were 61.48 ± 11.29 and 64.16 ± 12.38 respectively. There was no significant difference in patients' mean age in between the groups (p= 0.634). However, there were significant differences among the three groups in the incidences of the multivessel disease, renal insufficiency, Killip grade III/IV, and emergency PCI (p < 0:05 for all), as well as the levels of high-sensitivity C- creatine kinase isoenzyme MB (CK-

MB) ($p < 0:05$ for all). There were total 45 (22.5%) smokers in the study of which 25 were in group I and 20 in group II. There was no significant difference in number of smokers in between the two groups (p= 0.314). There were total of 62 patients with history of alcohol consumption in the study. There was no significant difference in number of patients with history of alcohol consumption between the two groups. The history of hypertension was present in 58 patients out of which 26 patients were in Group I and 32 patients in Group II. There was no statistically significant difference in number of hypertensives between the two groups. Studies have found that admission hyperglycemia was the greatest risk factor for patients with acute myocardial infarction without diabetes. The 30-day mortality rate of patients without diabetes increased when the admission BG level exceeded 6.1 mmol/L, while the admission BG threshold for the 30-day mortality rate was higher in diabetic patients. Additionally, the increased risk of death associated with high BG level was not limited to known diabetic patients; rather, the mortality rate of patients without diabetes was higher than that of diabetic patients. [16,17] Shacham Y et al [18] reported that admission hyperglycemia was an independent risk factor for acute kidney injury in nondiabetic ST-segment elevation myocardial infarction patients undergoing primary PCI.

Mean heart rate, systolic blood pressure and diastolic blood pressure between the two groups. There was a statistically significant difference in heart rate, SBP and DBP between the two groups. The incidences of severe pump failure, malignant arrhythmia, and death were significantly higher in groups B and C than in group A ($p < 0:05$). The incidences of severe pump failure, malignant arrhythmia, and death were higher in group C than in group B ($p < 0:05$). Kurmus O et al [19] reported that elevated admission BG level attenuated the coronary collateral flow in patients with ST-elevation myocardial infarction. Oka S et al [20] pointed out that glycemic variability was associated with myocardial damage after PCI in nondiabetic ST-segment elevation myocardial infarction patients. Microvascular dysfunction has also been confirmed in acute myocardial infarction patients with hyperglycemia in the study of Simsek et al [21] that evaluated the association of acute-to-chronic glycemic ratio and no reflow in patients with ST-segment elevation myocardial infarction undergoing primary PCI. Shock index on admission was associated with coronary slow/no reflow in patients with acute myocardial infarction undergoing emergent PCI. Wang et al [22] found a higher incidence of no blood flow in patients with hyperglycemia after successful reperfusion.

The relationship between glycemic level on-admission and short term prognosis has been thoroughly investigated in previous studies, however the mechanisms underlying the association between high serum glucose levels and mortality are not fully understood. It is indeed not clear if hyperglycemia is directly implicated in cellular damage or just an associated epiphenomenon and a marker of high stress levels and adrenergic response. [23,24] Total 30 patients developed cardiogenic shock. 10 patients in group I and 20 patients in group II developed cardiogenic shock. There was statistically significant (p= 0.025) increase in number of patients developing cardiogenic shock in group II. A total of 40 patients developed arrhythmias of which 10 patients were in group I and 40 patients in group II. There was a statistically significant increase in number of patients with arrhythmias in group II (p= 0.028). Total 20 patients in the study developed an AV block of ≥2nd degree. 6 patients in group I developed AV block (≥2nd degree) and 14 patients in group II developed AV block. There was a statistically significant (p=0.045) increase in patients developing AV block in group II. In acutely hyperglycemic mice, the level of tissue plasminogen activator was decreased and the level of plasminogen activation inhibitor was increased. Hyperglycemia in type 2 diabetic patients (abnormal glycemic clamp technique) was associated with increased activity of thromboxane A2 (TXA2) and von Willebrand factor. Acute hyperglycemia caused fibrinogen t1/2 to decrease and induced platelet aggregation, thereby increasing the levels of fibrinogen A, prothrombin, and factor VII levels. These changes indicate a prothrombotic state. The increased BG level was accompanied by increased vascular inflammatory markers. [25,26]

Conclusion

Therefore, hyperglycemia has different effects on the prognosis of patients with diabetes or undiagnosed diabetes. Hyperglycemia is more predictive of adverse events in patients with undiagnosed diabetes compared to those with diagnosed diabetes. Although the pathophysiological mechanism underlying this phenomenon is unknown, there are several explanations. Some undiagnosed diabetic patients, especially those with severe hyperglycemia, may be at high risk because they have never been treated for diabetes. In addition, in patients with unknown diabetes and hyperglycemia, when acute myocardial infarction occurs, even if blood glucose was significantly elevated, insulin therapy was rarely used. In view of the possible beneficial effect of insulin on myocardial ischemia, this difference in treatment may explain the different prognosis. Finally, it is possible that similar BG level may represent a more serious condition in unknown diabetic patients. There are still many gaps in understanding the relationship between hyperglycemia and the adverse prognosis. Further

studies are needed to confirm whether hyperglycemia is an indicator of high mortality.

References

1. Authors/Task Force Members, Steg PG, James SK, Atar D, Badano LP, Lundqvist CB, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). European heart journal. 2012 Oct 1;33(20): 25 69-619.
2. Buntaine AJ, Shah B, Lorin JD, Sedlis SP. Revascularization strategies in patients with diabetes mellitus and acute coronary syndrome. Current cardiology reports. 2016 Aug; 18:1-9.
3. Angeli F, Reboldi G, Poltronieri C, Lazzari L, Sordi M, Garofoli M, Bartolini C, Verdecchia P. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. Therapeutic advances in cardiovascular disease. 2015 Dec;9(6):412-24.
4. Malmberg K, Norhammar A, Wedel H, Rydén L. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. Circulation. 1999 May 25;99(20): 2626-32.
5. Timmer JR, Hoekstra M, Nijsten MW, van der Horst IC, Ottervanger JP, Slingerland RJ, Dambrink JH, Bilo HJ, Zijlstra F, van't Hof AW. Prognostic value of admission glycosylated hemoglobin and glucose in nondiabetic patients with ST-segment–elevation myocardial infarction treated with percutaneous coronary intervention. Circulation. 2011 Aug 9;124 (6):704-11.
6. Malmberg K, Norhammar A, Wedel H, Rydén L. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. Circulation. 1999;99(May (20)):262 6–2632.
7. Timmer JR, Hoekstra M, Nijsten MW, et al. Prognostic value of admission glycosylated hemoglobin and glucose in nondiabetic patients with STsegment-elevation myocardial infarction treated with percutaneous coronary intervention. Circulation. 2011;124(August (6)):704–711.
8. Cui CY, Zhou MG, Cheng LC, Ye T, Zhang YM, Zhu F, Li SY, Jiang XL, Chen Q, Qi LY, Chen X. Admission hyperglycemia as an independent predictor of long-term prognosis in acute myocardial infarction patients without diabetes: A retrospective study. Journal of diabetes investigation. 2021 Jul;12(7):1244-51.
9. Ding XS, Wu SS, Chen H, Zhao XQ, Li HW. High admission glucose levels predict worse short-term clinical outcome in non-diabetic patients with acute myocardial infraction: a retrospective observational study. BMC Cardiovascular Disorders. 2019 Dec;19(1):1-9.
10. Kim EJ, Jeong MH, Kim JH, Ahn TH, Seung KB, Oh DJ, Kim HS, Gwon HC, Seong IW, Hwang KK, Chae SC. Clinical impact of admission hyperglycemia on in-hospital mortality in acute myocardial infarction patients. International journal of cardiology. 2017 Jun 1;2 36:9-15.
11. Chung JW, Park YS, Seo JE, Son Y, Oh CW, Lee CH, Nam JH, Lee JH, Son JW, Kim U, Park JS. Clinical impact of dysglycemia in patients with an acute myocardial infarction. Diabetes & Metabolism Journal. 2021 Mar 1;45 (2):270-4.
12. Zhao Q, Zhang TY, Cheng YJ, Ma Y, Xu YK, Yang JQ, Zhou YJ. Prognostic significance of relative hyperglycemia after percutaneous coronary intervention in patients with and without recognized diabetes. Current vascular pharmacology. 2021 Jan 1;19(1):91-101.
13. Shahid M, Zarif HM, Farid MS, Abid MS, Akhtar B, Khan MR. Prognostic value of hyperglycemia on admission on in-hospital outcomes in patients presenting with ST-elevation myocardial infarction. Cureus. 2020 Feb 17; 12(2).
14. Ding XS, Wu SS, Chen H, Zhao XQ, Li HW. High admission glucose levels predict worse short-term clinical outcome in non-diabetic patients with acute myocardial infraction: a retrospective observational study. BMC Cardiovascular Disorders. 2019 Dec;19(1):1-9.
15. Cui CY, Zhou MG, Cheng LC, Ye T, Zhang YM, Zhu F, Li SY, Jiang XL, Chen Q, Qi LY, Chen X. Admission hyperglycemia as an independent predictor of long-term prognosis in acute myocardial infarction patients without diabetes: A retrospective study. Journal of diabetes investigation. 2021 Jul;12(7):1244-51.
16. Kosiborod M. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. Endocrinology and Metabolism Clinics. 2018 Mar 1;47(1):185-202.
17. Deedwania P, Kosiborod M, Barrett E, Ceriello A, Isley W, Mazzone T, Raskin P. Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2008 Mar 25;117(12):1610-9.
18. Shacham Y, Gal-Oz A, Leshem-Rubinow E, Arbel Y, Keren G, Roth A, Steinvil A. Admission glucose levels and the risk of acute kidney

injury in nondiabetic ST segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention. Cardiorenal medicine. 2015 May 30;5(3):191-8.
19. Kurmus O, Aslan T, Ekici B, Baglan Uzunget S, Karaarslan S, Tanindi A, Erkan AF, Akgul Ercan E, Kervancıoglu C. Impact of admission blood glucose on coronary collateral flow in patients with ST-elevation myocardial infarction. Cardiology Research and Practice. 2018 Oct;2018.
20. Oka S, Deyama J, Umetani K, Harama T, Shimizu T, Makino A, Sano K, Nakamura M. Glycemic variability is associated with myocardial damage in nondiabetic patients with ST-elevation myocardial infarction. Cardiovascular endocrinology & metabolism. 2018 Jun;7(2):47.
21. Şimşek B, Çınar T, Ozan V, İnan TD, Zeren G, Avcı İİ, Güngör B, Yılmaz F, Tanboğa İH, Karabay CY. The association of acute-to-chronic glycemic ratio with no-reflow in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Kardiologia Polska (Polish Heart Journal). 2021;79(2):170-8.
22. Wang Q, Shen H, Mao H, Yu F, Wang H, Zheng J. Shock index on admission is associated with coronary slow/no reflow in patients with acute myocardial infarction undergoing emergent percutaneous coronary intervention. Journal of Interventional Cardiology. 2019 Jul 25;2019.
23. McCowen KC, Malhotra A, Bistrian BR. Stress-induced hyperglycemia. Crit Care Clin. 2001;17(January (1)):107–124.
24. Huberlant V, Preiser JC. Year in review 2009: critical care–metabolism. Crit Care. 2010;14 (6):238.
25. Vanessa Fiorentino T, Prioletta A, Zuo P, Folli F. Hyperglycemia-induced oxidative stress and its role in diabetes mellitus related cardiovascular diseases. Current pharmaceutical design. 2013 Oct 1;19(32):5695-703.
26. Yahagi K, Kolodgie FD, Lutter C, Mori H, Romero ME, Finn AV, Virmani R. Pathology of human coronary and carotid artery atherosclerosis and vascular calcification in diabetes mellitus. Arteriosclerosis, thrombosis, and vascular biology. 2017 Feb;37(2):191-204.