Original research article

An observational study to assess the prognostic implications of admission hyperglycemia in non-diabetic acute myocardial infarction patients

[1]Dr. Archana, [2]Dr. Abhishek Kumar

[1]Associate Professor, Department of Medicine, Rama Medical College, Kanpur, Uttar Pradesh, India

[2]MBBS MD Medicine DNB Cardiology

Corresponding Author:
Dr. Archana

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: This was a retrospective analysis of prospectively enrolled consecutive NSTE-ACS patients treated at the Department of Medicine, Rama Medical College, Kanpur, Uttar Pradesh, India for the period of 1.6 years. A total of 500 patients with NSTE-ACS and high BG without history of diabetes were enrolled.

Results: There was no significant difference among the three groups in terms of age, sex, hypertension, hyperlipidemia, smoking, and history of myocardial infarction (*p*> 0:05 for all). 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). 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). Logistic regression analysis was performed with in-hospital death as the dependent variable and the previously identified risk factors as independent variables. The results showed that hyperglycemia, age, renal insufficiency, and severe pump failure were risk factors of in-hospital death.

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

Introduction

Acute myocardial infarction (AMI) is a serious type of coronary heart disease and an important cause of death from cardiovascular disease. Despite the tendency to standardize the diagnosis and treatment of AMI patients in recent years, mortality is still high [1]. Quick identification of high-risk patients, strengthening the treatment and nursing, and improving prognosis are still issues that require attention. Major advances in cardiovascular disease, and specifically the treatment of acute coronary syndrome (ACS), have had a significant impact on the morbidity and mortality of patients with acute myocardial infarctions (AMI). Despite these advances, diabetes continues to put patients with and without a prior history of myocardial infarction at significant cardiovascular risk [2]. Although declining, short and long term mortality rates in patients presenting for ST-elevation myocardial infarction (STEMI) remain highly preoccupying [3]. Compared to non-diabetic patients, diabetic ones are known to carry worse early and late outcomes [4]. 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 [5]. 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.

Hyperglycemia during hospital admission is common in patients with AMI and independently associated with worse prognosis, although the association may be nonlinear, and data confict as to whether this association varies by diabetes status. Admission hyperglycemia occurs in 25-50% of patients, depending on the defnition of admission hyperglycemia. Tere is still no consensus on what blood glucose level defnes admission hyperglycemia. It is well known that diabetes is a common comorbidity in patients with cardiovascular diseases. Patients with AMI and diabetes show a more than two-fold higher risk for short and long-term mortality than patients without diabetes [8].

Elevated admission glucose levels in non-diabetic patients with acute myocardial infarction are independently associated with large infarct sizes and a higher mortality rate when compared with patients with normal glucose levels [9]. A strong correlation between glycaemia and shock or development of heart failure has also been reported [10, 11].

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

This was a retrospective analysis of prospectively enrolled consecutive NSTE-ACS patients treated at the Department of Medicine, Rama Medical College, Kanpur, Uttar Pradesh, India for the period of 1.6 years. NSTE-ACS was diagnosed on the basis of typical angina symptoms lasting for >10 minutes, accompanied by at least one of the following: ST-segment depression ≥ 0:5 mm, 0.5–1.0 mm transient ST-segment elevation in two consecutive leads for <30 minutes, T-wave inversion > 1 mm before the chest pain or within 12 hours after the chest pain, and/or myocardial enzymes (cardiac troponin T (TnT) or creatine kinase isozymes MB (CK- MB)) exceeding the upper limit of the normal values. Patients were excluded if they had past diabetes, incomplete clinical and coronary angiography data, admission BG level > 20 mmol/L, symptoms of ketoacidosis, and/or new-onset diabetes. A total of 500 patients with NSTE-ACS and high BG without history of diabetes were enrolled.

Research and Treatment Methods

Patients with suspected ACS underwent an electrocardiogram (ECG) and measurement of the BG level (hexokinase method, Olympus AU400) and myocardial injury markers. ACS was classified by the cardiovascular doctor into unstable angina pectoris, acute ST-segment elevation myocardial infarction, and acute NSTE myocardial infarction based on the ECG and levels of myocardial injury markers. Emergency coronary angiography was performed on patients in a critical condition, such as intractable or recurrent angina pectoris with dynamic ST-segment changes, heart failure, life-threatening arrhythmia, or hemodynamic instability. Stents were implanted in these patients according to the disease condition after the target vessel was determined. Other patients in a less critical state underwent percutaneous coronary intervention (PCI).

After admission to the Department of Cardiology, the BG level of the patients was checked and ACS was classified into diff erent types. We identified 760 NSTE-ACS with hyperglycemia but excluded 260 patients due to history of diabetes, incomplete data, BG level > 20 mmol/L, symptoms of keto- acidosis, or new-onset diabetes mellitus. Finally, 498 NSTE-ACS patients were included in the study. Based on the BG level, NSTE-ACS patients were divided into three groups: A (BG < 7:8 mmol/L), B (7:8 mmol/L ≤ BG < 11:1 mmol/L), and C (BG ≥ 11:1 mmol/L). The risk factors for ACS were recorded for each group, including age, hypertension, hyperlipidemia, smoking history, clinical biochemical indexes, inflammatory markers, and left ven-tricular ejection fraction as measured by echocardiography. SPSS software (IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. Diff erences were considered statistically significant at $p < 0:05$.

Data Quality Control

The quality of the statistical data aff ects the research accuracy. Data quality control requires scientific and rigorous work. In the context of big data, the quality and efficiency of hospital data should be continuously improved.

All of the departments providing the data were incorporated into the information construction by our hospital to establish an ideal data quality management system. The hospital employees continuously regularly their skills and were familiar with the operation process of the information sys- tem. Our hospital regularly monitored the data operation and randomly checked the quality and standardization of the statistical to identify and solve potential problems. This ensured smooth information interaction in the hospital and improved the accuracy of the information. It also provided a solid foundation for the data quality control in our research.

Statistical Methods

SPSS software (version 25; IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. Categorical variables are expressed as numbers or percentages. Means between the multiple groups were compared using one-way ANOVA. Multivariate logistic stepwise regression was used to calculate the odds ratio (OR) for the predictors of in-hospital death and their impact on the outcomes.

Results

Table 1: Comparison of the baseline characteristics of the three groups

Group (*n*)	A (*n* = 100)	B (*n* = 200)	C (*n* = 200)	*p* value
Male, *n* (%)	75 (75)	140 (70)	144 (72)	0.84
Age (year)	62±8	64±6	72±8	0.68
Hypertension, *n* (%)	81 (81)	170 (85)	180 (90)	0.88
Hyperlipidemia, *n* (%)	54 (54)	96 (48)	120 (60)	0.36
Smoking, *n* (%)	61 (61)	126 (63)	144 (72)	0.76
Renal inadequacy, *n* (%)	6 (4.8)	18 (11)	28 (13.3)	0.07
Old myocardial infarction, *n* (%)	10 (10)	36 (18)	44 (22)	0.28
Triple vessel disease, *n* (%)	35 (35)	28 (56)	172 (86)	<0.01
Emergency PCI, *n* (%)	66 (66)	150 (75)	160 (80)	0.02
Admission blood glucose (mmol/L)	6:2±1:3	9:3±1:5	17:5±4:4	<0.01
TnT, *n* (%)	9 (9)	76 (38)	104 (52)	<0.05
CK-MB, *n* (%)	5 (5)	48 (24)	90 (45)	<0.05
Killip grading III/IV, *n* (%)	12 (12)	52 (26)	100 (50)	0.01
Hs-CRP (mg/L)	1:31±0:93	2:13±0:25	3:06±2:61	<0.01

There was no significant diff erence among the three groups in terms of age, sex, hypertension, hyperlipidemia, smoking, and history of myocardial infarction (*p*> 0:05 for all). However, there were significant diff erences 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).

Table 2: Comparison of in-hospital outcomes of the three groups

Groups	Number	Pump failure, *n* (%)	Malignant arrhythmia, *n* (%)	Target lesion revascularization, *n* (%)	Death, *n* (%)
A	100	12 (12)	9 (9)	3 (3)	1 (1)
B	200	52 (26)	22 (11)	8 (4)	12 (6)
C	200	72 (36)	50 (25)	12 (6)	24 (12)

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).

Table 3: Multivariate logistic regression analysis of in-hospital death

Item	Odds ratio	95% CI	*p* value
Age	1.04	(0.91, 1.14)	0.25
Hyperglycemia at admission	1.82	(1.26, 2.41)	<0.01
Killip grading III/IV	2.18	(1.03, 3.96)	0.03
Renal insufficiency	1.14	(1.03, 1.21)	0.07

Logistic regression analysis was performed with in-hospital death as the dependent variable and the previously identified risk factors as independent variables. The results showed that hyperglycemia, age, renal insufficiency, and severe pump failure were risk factors of in-hospital death.

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 inhospital death and complications [12, 15]. 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 [16, 17].

There was no significant diff erence among the three groups in terms of age, sex, hypertension, hyperlipidemia, smoking, and history of myocardial infarction (*p*> 0:05 for all). However, there were significant diff erences 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). 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 [18, 19]. Yacov *et al* [20] reported that admission hyperglycemia was an independent risk factor for acute kidney injury in nondiabetic ST-segment elevation myocardial infarction patients undergoing primary PCI.

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 ($p< 0:05$). Ozge *et al* [21] reported that elevated admission BG level attenuated the coronary collateral flow in patients with ST-elevation myocardial infarction. Satoshi *et al* [22] 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* [23] 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* [24] 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 [25, 26]. Logistic regression analysis was performed with in-hospital death as the dependent variable and the previously identified risk factors as independent variables. The results showed that hyperglycemia, age, renal insufficiency, and severe pump failure were risk factors of in-hospital death. 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 [27, 28].

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. Li J, Li X, Wang Q, Hu S, Wang Y, Masoudi FA, *et al*. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. The Lancet. 2015 Jan 31;385(9966):441-51.
2. Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. New England journal of medicine. 1998 Jul 23;339(4):229-34.
3. Steg PG, James SK, Atar D. 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). Eur Heart J. 2012;33:2569-2619.
4. Buntaine AJ, Shah B, Lorin JD, Sedlis SP. Revascularization strategies in patients with diabetes mellitus and acute Coronary syndrome. Curr Cardiol Rep. 2016;18(8):79.
5. Angeli F, Reboldi G, Poltronieri C. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. Ther Adv Cardiovasc Dis. 2015;9(6):412-424.

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(20):2626-2632.
7. Timmer JR, Hoekstra M, Nijsten MW. Prognostic value of admission glycosylated hemoglobin and glucose in nondiabetic patients with STsegment-elevation myocardial infarction treated with percutaneous coronary intervention. Circulation. 2011;124(6):704-711.
8. Upur H, Li JL, Zou XG, Hu YY, Yang HY, Abudoureyimu A, *et al*. Short and long-term prognosis of admission hyperglycemia in patients with and without diabetes after acute myocardial infarction: a retrospective cohort study. Cardiovascular diabetology. 2022 Jun 23;21(1):114.
9. Sanjuán R, Núñez JM, Blasco L. Prognostic Implications of Stress Hyperglycemia in Acute ST Elevation Myocardial Infarction. Prospective Observational Study. Revista Española de Cardiología. 2011;64(3):201-204.
10. Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increase risk of death after myocardial infarction in patient with or without diabetes: A systematic overview. Lancet. 2000;355:773-8.
11. Jaśkiewicz F, Supeł K, Koniarek W, Zielińska M. Admission hyperglycemia in patients with acute coronary syndrome complicated by cardiogenic shock. Cardiol J. 2015;22(3):290-5.
12. Kim EJ, Jeong MH, Kim JH, Ahn TH, Seung KB, Oh DJ, *et al*. Clinical impact of admission hyperglycemia on in-hospital mortality in acute myocardial infarction patients. International journal of cardiology. 2017 Jun 1;236:9-15.
13. Chung JW, Park YS, Seo JE, Son Y, Oh CW, Lee CH, *et al*. Clinical impact of dysglycemia in patients with an acute myocardial infarction. Diabetes & Metabolism Journal. 2021 Mar 1;45(2):270-4.
14. Zhao Q, Zhang TY, Cheng YJ, Ma Y, Xu YK, Yang JQ, *et al*. 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.
15. Shahid M, Zarif HM, Farid MS, Abid MS, Akhtar B, Khan MR, *et al*. Prognostic value of hyperglycemia on admission on in-hospital outcomes in patients presenting with ST-elevation myocardial infarction. Cureus. 2020 Feb 17, 12(2).
16. 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.
17. Cui CY, Zhou MG, Cheng LC, Ye T, Zhang YM, Zhu F, *et al*. 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.
18. Kosiborod M. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. Endocrinology and Metabolism Clinics. 2018 Mar 1;47(1):185-202.
19. Deedwania P, Kosiborod M, Barrett E, Ceriello A, Isley W, Mazzone T, *et al*. 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.
20. Shacham Y, Gal-Oz A, Leshem-Rubinow E, Arbel Y, Keren G, Roth A, *et al*. 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.
21. Kurmus O, Aslan T, Ekici B, Baglan Uzunget S, Karaarslan S, Tanindi A, *et al*. Impact of admission blood glucose on coronary collateral flow in patients with ST-elevation myocardial infarction. Cardiology Research and Practice. 2018 Oct; c2018.
22. Oka S, Deyama J, Umetani K, Harama T, Shimizu T, Makino A, *et al*. Glycemic variability is associated with myocardial damage in nondiabetic patients with ST-elevation myocardial infarction. Cardiovascular endocrinology & metabolism. 2018 Jun;7(2):47.
23. Şimşek B, Çınar T, Ozan V, İnan TD, Zeren G, Avcı İİ, *et al*. 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.
24. Wang Q, Shen H, Mao H, Yu F, Wang H, Zheng J, *et al*. 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; c2019.
25. McCowen KC, Malhotra A, Bistrian BR. Stress-induced hyperglycemia. Crit Care Clin. 2001;17(1):107-124.
26. Huberlant V, Preiser JC. Year in review 2009: critical care–metabolism. Crit Care. 2010;14(6):238.
27. Vanessa Fiorentino T, Prioletta A, Zuo P, Folli F. Hyperglycemia-induced oxidative stress and its

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 11, 2023

role in diabetes mellitus related cardiovascular diseases. Current pharmaceutical design. 2013 Oct 1;19(32):5695-703.

28. Yahagi K, Kolodgie FD, Lutter C, Mori H, Romero ME, Finn AV, *et al*. 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.