

## A Prognostic Implications of Admission Hyperglycemia in Non-Diabetic Acute Myocardial Infarction Patients

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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 in the Department of Medicine, Government medical College and Hospital, Madhepura, Bihar, India on 100 non diabetic STEMI patients admitted from May 2022 to June 2023. There were 50 patients in group I and 50 patients in group II.

**Results:** There were total 73 males and 27 females in the study. Group I had 15 females and 35 males. Group II had 12 females and 38 males. There was no significant difference between the number of males and females in two groups ( $p=0.723$ ). The mean age of patients in Group I and Group II were  $60.42 \pm 12.28$  and  $65.15 \pm 13.37$  respectively. There was no significant difference in patients' mean age in between the groups ( $p=0.550$ ). There were total 22 smokers in the study of which 10 were in group I and 12 in group II. There was no significant difference in number of smokers in between the two groups ( $p=0.282$ ). There were total of 29 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 31 patients out of which 13 patients were in Group I and 28 patients in Group II. There was no statistically significant difference in number of hypertensives 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

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### Introduction

Hyperglycemia during hospital admission is common in patients with AMI and independently associated with worse prognosis [1-4], although the association may be nonlinear [5] and data conflict as to whether this association varies by diabetes status. [4,6,7] Admission hyperglycemia occurs in 25–50% of patients, depending on the definition of admission hyperglycemia. [8] There is still no consensus on what blood glucose level defines admission hyperglycemia. It is well known that diabetes is a common comorbidity in patients with cardiovascular diseases. [9] Patients with AMI and diabetes show a more than two-fold higher risk for short and long-term mortality than patients without diabetes. [10,11] Previous studies showed a stronger association between a diagnosis of clinical diabetes

and incident mortality in hyperglycemia patients than non-hyperglycemia patients without diabetes when using the same prognostic cutoff value for both diabetic and non-diabetic patients. [1] Contributors to such diabetes status-based differences are not clear, although disparities in the prevalence of uncontrolled blood glucose and mortality are a possibility. Data are also lacking on diabetes status differences in the prognostic relevance of the blood glucose levels for defining admission hyperglycemia.

Although less is known about the association between admission hyperglycemia and mortality by diabetes status, recent studies demonstrated that admission hyperglycemia was an independent

predictor of mortality in AMI patients without diabetes when used the same or different cutoff values for diabetic and non-diabetic patients. [4,7] 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.

Cardiovascular magnetic resonance imaging (CMRI) allows for high-resolution assessment of myocardial necrosis and microvascular damage providing a robust and highly reproducible in vivo tissue characterization in patients with MI. [12-14] To date, this imaging technique has only been applied in a limited number of patients to assess the relationship between hyperglycemia and myocardial damage in MI. [15,16] Particularly CMRI data from large unselected, consecutive patient series with evolving STEMI including patients with and without established DM treated by contemporary acute MI management are lacking.

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 in the Department of Medicine, Government medical College and Hospital, Madhepura, Bihar, India from May 2022 to June 2023, on 100 non diabetic STEMI patients admitted from. There were 50 patients in group I and 50 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
<b>Gender</b>			
Male	35	38	0.723
Female	15	12	
Mean age	60.42 ± 12.28	65.15 ± 13.37	0.550

There were total 73 males and 27 females in the study. Group I had 15 females and 35 males. Group II had 12 females and 38 males. There was no significant difference between the number of males and females in two groups (p= 0.723). The mean age

of patients in Group I and Group II were 60.42 ± 12.28 and 65.15 ± 13.37 respectively. There was no significant difference in patients' mean age in between the groups (p= 0.550).

**Table 2: Personal and past history**

Parameters	Group I	Group II	P Value
<b>Smoking</b>			
Yes	10	12	0.282
No	40	38	
<b>Alcohol</b>			
Yes	14	15	0.643
No	36	35	
<b>Hypertension</b>			
Yes	13	18	0.545
No	37	32	

There were total 22 smokers in the study of which 10 were in group I and 12 in group II. There was no significant difference in number of smokers in between the two groups ( $p=0.282$ ). There were total of 29 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 31 patients out of which 13 patients were in Group I and 18 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)	76.84 ± 13.57	82.84 ± 11.59	0.032
Mean SBP (mmHg)	125.45 ± 24.76	114.56 ± 25.25	0.001
Mean DBP (mmHg)	79.01 ± 14.66	74.46 ± 16.14	<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	5	12	0.028
Arrhythmias	5	20	0.032
AV Block	3	7	0.040

Total 17 patients developed cardiogenic shock. 5 patients in group I and 12 patients in group II developed cardiogenic shock. There was statistically significant ( $p=0.028$ ) increase in number of patients developing cardiogenic shock in group II. A total of 25 patients developed arrhythmias of which 5 patients were in group I and 20 patients in group II. There was a statistically significant increase in number of patients with arrhythmias in group II ( $p=0.032$ ). Total 10 patients in the study developed an AV block of  $\geq 2$ nd degree. 3 patients in group I developed AV block ( $\geq 2$ nd degree) and 7 patients in group II developed AV block. There was a statistically significant ( $p=0.040$ ) increase in patients developing AV block in group II.

### Discussion

Acute myocardial infarction (AMI) is one of the highest morbidity and mortality diseases in the world. [17] Although timely and effective revascularization and drug use have improved the clinical outcomes of AMI, the mortality rate of AMI remains high. Additionally, other clinical factors affecting the mortality of patients with AMI are

considered. Hyperglycemia is a universal clinical phenomenon in critically ill patients, and more and more evidence has shown that it is related to the severity and mortality of the disease. [18] Diabetes promotes the occurrence and development of AMI. For patients with AMI with diabetes, the prognosis is relatively poor and the mortality rate is high. [19]

There were total 73 males and 27 females in the study. Group I had 15 females and 35 males. Group II had 12 females and 38 males. There was no significant difference between the number of males and females in two groups ( $p=0.723$ ). The mean age of patients in Group I and Group II were  $60.42 \pm 12.28$  and  $65.15 \pm 13.37$  respectively. There was no significant difference in patients' mean age in between the groups ( $p=0.550$ ). There were total 22 smokers in the study of which 10 were in group I and 12 in group II. There was no significant difference in number of smokers in between the two groups ( $p=0.282$ ). There were total of 29 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 31 patients out of which 13 patients were in Group I and 28 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. There was a statistically significant increase in heart rate in group II i.e. patients with hyperglycemia. This was in concordance with the previous studies by Kadri et al and Suleiman et al and Modenesi et al. [20-22]

Some studies showed that persisting hyperglycemia was a more accurate and stronger independent predictor of risk than admission blood glucose. Hyperglycemia (blood glucose  $\geq 8.9$  mmol/L), persists from admission to at least 24 h after symptom onset, is associated both with reduced myocardial perfusion despite patency of the infarct-related artery and with pre-discharge left ventricular impairment. [23] In another study, persistent hyperglycemia in myocardial infarction has a stronger relation with 30-day MACE than elevated glucose at admission. [24] Fasting glucose was superior to admission glucose with regard to 30-day mortality in previous study. [21] The superiority of FBG over random glucose levels in predicting outcome probably results from factors such as differences in the amount of caloric intake and time since the last meal. In a recent study, random blood glucose and FBG were positively correlated with the Gensini score in AMI patients, and FBG was an independent risk factor for the Gensini score in AMI patients. [25] These findings demonstrate that acute and continuing elevation of blood glucose, rather than an underlying "diabetic state", may promote microvascular dysfunction, contributing to poorer outcomes. In 1219 non-diabetic patients after AMI, higher admission glucose concentrations predicted greater mortality, while larger reductions in glucose over 24 h predicted lower 30-day mortality. Baseline glucose and the 24-h change in glucose remained significant predictors of 180-day death. [26]

Total 17 patients developed cardiogenic shock. 5 patients in group I and 12 patients in group II developed cardiogenic shock. There was statistically significant ( $p=0.028$ ) increase in number of patients developing cardiogenic shock in group II. A total of 25 patients developed arrhythmias of which 5 patients were in group I and 20 patients in group II. There was a statistically significant increase in number of patients with arrhythmias in group II ( $p=0.032$ ). Total 10 patients in the study developed an AV block of  $\geq 2$ nd degree. 3 patients in group I developed AV block ( $\geq 2$ nd degree) and 7 patients in group II developed AV block. There was a statistically significant ( $p=0.040$ ) increase in patients developing AV block in group II. The

endothelial dysfunction inactivates nitric oxide and increases oxidative stress, responsible for the production of oxygen reactive species. [27] The production of those radicals activates transcription and growth factors and secondary mediators. Through direct tissue lesion or activation of those secondary mediators, hyperglycemia-induced oxidative stress causes additional lesion to myocytes. [27,28] There is evidence that the prothrombotic state generated by hyperglycemia originates from reduced plasma fibrinolytic activity and action of tissue plasminogen activator. [29]

### 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.

### References

1. Paolisso P, Foà A, Bergamaschi L, Angeli F, Fabrizio M, Donati F, Toniolo S, Chiti C, Rinaldi A, Stefanizzi A, Armillotta M, Sansonetti A, Magnani I, Iannopolo G, Rucci P, Casella G, Galie N, Pizzi C. Impact of admission hyperglycemia on short and long-term prognosis in acute myocardial infarction: MINOCA versus MIOCA. *Cardiovasc Diabetol*. 2021 Sep 24;20(1):192.
2. Sia CH, Chan MH, Zheng H, Ko J, Ho AF, Chong J, Foo D, Foo LL, Lim PZ, Liew BW, Chai P, Yeo TC, Tan HC, Chua T, Chan MY, Tan JWC, Bulluck H, Hausenloy DJ. Optimal glucose, HbA1c, glucose-HbA1c ratio and stress-hyperglycaemia ratio cut-off values for predicting 1-year mortality in diabetic and non-diabetic acute myocardial infarction patients. *Cardiovasc Diabetol*. 2021 Oct 19;20(1):211.
3. Ferreira JA, Baptista RM, Monteiro SR, Gonçalves FM, Monteiro PF, Gonçalves LM. Admission hyperglycemia and all-cause mortality in diabetic and non-diabetic patients with acute myocardial infarction: a tertiary center analysis. *Intern Emerg Med*. 2021 Nov; 16(8):2109-2119.

4. Kim EJ, Jeong MH, Kim JH, Ahn TH, Seung KB, Oh DJ, Kim HS, Gwon HC, Seong IW, Hwang KK, Chae SC, Kim KB, Kim YJ, Cha KS, Oh SK, Chae JK; KAMIR-NIH registry investigators. Clinical impact of admission hyperglycemia on in-hospital mortality in acute myocardial infarction patients. *Int J Cardiol.* 2017 Jun 1;236:9-15.
5. Cid-Alvarez B, Gude F, Cadarso-Suarez C, Gonzalez-Babarro E, Rodriguez-Alvarez MX, Garcia-Acuna JM, Gonzalez-Juanatey JR. Admission and fasting plasma glucose for estimating risk of death of diabetic and nondiabetic patients with acute coronary syndrome: nonlinearity of hazard ratios and time-dependent comparison. *Am Heart J.* 2009 Dec;158(6):989-97.
6. Marenzi G, Cosentino N, Milazzo V, De Metrio M, Cecere M, Mosca S, Rubino M, Campodonico J, Moltrasio M, Marana I, Grazi M, Lauri G, Bonomi A, Veglia F, Manfrini R, Bartorelli AL. Prognostic Value of the Acute-to-Chronic Glycemic Ratio at Admission in Acute Myocardial Infarction: A Prospective Study. *Diabetes Care.* 2018 Apr;41(4):847-853.
7. Cui CY, Zhou MG, Cheng LC, Ye T, Zhang YM, Zhu F, Li SY, Jiang XL, Chen Q, Qi LY, Chen X, Yang SQ, Cai L. Admission hyperglycemia as an independent predictor of long-term prognosis in acute myocardial infarction patients without diabetes: A retrospective study. *J Diabetes Investig.* 2021 Jul;12(7):1244-1251.
8. Chakrabarti AK, Singh P, Gopalakrishnan L, Kumar V, Elizabeth Doherty M, Abueg C, Wang W, Gibson CM. Admission hyperglycemia and acute myocardial infarction: outcomes and potential therapies for diabetics and nondiabetics. *Cardiol Res Pract.* 2012; 2012:704314.
9. Grant PJ, Cosentino F. The 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: New features and the 'Ten Commandments' of the 2019 Guidelines are discussed by Professor Peter J. Grant and Professor Francesco Cosentino, the Task Force chairmen. *Eur Heart J.* 2019 Oct 14;40(39):3215-3217.
10. Arnold SV, Spertus JA, Jones PG, McGuire DK, Lipska KJ, Xu Y, Stolker JM, Goyal A, Kosiborod M. Predicting Adverse Outcomes After Myocardial Infarction Among Patients With Diabetes Mellitus. *Circ Cardiovasc Qual Outcomes.* 2016 Jul;9(4):372-9.
11. Nauta ST, Deckers JW, Akkerhuis KM, van Domburg RT. Short- and long-term mortality after myocardial infarction in patients with and without diabetes: changes from 1985 to 2008. *Diabetes Care.* 2012 Oct;35(10):2043-7.
12. Eitel I, Desch S, Fuernau G, Hildebrand L, Gutberlet M, Schuler G, Thiele H. Prognostic significance and determinants of myocardial salvage assessed by cardiovascular magnetic resonance in acute reperfused myocardial infarction. *Journal of the American College of Cardiology.* 2010 Jun 1;55(22):2470-9.
13. De Waha S, Desch S, Eitel I, Fuernau G, Zachrau J, Leuschner A, Gutberlet M, Schuler G, Thiele H. Impact of early vs. late microvascular obstruction assessed by magnetic resonance imaging on long-term outcome after ST-elevation myocardial infarction: a comparison with traditional prognostic markers. *European heart journal.* 2010 Nov 1;31(21):2660-8.
14. Kim HW, Farzaneh-Far A, Kim RJ. Cardiovascular magnetic resonance in patients with myocardial infarction: current and emerging applications. *Journal of the American College of Cardiology.* 2009 Dec 29;55(1):1-6.
15. Mather AN, Crean A, Abidin N, Worthy G, Ball SG, Plein S, Greenwood JP. Relationship of dysglycemia to acute myocardial infarct size and cardiovascular outcome as determined by cardiovascular magnetic resonance. *Journal of Cardiovascular Magnetic Resonance.* 2010 Oct 7;12(1):61.
16. Jensen CJ, Eberle HC, Nassenstein K, Schlosser T, Farzandeh M, Naber CK, Sabin GV, Bruder O. Impact of hyperglycemia at admission in patients with acute ST-segment elevation myocardial infarction as assessed by contrast-enhanced MRI. *Clinical Research in Cardiology.* 2011 Aug;100:649-59.
17. McAloon CJ, Boylan LM, Hamborg T, Stallard N, Osman F, Lim PB, Hayat SA. The changing face of cardiovascular disease 2000-2012: An analysis of the world health organisation global health estimates data. *Int J Cardiol.* 2016 Dec 1;224:256-264.
18. Bahloul M, Turki O, Chaari A, Bouaziz M. Incidence, mechanisms and impact outcome of hyperglycaemia in severe scorpion-envenomed patients. *Ther Adv Endocrinol Metab.* 2018 Jul;9(7):199-208.
19. Lee SA, Cho SJ, Jeong MH, Kim YJ, Kim CJ, Cho MC, Kim HS, Ahn Y, Koh G, Lee JM, Oh SK, Yun KH, Kim HY, Cho CG, Lee DH; KAMIR/KorMI Registry. Hypoglycemia at admission in patients with acute myocardial infarction predicts a higher 30-day mortality in patients with poorly controlled type 2 diabetes than in well-controlled patients. *Diabetes Care.* 2014 Aug;37(8):2366-73.
20. Kadri Z, Danchin N, Vaur L, Cottin Y, Guéret P, Zeller M, Lablanche JM, Blanchard D, Hanania G, Genès N, Cambou JP. Major impact

- of admission glycaemia on 30 day and one year mortality in non-diabetic patients admitted for myocardial infarction: results from the nationwide French USIC 2000 study. *Heart*. 2006 Jul 1;92(7):910-5.
21. Suleiman M, Hammerman H, Boulos M, Kapeliovich MR, Suleiman A, Agmon Y, Markiewicz W, Aronson D. Fasting glucose is an important independent risk factor for 30-day mortality in patients with acute myocardial infarction: a prospective study. *Circulation*. 2005 Feb 15;111(6):754-60.
  22. Na Z, Zhen L. GW25-e0795 Relationship between Stress Hyperglycemia and in hospital Mortality and Complications in Patients with Acute Myocardial Infarction. *Journal of the American College of Cardiology*. 2014 Oct 21 ;16(64):C126.
  23. Kosuge M, Kimura K, Ishikawa T, Shimizu T, Hibi K, Toda N, Tahara Y, Kanna M, Tsukahara K, Okuda J, Nozawa N, Umemura S. Persistent hyperglycemia is associated with left ventricular dysfunction in patients with acute myocardial infarction. *Circ J*. 2005 Jan; 69(1):23-8.
  24. van der Horst IC, Nijsten MW, Vogelzang M, Zijlstra F. Persistent hyperglycemia is an independent predictor of outcome in acute myocardial infarction. *Cardiovasc Diabetol*. 2007 Feb 6;6:2.
  25. Qin Y, Yan G, Qiao Y, Ma C, Liu J, Tang C. Relationship between Random Blood Glucose, Fasting Blood Glucose, and Gensini Score in Patients with Acute Myocardial Infarction. *Biomed Res Int*. 2019 Oct 15;2019:9707513.
  26. Goyal A, Mahaffey KW, Garg J, Nicolau JC, Hochman JS, Weaver WD, Theroux P, Oliveira GB, Todaro TG, Mojcik CF, Armstrong PW, Granger CB. Prognostic significance of the change in glucose level in the first 24 h after acute myocardial infarction: results from the CARDINAL study. *Eur Heart J*. 2006 Jun;27(11):1289-97.
  27. Zecchin HG, Nadruz Junior W, Saad MJ. Importance and management of diabetes and hyperglycemia in the setting of myocardial infarction. *Rev Soc Cardiol*. 2004;14(6):1017-30.
  28. Ceriello A. Acute hyperglycaemia: a 'new' risk factor during myocardial infarction. *Eur Heart J*. 2005;26(4):328-31.
  29. Huoya MDO, Penalva RA, Alves SR, Feitosa GS, Gadelha S, Ladeia AMT. Comparison of inflammatory biomarkers between diabetic and non-diabetic patients with unstable angina. *Arq Bras Cardiol*. 2009;92(4):269-74.