

A Hospital Based Study to Assess the Prognostic Implications of Admission Hyperglycemia in Non-Diabetic Acute Myocardial Infarction PatientsVijay Gadhia¹, Darshankumar Parmar², Sanket G. Makwana³¹Consultant, Department of General Medicine, Jeevandeep Hospital, Morbi, Gujarat, India²Consultant, Department of General Medicine, Aayush Multi-speciality Hospital, Morbi, Gujarat, India³Associate Professor, Department of General Medicine, C U Shah Medical College and Hospital, Surendranagar, Gujarat, India

Received: 05-03-2023 Revised: 08-04-2023 / Accepted: 20-05-2023

Corresponding author: Dr. Sanket G. Makwana

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 100 non diabetic STEMI patients admitted in Jeevandeep Hospital, Gujarat, India. The study was conducted on 100 non diabetic STEMI patients admitted in Jeevandeep Hospital, morbi, Gujarat, India for the period of one year. There were 50 patients in group I and 50 patients in group II.**Results:** There were total 58 males and 42 females in the study. Group I had 20 females and 30 males. Group II had 22 females and 28 males. There was no significant difference between the number of males and females in two groups ($p=0.850$). The mean age of patients in Group I and Group II were 63.47 ± 12.28 and 62.16 ± 11.36 respectively. Median age in group I and group II were 65 and 62 years respectively. There was no significant difference in patients' mean age in between the groups ($p=0.612$). There were total 22 (22%) smokers in the study of which 11 were in group I and 10 in group II. History of smoking was present in 22% and 20% of patients of Group I and Group II respectively. There was no significant difference in number of smokers in between the two groups ($p=0.314$). There were total of 30 patients with history of alcohol consumption in the study. Group I and Group II, both had 15 patients and 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 28 patients out of which 12 patients were in Group I and 16 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:** Hyperglycemia at admission in non-diabetic patients of acute ST elevation myocardial infarction is strongly associated with higher in hospital complications like cardiogenic shock, arrhythmias and AV block.**Keywords:** Non-Diabetic, Acute Myocardial Infarction, Hyperglycemia.

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.

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. [6] 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. [7,8] 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}

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 100 non diabetic STEMI patients admitted in department of General Medicine Jeevandeep Hospital, Morbi ,Gujarat, India for the period of one year. 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
Gender			
Male	30	28	0.850
Female	20	22	
Mean age	63.47 ± 12.28	62.16 ± 11.36	0.612

There were total 58 males and 42 females in the study. Group I had 20 females and 30 males. Group II had 22 females and 28 males. There was no significant difference between the number of males and females in two groups (p= 0.850). The mean

age of patients in Group I and Group II were 63.47 ± 12.28 and 62.16 ± 11.36 respectively. Median age in group I and group II were 65 and 62 years respectively. There was no significant difference in

patients' mean age in between the groups ($p= 0.612$).

Table 2: Personal and past history

Parameters	Group I	Group II	P Value
Smoking			
Yes	11	10	0.314
No	39	40	
Alcohol			
Yes	15	15	0.750
No	35	35	
Hypertension			
Yes	12	16	0.512
No	38	34	

There were total 22 (22%) smokers in the study of which 11 were in group I and 10 in group II. History of smoking was present in 22% and 20% of patients of Group I and Group II respectively. There was no significant difference in number of smokers in between the two groups ($p= 0.314$). There were total of 30 patients with history of alcohol consumption in the study. Group I and

Group II, both had 15 patients and 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 28 patients out of which 12 patients were in Group I and 16 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)	74.86 ± 12.68	80.82 ± 13.57	0.020
Mean SBP (mmHg)	123.47 ± 24.76	112.57 ± 25.28	0.001
Mean DBP (mmHg)	78.06 ± 12.62	72.48 ± 14.16	<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	10	0.023
Arrhythmias	5	20	0.025
AV Block	3	7	0.040

Total 15 patients developed cardiogenic shock. 5 patients in group I and 10 patients in group II developed cardiogenic shock. There was statistically significant ($p= 0.023$) 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 ($p= 0.025$). Total 10 patients in the study developed an AV block of ≥ 2 nd degree. 3 patients in group I developed AV block (≥ 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

Stress hyperglycemia represents increased blood glucose levels result of activation of neurohormonal processes in organism exposed to stress. Increased glucose level during stress is evoked by integrated hormonal, cytokine and nervous counter regulatory signals on glucose

metabolic pathways and, therefore, presented in the same time with hyperinsulinemia and insulin resistance. The mortality and morbidity of a diabetic patient is poor as compared to non-diabetic patient. [10] 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. [11] A strong correlation between glycaemia and shock or development of heart failure has also been reported. [12,13]

There were total 58 males and 42 females in the study. Group I had 20 females and 30 males. Group II had 22 females and 28 males. There was no significant difference between the number of males and females in two groups ($p= 0.850$). The mean age of patients in Group I and Group II were 63.47 ± 12.28 and 62.16 ± 11.36 respectively. Median age in group I and group II were 65 and 62 years respectively. There was no significant difference in patients' mean age in between the groups ($p= 0.612$). There were total 22 (22%) smokers in the

study of which 11 were in group I and 10 in group II. History of smoking was present in 22% and 20% of patients of Group I and Group II respectively. There was no significant difference in number of smokers in between the two groups ($p=0.314$). There were total of 30 patients with history of alcohol consumption in the study. Group I and Group II, both had 15 patients and 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 28 patients out of which 12 patients were in Group I and 16 patients in Group II. Hyperglycaemia (blood glucose ≥ 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. [14] In another study, persistent hyperglycemia in myocardial infarction has a stronger relation with 30-day MACE than elevated glucose at admission. [15] Fasting glucose was superior to admission glucose with regard to 30-day mortality in previous study. [16] 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. [17]

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. Probable explanation for this might be due to the reason that studies have reported that patients with stress hyperglycemia have poor LV function and lower ejection fraction. Previous studies have reported similar results with respect to mean SBP and DBP. [18,19] The mean heart rate in the present study was 79.39 ± 13.34 bpm. The mean heart rate in the study by Sanjuan R et al [11] was 79 ± 22 bpm which is close to the present study. There was a statistically significant difference in heart rate, SBP and DBP between the two groups. Total 15 patients developed cardiogenic shock. 5 patients in group I and 10 patients in group II developed cardiogenic shock. There was statistically significant ($p=0.023$) 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 ($p=0.025$). Total 10 patients in the study developed an AV block of ≥ 2 nd degree. 3 patients in group I developed AV block (≥ 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 exact mechanism through which hyperglycemia worsens the prognosis of ischemic patients has not been well established. Its pathophysiology is believed to be based on endothelial and microvascular dysfunction, causing a prothrombotic state produced by vascular inflammation. The endothelial dysfunction inactivates nitric oxide and increases oxidative stress, responsible for the production of oxygen reactive species. [20] 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. [20,21] There is evidence that the prothrombotic state generated by hyperglycemia originates from reduced plasma fibrinolytic activity and action of tissue plasminogen activator. [22,23]

Conclusion

Hyperglycemia at admission in non-diabetic patients of acute ST elevation myocardial infarction is strongly associated with higher in hospital complications like cardiogenic shock, arrhythmias and AV block. Hyperglycemia at admission is a strong predictor of early mortality during hospital stay. Though hyperglycemia at admission is a strong predictor of in hospital complications and mortality, it is not an independent predictor of either of them. Stress hyperglycemia is also associated with significantly lower systolic and diastolic blood pressure and higher heart rate at admission.

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. Paolisso P, Foà A, Bergamaschi L, Angeli F, Fabrizio M, Donati F, Toniolo S, Chiti C, Rinaldi A, Stefanizzi A, Armillotta M. Impact of admission hyperglycemia on short and long-term prognosis in acute myocardial infarction: MINOCA versus MIOCA. *Cardiovascular Diabetology*. 2021 Dec;20(1):1-0.
 7. 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; 236:9-15.
 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 infarction: a retrospective observational study. *BMC Cardiovascular Disorders*. 2019 Dec;19(1):1-9.
 10. Malmberg K, Rydén L, Hamsten A, Herlitz J, Waldenström A, Wedel H. Mortality prediction in diabetic patients with myocardial infarction: experiences from the DIGAMI study. *Cardiovascular research*. 1997 Apr 1;34(1):248-53.
 11. Chakdoufi, S., Moumen, A., & Guerboub, A. Dyslipidemia and Diabetic Retinopathy in Moroccans Type 2 Diabetics Patients: A Cross-Sectional Study. *Journal of Medical Research and Health Sciences*, 2023; 6(3): 2471–2479.
 12. Sanjuan R, Nunez J, Blasco ML, Minana G, Martínez-Maicas H, Carbonell N, Palau P, Bodí V, Sanchis J. Prognostic implications of stress hyperglycemia in acute ST-elevation myocardial infarction. Prospective observational study. *Revista Española de Cardiología (English Edition)*. 2011 Mar 1;64(3):201-7.
 13. Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *The Lancet*. 2000 Mar 4;355(9206):773-8.
 14. Jaśkiewicz F, Supeł K, Koniarek W, Zielińska M. Admission hyperglycemia in patients with acute coronary syndrome complicated by cardiogenic shock. *Cardiology Journal*. 2015;22(3):290-5.
 15. Kosuge M, Kimura K, Ishikawa T, Shimizu T, Hibi K, Toda N, Tahara Y, Kanna M, Tsukahara K, Okuda J, Nozawa N. Persistent hyperglycemia is associated with left ventricular dysfunction in patients with acute myocardial infarction. *Circulation Journal*. 2005;69(1):23-8.
 16. Van der Horst IC, Nijsten MW, Vogelzang M, Zijlstra F. Persistent hyperglycemia is an independent predictor of outcome in acute myocardial infarction. *Cardiovascular Diabetology*. 2007 Dec;6(1):1-8.
 17. Suleiman M, Hammerman H, Boulous 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.
 18. 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 research international*. 2019 Oct 15; 2019.
 19. 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.
 20. Suleiman M, Hammerman H, Boulous 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.

21. 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.
22. Ceriello A. Acute hyperglycaemia: a 'new' risk factor during myocardial infarction. *Eur Heart J.* 2005;26(4):328- 31.
23. 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.