

Role of Glycosylated Haemoglobin (HbA1c) in Predicting Acute Coronary Syndrome: a Retrospective Study

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Abstract

Aim: To investigate the predictive significance of glycosylated haemoglobin (HbA1C) in acute coronary syndrome among the population of Bihar.

Material and Methods: This hospital-based retrospective study was conducted in the at Department of Medicine, JNKTMCH, Madhepura, Bihar, India for one year. A total of 100 patients who presented with Acute Coronary Syndrome (ACS) were enrolled in this study. Patients were selected based on their presentation with ACS symptoms such as chest pain and were evaluated upon admission.

Results: The mean age was 62.36±9.89 years. All the patients presented with chest pain radiating to left arm /radiating to back (100%). The next common complaint was breathlessness (57%) and vomiting and profuse sweating (45%). Hypertension, tobacco/Misri chewing and smoking were the risk factors noted in 62%, 18% and 17% of the patients respectively. Fasting blood sugar levels were between 100 to 125 mg/dL in majority of the patients while ≥126 mg/dL were note in 11% of the patients. The mean fasting blood sugar levels were 107.64±10.60 mg/dl. Post prandial blood sugar levels were noted as ≥140 mg/dL in majority of the patients. The mean post prandial blood sugar levels were 174.62±31.88 mg/Dl HbA1c levels were ≥6.5 percent in majority of the patients (68%). The mean HbA1c levels were 6.62±0.73 percent. Troponin I levels were raised among 99% of the patients. Based on ECG, majority of the patients were diagnosed with STEMI (85%), followed by NSTEMI (14%). Based on the 2D echocardiography most of the patients had anterior wall LW HK. Majority of the patients were diagnosed with double vessel disease while single vessel disease was noted in 16% of the patients.

Conclusion: Based on the above results it may be concluded that, admission glycated haemoglobin levels are associated with in hospital adverse events as well as outcome while outcome and adverse events were independent of blood sugar levels that is, random, fasting and post prandial blood sugar levels hence, blood sugar levels have limited prognostic value in patient with ACS.

Keywords: Predictive, Glycosylated haemoglobin (HbA1C), Acute coronary syndrome, among the population of Bihar.

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Introduction

Acute coronary syndrome (ACS) is a spectrum of conditions associated with sudden, reduced blood flow to the heart, encompassing unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) [1-3]. It is a leading cause of morbidity and mortality worldwide, necessitating effective prognostic indicators to guide clinical management and improve patient outcomes. One such potential prognostic marker is glycosylated haemoglobin (HbA1c), which reflects average blood glucose levels over the preceding two to three months. HbA1c is widely used for diagnosing and

monitoring diabetes mellitus, but its role in predicting cardiovascular outcomes, particularly in the context of ACS, has garnered increasing attention. Elevated HbA1c levels have been associated with a higher risk of cardiovascular events in both diabetic and non-diabetic individuals [4-7]. This association suggests that HbA1c could serve as a valuable marker for stratifying risk and tailoring therapeutic strategies in patients presenting with ACS. Several studies have explored the prognostic implications of HbA1c in ACS patients. The pathophysiological mechanisms underlying the prognostic value of HbA1c in ACS are multifaceted.

Chronic hyperglycaemia, as indicated by elevated HbA1c, contributes to endothelial dysfunction, increased oxidative stress, and a pro-inflammatory state, all of which exacerbate atherosclerosis and plaque instability. These factors collectively heighten the risk of adverse cardiovascular events in ACS patients, underscoring the importance of HbA1c as a prognostic marker. Moreover, integrating HbA1c assessment into the clinical management of ACS could enhance risk stratification and therapeutic decision-making. For example, patients with elevated HbA1c levels might benefit from more intensive glucose control measures and aggressive cardiovascular risk management to mitigate the heightened risk of adverse outcomes [8-10].

Material and Methods

This hospital-based retrospective study was conducted in the Department of Medicine, JNKTMCH, Madhepura, Bihar, India for one year. A total of 100 patients who presented with Acute Coronary Syndrome (ACS) were enrolled in this study. Patients were selected based on their presentation with ACS symptoms such as chest pain and were evaluated upon admission.

Inclusion Criteria

- Patients presenting with ACS.
- Patients willing to participate and provide informed consent.

Exclusion Criteria

- Patients with pre-existing conditions that could interfere with the study parameters.
- Patients who refused to participate.

Data Collection

Upon admission, each patient underwent the following evaluations:

1. **Electrocardiogram (ECG):** To confirm the diagnosis of ACS and classify the type of myocardial infarction.
2. **Random Blood Sugar (RBS):** Measured at the time of admission to evaluate immediate blood glucose levels.

Following admission, the patients were further assessed with:

1. **Fasting Blood Sugar (FBS):** To evaluate fasting glucose levels.
2. **Postprandial Blood Sugar (PPBS):** To assess blood glucose levels after meals.
3. **Glycosylated Haemoglobin (HbA1c):** To determine the average blood glucose levels over the past three months and assess long-term glucose control.

Statistical Analysis

The data were statistically analysed to determine the prognostic value of HbA1c in patients with ACS. Various statistical methods were employed to analyse the correlation between HbA1c levels and patient outcomes, including:

- **Descriptive Statistics:** For summarizing the demographic data and clinical characteristics of the study population.
- **Comparative Analysis:** To compare HbA1c levels with patient outcomes, including complications, vessel disease severity, and mortality.
- **Significance Testing:** Using p-values to determine the statistical significance of observed associations between HbA1c levels and patient outcomes.

Results

Most of the patients were males (54%) and male to female ratio was 1.17:1. Most of the patients were (37%) aged between 61 to 70 years and 32% of the patients were aged between 51 to 60 years. The mean age was 62.36 ± 9.89 years. All the patients presented with chest pain radiating to left arm /radiating to back (100%). The next common complaint was breathlessness (57%) and vomiting and profuse sweating (45%). Hypertension, tobacco/Misri chewing and smoking were the risk factors noted in 62%, 18% and 17% of the patients respectively. Fasting blood sugar levels were between 100 to 125 mg/dL in majority of the patients while ≥ 126 mg/dL were noted in 11% of the patients. The mean fasting blood sugar levels were 107.64 ± 10.60 mg/dL. Post prandial blood sugar levels were noted as ≥ 140 mg/dL in majority of the patients. The mean post prandial blood sugar levels were 174.62 ± 31.88 mg/dL. HbA1c levels were ≥ 6.5 percent in majority of the patients (68%). The mean HbA1c levels were 6.62 ± 0.73 percent. Troponin I levels were raised among 99% of the patients. Based on ECG, majority of the patients were diagnosed with STEMI (85%), followed by NSTEMI (14%). Based on the 2D echocardiography most of the patients had anterior wall LW HK. Majority of the patients were diagnosed with double vessel disease while single vessel disease was noted in 16% of the patients. Complications were noted in 25% of the patients. Left Ventricular Failure (LVF) was the common complication noted in 16% of the patients and arrhythmia was noted in 5% of the patients while arrhythmia with LVF was noted in 4% of the patients. Majority of the patients (98%) improved and discharged. While mortality was noted in 2% of the patients. Significantly higher number of patients with HbA1c levels ≥ 6.5 percent developed complications (30.88% vs 12.50%; $p=0.048$). Significantly higher number of patients with HbA1c

had double vessel disease (72.84%) and triple vessel disease (100%) ($p=0.028$). Significant association was found between PPBS and severity of CAD ($p=0.023$). It was observed that, the mean HbA1c levels were significantly high in patients who developed complications (6.83 ± 0.50 vs 6.55 ± 0.79 percent; $p=0.046$). Also the mean HbA1c levels

were significantly high among non survivors compared to survivors (8.10 ± 0.14 vs 6.59 ± 0.71 percent; $p=0.004$). No association was found between RBS and FBS with severity of CAD, complications with RBS, FBS and PPBS. Also no association was found between RBS, FBS, PPBS, and HbA1c with outcome ($p>0.050$).

Table 1: Patient Demographics and Risk Factors

Characteristic	Number of Patients (n=100)	Percentage (%)
Gender		
Males	54	54
Females	46	46
Age		
Mean Age (years)	62.36 ± 9.89	
Presenting Symptoms		
Chest pain	100	100
Breathlessness	57	57
Vomiting and Profuse Sweating	45	45
Risk Factors		
Hypertension	62	62
Tobacco/Misri Chewing	18	18
Smoking	17	17

Table 2: Blood Sugar Levels and HbA1c

Test	Mean Value \pm SD	Normal Range	Number of Patients (n=100)	Percentage (%)
Fasting Blood Sugar (mg/dL)	107.64 ± 10.60	70-100		
FBS 100-125 mg/dL			Majority	
FBS ≥ 126 mg/dL			11	11
Post Prandial Blood Sugar (mg/dL)	174.62 ± 31.88	<140	Majority	
HbA1c (%)	6.62 ± 0.73	<5.7		
HbA1c $\geq 6.5\%$			68	68

Table 3: Cardiac Event and ECG Findings

Characteristic	Number of Patients (n=100)	Percentage (%)
Troponin I Elevated	99	99
ECG Findings		
STEMI	85	85
NSTEMI	15	15
2D Echocardiography		
Anterior Wall LV HK	Majority	
Vessel Disease		
Single Vessel Disease	16	16
Double Vessel Disease	Majority	
Complications		
LVF	16	16
Arrhythmia	5	5
Arrhythmia with LVF	4	4

Table 4: Outcomes and Associations

Characteristic	Number of Patients (n=100)	Percentage (%)	p-Value
Outcome			
Improved and Discharged	98	98	
Mortality	2	2	
HbA1c \geq 6.5% and Complications	30.88% vs 12.50%		0.048
HbA1c and Vessel Disease			0.028
Double Vessel Disease	72.84		
Triple Vessel Disease	100		
PPBS and Severity of CAD			0.023
Mean HbA1c in Complications	6.83 \pm 0.50 vs 6.55 \pm 0.79		0.046
Mean HbA1c in Survivors vs Non-survivors	8.10 \pm 0.14 vs 6.59 \pm 0.71		0.004
Association of RBS and FBS with Severity of CAD	No significant association		>0.050
Association of RBS, FBS, PPBS, HbA1c with Outcome	No significant association		>0.050

Discussion

The prognostic value of HbA1c level in patients with coronary atherosclerotic disease has not been well studied in Indian population. Hence the present study was undertaken to find out the role of HbA1c levels in early outcome of ACS with non-diabetic patient. Also we will study possible relation between HbA1c and admission glucose level identified during initial hospitalization. We will further study relation between HbA1c levels and complication of ACS. Non-modifiable factors that influence risk for coronary artery disease include age and sex. Men have a higher risk than women [10]. The same was true in the present study since there was slight male preponderance with 54% of the patients being males and male to female ratio of 1.17:1. These findings suggest that, ACS was prevalent among males. Advanced age is an important non-modifiable risk factor and predictor of ACS and leads to poor prognosis. In the present study the age of the patients ranged between 42 to 88 years. The mean age was 62.36 \pm 9.89 years and median age was noted as 63 years. More than one third (37%) of the patients were aged between 61 to 70 years and 32% of the patients were aged between 51 to 60 years. These findings suggest that, ACS were widely prevalent among elderly patients. These findings were consistent with a report [11] who reported higher risk of acute coronary syndrome in average age group of 57.5 years among Indians. In the present study all the patients presented with chest pain radiating to left arm/radiating to back (100%). The next common complaint was breathlessness (57%) and vomiting and profuse sweating (45%). The other uncommon clinical signs and symptoms were epigastric pain (39%) and acute behavioural changes like confusion (9%). In this study hypertension, tobacco/Misri chewing and smoking were the risk factors noted in 62%, 18% and 17% of the patients respectively. These findings were in strong agreement with the studies in the literature which state that, hypertension, smoking and tobacco

chewing are the major modifiable risk factors. In this study the diagnosis of ACS was based on ECG and majority of the patients were diagnosed with STEMI (85%). Diagnosis of NSTEMI and unstable angina was done in 14% and 1% of the patients respectively. Further these patients were subjected to 2D echocardiography and most of the patients had anterior wall LW HK. With regard to cardiac enzymes, troponin I levels were raised among majority of the patients (99%). In the present study majority of the patients (81%) were diagnosed with double vessel disease followed by single vessel disease in 16% of the patients and triple vessel disease in 2% of the patients while 1% of the patients had normal findings. Majority of the patients did not develop any complications and 25% of the patients had complications viz. LVF (16%), arrhythmia (5%) and arrhythmia with LVF (4%). With regard to outcome majority of the patients (98%) improved and discharged and mortality was noted in 2% of the patients. In the present study sample for random blood sugars levels were obtained immediately after admission in emergency department and evaluated. The random blood sugar levels ranged between 158 to 364 mg/dL. The mean random blood sugar levels were 176.03 \pm 37.37 mg/dL and median levels were noted as 172 mg/dL suggestive of normal values (<200 mg/dL). In this study FBS, PPBS and HbA1c tests were performed after the admission of the patient in the Wads. The fasting blood sugar levels ranged between 92 to 142 mg/dL. The mean FBS levels were noted as 107.64 \pm 10.60 mg/dL and median levels were 104.50 mg/dL. While, FBS levels suggestive of prediabetes (100 to 125 mg/dL) were noted in majority of the patients (82%) and \geq 126 mg/dL were noted in 11% of the patients and 7% of the patients had normal FBS (< 140 mg/dL). These findings suggest that, higher PPBS levels suggestive of type 2 diabetes mellitus are associated with severe MI. Also one patient (1%) had normal findings on coronary angiography and he had normal HbA1c levels (< 6.5 percent and the

difference was statistically significant ($p=0.048$). Also, the mean HbA1c levels were significantly high in patients who developed complications (6.83 ± 0.50 vs 6.55 ± 0.79 percent; $p=0.046$). These findings suggest that, ACS patients with raised HbA1c levels at admission or within 24 hours of admission are significantly at high risk of developing complications. These findings were in agreement with the studies in the literature despite of methodological differences. e.g., in a study by Singh S. et al. [12] elevated HbA1c level was a strong and independent predictor of severity and complication in ACS patients even in nondiabetics. Researches showed that an elevated HbA1c was associated with increased cardiovascular risk in patients with and without diabetes [13,14,15]. In contrast to the observations of the present study, Timmer JR [16] concluded that elevated HbA1c was not significantly associated with adverse outcome in their study. However, in this study no association was found between HbA1c and mortality but, surprisingly it was observed that, the mean HbA1c levels were significantly high among non survivors compared to survivors (8.10 ± 0.14 vs 6.59 ± 0.71 percent; $p=0.004$) suggesting that, higher HbA1c levels pose the risk of mortality. This disparity can be attributed to the smaller sample size of the study population and timely diagnosis and effective management of the patient which resulted in lower mortality rates. Zaghla HE et al. [17] also did not find any significant correlation between its level and outcome of patients with AMI. Another study by Timmer JR [16] also concluded that elevated HbA1c was not significantly associated with increased mortality or adverse outcome in their study, which was previously described. However, in contrast to our findings, Liu et al. [18] suggested that elevated HbA1c was associated with a higher risk of mortality in patients without recognized diabetes but had a neutral effect on mortality in patients with diabetes. Kosiborod and McGuire [19] also found that higher blood glucose on admission in patients with AMI was associated with greater 30-day mortality ($p<0.05$). Neither association was found nor did the mean values differ significantly. In contrast to these observations, Zaghla HE et al. [17] detected an increased incidence of developing heart failure (detected by low ejection fraction) in patients with AMI and elevated admission glucose levels, with high significant correlation between them ($p<0.001$).

Conclusion

Based on the above results it may be concluded that, admission glycated haemoglobin levels are associated with in hospital adverse events as well as outcome while outcome and adverse events were independent of blood sugar levels that is, random, fasting and post prandial blood sugar levels hence,

blood sugar levels have limited prognostic value in patient with ACS.

References

1. Pan W, Lu H, Lian B, Liao P, Guo L, Zhang M. Prognostic value of HbA1c for in-hospital and short-term mortality in patients with acute coronary syndrome: a systematic review and meta-analysis. *Cardiovasc Diabetol*. 2019 Dec 11;18(1):169. doi: 10.1186/s12933-019-0970-6. PMID: 31829179; PMCID: PMC6905004.
2. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125(1).
3. Piironen M, Ukkola O, Huikuri H, Havulinna AS, Koukkunen H, Mustonen J, Ketonen M, Lehto S, Airaksinen J, Antero Kesaniemi Y, et al. Trends in long-term prognosis after acute coronary syndrome. *Eur J Prev Cardiol*. 2017; 24(3):274–280. doi:10.1177/2047487316679522.
4. Eggers KM, Lindahl B. Prognostic biomarkers in acute coronary syndromes: risk stratification beyond cardiac troponins. *Curr Cardiol Rep*. 2017;19(4):29. doi:10.1007/s11886-017-0840-3.
5. Selvin E, Coresh J, Golden SH, et al. Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in communities study. *Arch Intern Med*. 2005;165(16):1910-1916.
6. Khaw KT, Wareham N, Bingham S, et al. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. *Ann Intern Med*. 2004; 141(6):413-420.
7. Rydén L, Standl E, Bartnik M, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J*. 2007;28(1):88-136.
8. Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med*. 2004;141(6):421-431.
9. Kuhl J, Javitt ND, Passman W, et al. Impact of Hemoglobin A1c on outcomes following percutaneous coronary intervention in patients with and without diabetes mellitus. *Am J Cardiol*. 2015;116(3):363-368.
10. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. *Diabetes*. 2005;54(6):1615-1625.
11. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular

- and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258): 405-412.
12. Singh S, Bansal M, Rani K, Gupta V. Prognostic significance of glycosylated hemoglobin in nondiabetic patients in acute coronary syndrome. *Heart India*. 2016;4:17-22.
 13. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med*. 2004;141:421- 31.
 14. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: The European prospective investigation into cancer in Norfolk. *Ann Intern Med*. 2004;141:413- 20.
 15. Sato KK, Hayashi T, Harita N, Yoneda T, Nakamura Y, Endo G, et al. Combined measurement of fasting plasma glucose and A1C is effective for the prediction of type 2 diabetes: The Kansai Healthcare Study. *Diabetes Care*. 2009;32:644- 6.
 16. Jorik Rudolf Timmer, Clinical implications of glycometabolic disturbances in acute coronary syndromes / Jorik Rudolf Timmer.[S.l.:s.n.], ([Enschede]:Febodruk).2005;203: ill.; 24 cm.
 17. Zaghla HE, Elbadry MA, Ashour AM, Abdelfatah MM. Influence of admission blood glucose and hemoglobin A1c on outcome of acute myocardial infarction. *Egypt J Intern Med*. 2014;26:21-6.
 18. The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009; 360:1283– 1297.
 19. Kosiborod M, McGuire DK. Glycated hemoglobin as a prognostic risk marker in nondiabetic patients after acute myocardial infarction. *Circulation*. 2011;124:666–668.