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Glycosylated Haemoglobin as A Marker of Severity in Patients with Acute Myocardial Infarction

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Abstract: Hyperglycaemia is an independent risk factor for cardiovascular diseases (CVD). Glycosylated hemoglobin A1c (HbA1c) is a pivotal bio-marker reflecting fasting and postprandial plasma glucose concentration over the preceding 2–3 months. And also, it has been regarded as an important tool in diabetes diagnosis and management. The study evaluated the utility of HBA1c in determining the severity of Acute Myocardial Infarction in Tertiary Care Hospitals. The prospective analytical cross-sectional study was carried out among 169 patients aged 18 years and above admitted with Acute myocardial infarction at a tertiary care center from November 2021 to October 2022. The severity of MI was done using TIMI Score for STEMI/ NSTEMI. The collected data were analyzed with proper statistical methods using MS Excel 2016. Data were summarized in percentages and proportions. P value <0.05 was considered statistically significant. The mean age of the patients was 60.50 ±10.94 years, with the majority of cases being male. (63.91%) There was a strong association between the risk category and HbA1c with statistically significant differences. TIMI risk score had a strong positive correlation with HbA1c. (P<0.0001) The present study concludes a significant correlation between HbA1c levels and the severity of Acute Myocardial Infarction.

Key Words: Glycosylated Haemoglobin, Severity, Acute Myocardial Infarction, HbA1c, TIMI risk score

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1. INTRODUCTION

Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non–ST-segment elevation myocardial infarction (NSTEMI) or unstable angina. It is a type of coronary heart disease (CHD) responsible for one-third of deaths in people older than 35. Some forms of CHD can be asymptomatic, but ACS is always symptomatic. The common risk factors for the disease are smoking, hypertension, diabetes, hyperlipidemia, male sex, physical inactivity, family obesity, and poor nutritional practices. It is almost always associated with the rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct-related artery.[1,2] Diabetes mellitus is a disease with a major impact on the vascular tree with both microvascular and macrovascular complications.[3] It is well known that microvascular complications occur long before the patient has overt diabetes. Hyperglycaemia is an independent risk factor for cardiovascular diseases (CVD). Hyperglycaemia accelerates the process of atherosclerosis by the formation of glycated proteins and products, which act by increasing endothelial dysfunction and leading to macrovascular complications. [4,5] Diabetic individuals face a well-established two-to-four-fold relative risk increase for the development of cardiovascular disease compared to their nondiabetic peers of similar age, sex, and ethnicity. Furthermore, upon developing cardiovascular disease, diabetic patients fare worse, with a two to four times higher mortality than adults without diabetes. As a common manifestation of cardiovascular disease, patients with diabetes mellitus are at high risk for developing acute coronary syndrome (ACS).[6] Glycosylated Hemoglobin A1c (HbA1c) is a pivotal bio-marker reflecting fasting and postprandial plasma glucose concentration over the preceding 2–3 months. And also, it has been regarded as an important tool in diabetes diagnosis and management. It has been reported that elevated HbA1c levels probably mean long-term insulin resistance and severe consequences such as hyperglycemia, dyslipidemia, hypercoagulability, and system inflammatory response.[5] Hyperglycaemia is an independent risk factor for cardiovascular diseases (CVD). Hyperglycaemia accelerates the process of atherosclerosis by the formation of glycated proteins and products, which act by increasing endothelial dysfunction and leading to macrovascular complications.[5] The aim of this study, therefore, was to evaluate the utility of HBA1c in determining the severity of Acute Myocardial Infarction.

2. MATERIALS AND METHODS

The prospective analytical cross-sectional study was conducted among patients aged 18 years and above admitted at tertiary care centers from November 2021 to October 2022. The study was conducted after obtaining clearance from the institute's Ethical Committee. A total sample size of 169 patients aged 18 years and above admitted with Acute myocardial infarction as per the Fourth Universal Definition of Myocardial Infarction was selected[7].

2.1 Inclusion Criteria

1) Acute myocardial infarction as per the fourth universal definition.

2.2 Exclusion Criteria

1) Patients with Sickle cell disease/ trait.
2) Iron deficiency anemia, sepsis.
3) Hemoglobinopathy or hypothyroidism.
4) Pregnant women and hemolytic anemias. Detailed history and clinical examination along with relevant laboratory and radiological examination, including ECG, 2D Echocardiography, Cardiac enzymes, and Lipid profile, was assessed to determine the severity of myocardial infarction. The treatment was given as per standard treatment protocol. Patients were followed up till hospital stay, and all complications like arrhythmias, cardiac failure, stroke, and cardiogenic shock were noted. The severity of MI was done using TIMI Score for STEMI/ NSTEMI.

The institutional ethical committee approved the protocol of this study. Informed consent was obtained from all participants.

3. STATISTICAL ANALYSIS

The collected data were analyzed with proper statistical methods using MS Excel 2016. Data were summarized in percentages and proportions. The chi-square test and Fisher Exact test have been used whenever the data is presented in terms of frequency, and the student t-test has been used to test significance when the results are presented as mean ± standard deviation (SD). The odds ratio (OR) and its confidence interval (CI) have been computed for events of interest. Multivariate logistic regression analysis has been used to assess the risk factors for predicting the event. P value <0.05 was considered statistically significant.

4. RESULTS

The demographic profile of the patients is shown below in Table 1. Most of the patients in the present study were more than 50 years of age. The mean age of the study population was 60.50 ± 10.94 years, with male predominance (63.91%).

Table 1: Distribution according to demographic variables:

Variables		No. of Patients (n=169)	Percentage
Age group (years)	≤40	08	4.73
	41-50	29	17.15
	51-60	55	32.54
	61-70	49	28.99
	>70	28	16.56
Gender	Male	108	63.91
	Female	61	36.09
Co-morbidities	Diabetes Mellitus	80	47.33
	Hypertension	75	44.37
	HISTORY OF IHD	08	4.73

Table 2: Distribution according to HbA1c (N = 169)		
HbA1c (%)	No. of patients	Percentage
<5.7	08	4.74
5.7-6.4	24	14.20
≥6.5	137	81.06
Total	169	100

It was seen that 137(81.06%) patients had HbA1c ≥ 6.5, while 5.7-6.4% HbA1c was observed among 24 (14.2%) patients. On the other hand, hbA1c levels less than 5.7 were observed in 8 (4.74%) patients.

Table 3: Distribution according to risk categories:		
Risk Category	No. of patients	Percentage
Low	23	13.61
Intermediate	41	24.26
High	105	62.13
Total	169	100

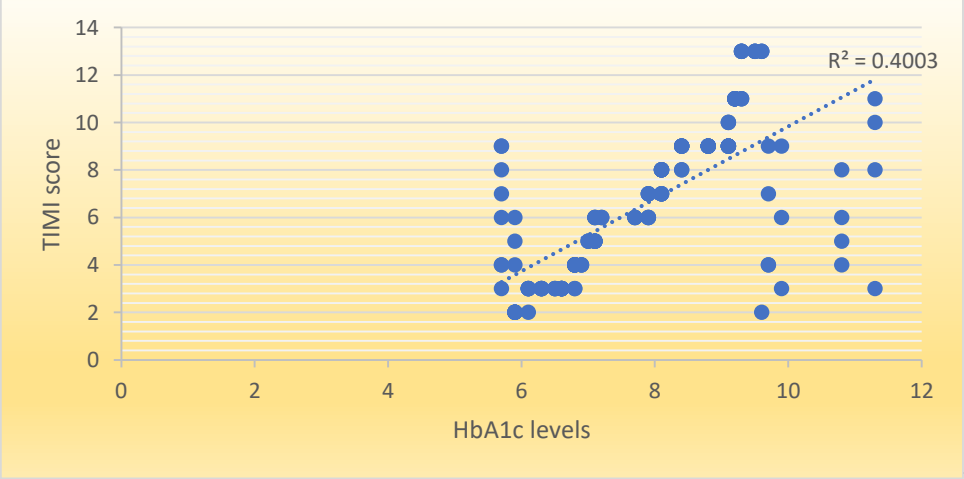
In the study population, it was observed that 23 (13.61%) patients were in the low-risk category, 41(24.26%) patients were in the Intermediate risk category, and 105 (62.13%) patients were in the high-risk category. It was seen that the majority of the patients were in the high-risk category (62.13%), followed by the intermediate-risk group (24.26%) and the low-risk group (13.61%).

Table 4: Comparison of HbA1c findings according to risk categories.				
HbA1C	Low risk	Intermediate risk	High risk	P value
<5.7	06 (26.1%)	02 (4.9%)	00 (00%)	P<0.000 (Significant)
5.7-6.4	12 (52.2%)	10 (24.4%)	02 (1.9%)	
≥ 6.5	05 (21.7%)	29 (70.7%)	103 (98.1%)	
Total	23 (100%)	41 (100%)	105 (100%)	

It was seen that the majority of the patients in the present study were more in the high-risk group with HbA1c ≥ 6.5 (98.1%) compared to the low-risk group (21.7%). It shows a strong association between the risk category and HbA1c with a statistically significant difference. (P<0.0001)

Table 5: Correlation between TIMI risk score with HbA1c			
R	R^2	P value	Statistical significance
0.6327	0.4003	< 0.00001	Statistically significant

The value of R is 0.6327. It is a moderate positive correlation, which means there is a tendency for high X variable scores to go with high Y variable scores (and vice versa). The value of R2, the coefficient of determination, is 0.4003. It shows that the TIMI risk score had a strong positive correlation with HbA1c. (<0.0001).



5. DISCUSSION

The present prospective analytical cross-sectional study was undertaken to predict the utility of HbA1c as a marker of severity in patients with acute myocardial infarction. In the present study, the majority of the patients in the present study were more than 50 years of age. The mean age of the study population was 60.50 ±10.94yrs. Similar findings were seen in the study by Muhammad Asif Bhalli et al.[8] in acute myocardial infarction, with the mean age of patients being 59 ± 14.2 years.

Gorre Chandrashekar et al.[9] observed age of the study group ranged from 25 to 90 years, with a mean age of 54.78 ± 13.27 years. Ratan Ram et al.[10] studied acute myocardial infarction at an observed mean age of 57.3 ±9.5 years. In comparison with other studies, patients in our study were younger, corroborating with the emerging evidence from various recent studies that CAD occurred a decade earlier in the Indian population. It also emphasizes the growing prevalence of CAD and changes in the at-risk population. It was seen that the majority of the patients were males (63.91%) with 1.77 :1 of male: female proportion. Koek HL et al. [11] showed the incidence of MI to be 72% in males and 24% in females. Similar studies by Bhalli et al.[8] and Chandrashekhar et al.[9] in AMI showed male preponderance, 87.8%, and 68.9%, respectively. In the present study, it was seen that 81.06% of patients had HbA1c >6.5, i.e., in an uncontrolled state. Santosh Gosavi et al. [12] found a correlation between HbA1c levels and complications and outcomes in patients with acute myocardial infarction and observed 52.5% had HbA1c levels of 7% or more. The majority of the patients were in the high-risk category (62.13%), followed by the intermediate-risk group (24.26%) and low-risk group (13.61%). The findings were comparable with Abu-Assi E et al. [13], where Low risk was 22.7%, Intermediate was 28.2%, and High risk was 49%. Similar observations were also reported by Venkatesh Munusamy[14], de Araujo Goncalves P, et al.[15], Anil Avci et al.[16], and Neeland et al.[17]. On the contrary, M.A. Cakar et al.[18] observed the majority of the patients were in low-risk groups, followed by intermediate and high-risk groups. (39.6%, 34.3%, and 26.1%, respectively). In the present study, the association of HbA1c and risk category shows a significant difference, i.e., the high-risk group had ≥6.5 HbA1c. The value of R2, the coefficient of determination, is 0.4003. The correlation of TIMI score and HbA1c shows a significant positive correlation. (P<0.0001) Santosh Gosavi et al. [12] found a correlation between HbA1c levels, complications, and outcomes in acute myocardial infarction patients. Observed high HbA1c in the elderly population should be considered a risk factor for mortality. Hence, active management should be done to keep HbA1c levels strictly below 7 in this population. Li-Feng Hong et al. [19] studied the relationship of HbA1c with severity and outcome in patients with stable CAD and observed high HbA1c was associated with three-vessel disease. The area under the receiver operating characteristic curve (AUC = 0.67, 95% CI: 0.63-0.71, P < 0.001) and multivariate logistic regression analysis suggested that HbA1C was an independent predictor of severity of CAD (OR = 1.60, 95% CI: 1.29-1.99, P < 0.001) even after adjusting for gender, age, the risk factor of CAD, lipid profile and fasting blood glucose. Several studies showed that although crude mortality data was higher in patients with elevated HbA1c following adjustment for many cardiovascular risk factors, HbA1c values failed to predict mortality independently. Others suggested that HbA1c level potently predicted in-hospital and long-term death. [20,21] It has been demonstrated that DM is a risk for the development of CAD, and individuals with DM will suffer from more intensive atherosclerotic lesions and cardiovascular events. Previous studies have already suggested an association of high-normal glucose and HbA1C levels with the presence of CAD in various individuals, such as in patients with or without diabetes, in asymptomatic persons, and even in the general population with undiagnosed diabetes. A high level of plasma HbA1C (>6.3%) was an independent predictor for the presence and severity of AMI and the early outcome of patients with AMI. Long-term follow-up may be needed for further revealing more information regarding the role of HbA1C in AMI.

6. CONCLUSION

The present study concludes a significant correlation between HbA1c levels and the severity of Acute Myocardial Infarction. Indeed, HbA1C has been proposed as a reliable tool for diagnosing DM and identifying individuals at high risk of cardiovascular events with and without DM. Type 2 diabetes mellitus (T2DM) and its complications seriously affect public health worldwide. Myocardial infarction (MI) is the primary cause of death in patients with T2DM.

7. AUTHORS CONTRIBUTION STATEMENT

Dr. Kumar Ujjwal gathered the data for this study. Dr. D. P. Lakra and Dr. M. Khande conceptualized, and necessary inputs were given to the study's design. Dr. M. Khande and Dr. Kumar Ujjwal analyzed these data. All authors discussed the methodology and results and contributed to the final manuscript.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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