ORIGINAL RESEARCH PAPER

General Medicine

AN OBSERVATIONAL CROSS SECTIONAL STUDY OF THE RELATION BETWEEN GLYCOSYLATED HEMOGLOBIN A1C AND THE SEVERITY OF CORONARY ARTERY DISEASE IN NON DIABETIC PATIENTS PRESENTING TO TERTIARY CARE CENTRE IN SOUTH WESTERN MAHARASHTRA

KEY WORDS: HbA1c, Coronary Artery Disease, Acute Coronary Syndrome, Prediabetes, Angiography

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ABSTRACT

Glycosylated hemoglobin (HbA1c) reflects average blood glucose levels over the preceding two to three months and is widely used for diabetes diagnosis and monitoring. However, its relationship with coronary artery disease (CAD) severity in non-diabetic patients remains inadequately explored. This observational cross-sectional study was conducted in a tertiary care center in South Western Maharashtra and included 140 non-diabetic patients presenting with acute coronary syndrome who underwent coronary angiography. CAD severity was categorized based on the number of significantly diseased vessels. The study demonstrated a progressive rise in mean HbA1c levels with increasing angiographic severity of CAD. Patients with prediabetic HbA1c levels showed significantly higher prevalence of multivessel disease compared to those with normal HbA1c levels. A strong positive correlation was observed between HbA1c and CAD severity, and HbA1c emerged as an independent predictor of severe coronary involvement. The findings suggest that HbA1c, even within non-diabetic range, may serve as a useful marker for cardiovascular risk stratification in acute coronary syndrome.

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, accounting for approximately 17.9 million deaths annually and representing 32% of all global deaths.[1] Among these, coronary artery disease (CAD) is the predominant contributor and is characterized by atherosclerotic plaque formation within the coronary arteries, leading to clinical manifestations ranging from stable angina to acute coronary syndrome (ACS).[2] ACS includes unstable angina, non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI), which represent varying degrees of coronary artery occlusion and myocardial injury.

The pathophysiology of ACS involves a complex interplay of endothelial dysfunction, inflammation, lipid accumulation, and thrombosis. Although traditional risk factors such as hypertension, dyslipidemia, smoking, and diabetes mellitus are well established, there is growing interest in identifying novel biomarkers that may enhance cardiovascular risk stratification and guide therapeutic decision-making.[3] Glycosylated hemoglobin A1c (HbA1c), which reflects the average blood glucose levels over the preceding two to three months, has gained attention in this context.[4]

HbA1c is formed through the non-enzymatic glycation of hemoglobin and is widely used in the diagnosis and monitoring of diabetes mellitus. Emerging evidence suggests that HbA1c may serve as a prognostic marker in CAD even among individuals without overt diabetes.[4] Chronic hyperglycemia, even at levels below the diabetic threshold, may induce oxidative stress, promote endothelial dysfunction, enhance platelet aggregation, and accelerate advanced glycation end-product formation, all of which contribute to the progression of atherosclerosis.[5]

The burden of CAD is disproportionately high in South Asian populations, including India, where it manifests nearly a decade earlier than in Western countries.[6] In India, the prevalence of prediabetes is estimated to be 10–15%, representing a substantial population at increased cardiovascular risk.[7] Previous studies examining the relationship between HbA1c and CAD severity have shown inconsistent results. A meta-analysis demonstrated that elevated HbA1c levels are associated with increased mortality and adverse cardiovascular outcomes in non-diabetic patients with coronary artery disease.[8] However, some investigations have not confirmed a significant association after adjusting for conventional risk factors.

The severity of CAD is commonly assessed using angiographic scoring systems that quantify the extent and complexity of coronary lesions.[9] However, data regarding the association between HbA1c levels and angiographic CAD severity in non-diabetic patients presenting with ACS in transitional regions such as South Western Maharashtra remain limited.

In this context, the present study aims to evaluate the association between HbA1c levels and angiographically determined severity of coronary artery disease in non-diabetic patients presenting with acute coronary syndrome at a tertiary care center in South Western Maharashtra.

MATERIALS AND METHODS

This observational cross-sectional study included 140 non-diabetic patients presenting with acute coronary syndrome who underwent coronary angiography at a tertiary care center in South Western Maharashtra. Patients with HbA1c levels less than 6.5% and no prior diagnosis of diabetes mellitus were included. Patients with known diabetes mellitus, severe anemia, chronic kidney disease, or other systemic illnesses affecting HbA1c measurement were excluded.

Venous blood samples were collected at admission for HbA1c estimation using standardized laboratory techniques. Coronary angiography was performed using standard procedures. CAD severity was categorized based on angiographic findings into normal coronaries, single vessel disease, double vessel disease, and triple vessel disease. Angiographic assessment was carried out by experienced interventional cardiologists who were blinded to laboratory parameters.

Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment.

Inclusion Criteria:

- Non-diabetic individuals (defined as those without a previous diagnosis of diabetes mellitus and with fasting plasma glucose <126 mg/dL)
- Individuals presenting with symptoms consistent with

ACS, including unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI)
- Patients who underwent coronary angiography to assess the severity of coronary artery disease (CAD)
- Patients aged 18 years and above

Exclusion Criteria:
- Diabetic individuals (defined as those with a previous diagnosis of type 1 and type 2 diabetes mellitus, currently on anti-diabetic medications, or with fasting plasma glucose ≥126 mg/dL)
- Pregnant women
- Patients with severe comorbidities such as end-stage renal disease (estimated glomerular filtration rate <30 mL/min/1.73m²), advanced liver disease (Child-Pugh class B or C), or malignancies
- Individuals with case of coronary artery disease in past .

Statistical Analysis

All statistical analyses were performed using SPSS software version 25.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were expressed as frequencies and percentages.

Normality was assessed using the Shapiro–Wilk test. Comparisons between groups were performed using one-way ANOVA for normally distributed variables and the Kruskal–Wallis test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate. Correlation between HbA1c and angiographic scores was evaluated using Spearman's rank correlation coefficient. Multiple linear regression analysis was performed to identify independent predictors of CAD severity after adjusting for confounding variables. Receiver operating characteristic (ROC) curve analysis was conducted to determine optimal HbA1c cutoff values. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The study included 140 non-diabetic patients presenting with acute coronary syndrome. Mean HbA1c levels increased progressively from 5.18±0.15% in patients with normal coronaries to 6.18±0.24% in those with triple-vessel disease (p<0.001), demonstrating a strong positive correlation (r=0.742).[1] HbA1c emerged as the strongest independent predictor of severe CAD (OR=8.92, 95% CI: 4.21–18.9, p<0.001).

Table 1- HbA1c vs CAD Severity By Age Groups

Age Group	CAG Finding	n	HbA1c (Mean ± SD)	p-value
<50 years (n=53)	Normal	8	5.12 ± 0.18	0.021
	Single	18	5.48 ± 0.25	
	Double	21	5.79 ± 0.28	
	Triple	6	6.15 ± 0.22	
50-65 years (n=74)	Normal	4	5.21 ± 0.12	<0.001
	Single	20	5.55 ± 0.31	
	Double	28	5.88 ± 0.33	
	Triple	22	6.19 ± 0.26	
>65 years (n=13)	Normal	0	-	0.045
	Single	4	5.58 ± 0.29	
	Double	5	5.92 ± 0.35	
	Triple	4	6.22 ± 0.24	

Patients with prediabetic HbA1c levels (5.7–6.4%) showed an 80.6% prevalence of multivessel disease compared to 41.2% in the normal HbA1c group (p<0.001). The prediabetic group also experienced longer hospital stays and a significantly higher incidence of major adverse cardiac events.

These findings support the hypothesis that chronic glycemic exposure, even within non-diabetic ranges, contributes to coronary atherosclerosis progression. The association between elevated HbA1c and CAD severity may be explained by mechanisms including oxidative stress, endothelial dysfunction, inflammation, and advanced glycation end-product formation. The results align with prior studies demonstrating that elevated HbA1c levels are associated with increased mortality and adverse cardiovascular outcomes in non-diabetic CAD patients.

CONCLUSION

HbA1c demonstrates a strong independent association with coronary artery disease severity in non-diabetic patients presenting with acute coronary syndrome. Elevated HbA1c levels correlate with increased prevalence of multivessel disease and adverse clinical outcomes. HbA1c may therefore serve as a valuable marker for cardiovascular risk stratification beyond traditional risk factors.

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