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Role of HbA1C & Glycated Albumin as Predictors of Cardiovascular Outcome Post-Myocardial Infarction in Diabetic Patients: A Matched Case-Control Study

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Keywords

cardio-vascular diseases;
diabetes mellitus;
glycated albumin;
HbA1C;
myocardial infarction;

Abstract

Background: Diabetes mellitus significantly increases the risk of adverse cardiovascular outcomes following ST-elevation myocardial infarction (STEMI). Glycaemic markers like HbA1C and glycated albumin (GA) may serve as prognostic indicators, but their predictive validity in Indian diabetic populations remains underexplored. Thus, this study was conducted to evaluate the prognostic value of HbA1C and GA in predicting adverse cardiovascular outcomes post-MI in diabetic patients. **Methods:** A matched case-control study was conducted among 260 type II diabetic STEMI patients in a tertiary care hospital. Cases were those developing post-MI complications; age- and sex-matched controls who did not. Glycaemic markers and clinical risk factors were analyzed using conditional logistic regression and ROC analysis. **Results:** Raised HbA1C and GA levels were significantly associated with higher odds of post-MI complications (aOR: 5.55 and 10.9, respectively). GA showed superior diagnostic accuracy (AUC: 0.948) and specificity (57.6%) over HbA1C. **Conclusion:** GA is a promising biomarker for risk stratification in diabetic patients post-MI and may complement HbA1C in clinical practice.

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Contents

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1 Introduction

Cardiovascular disease (CVD) has emerged as a leading cause of morbidity and mortality globally and in India. Myocardial infarction (MI), a major clinical manifestation of ischemic heart disease, accounts for a substantial proportion of premature deaths and disability-adjusted life years in India, with an increasing incidence in younger populations (Prabhakaran et al., 2016). Simultaneously, India is witnessing a rapid rise in the prevalence of type II diabetes mellitus (T2DM), with over 74 million cases estimated in 2023—ranking second globally (International Diabetes Federation, 2021). Diabetes not only predisposes individuals to macrovascular complications but also contributes significantly to acute microvascular injury, including endothelial dysfunction and impaired coronary microcirculation, which may exacerbate myocardial damage during infarction (Mengstie et al., 2022).

In diabetic patients, the incidence of MI is significantly higher compared to non-diabetics. Studies such as the Chennai Urban Population Study reported a threefold greater prevalence of MI among individuals with diabetes (Mohan et al., 2001). Additionally, the CREATE registry and other Indian STEMI cohorts have found that 30–40% of MI patients present with diabetes, and these patients tend to have more severe infarcts, higher rates of complications such as heart failure, and worse long-term cardiovascular outcomes (Xavier et al., 2008). Even after reperfusion therapy, such as thrombolysis or primary percutaneous coronary intervention (PCI), patients with ST-elevation myocardial infarction (STEMI) remain at considerable risk for adverse cardiovascular events, including reinfarction, stroke, cardiac failure, arrhythmias, and mortality (Ibanez et al., 2018). This residual risk is often higher in diabetic patients, attributed in part to persistent subclinical inflammation, endothelial dysfunction, and altered platelet activity. [7] However, despite the growing burden of MI in India, there is a notable absence of reliable blood-based biomarkers that can predict adverse post-MI outcomes, particularly in diabetic or dysglycemic populations (Deedwania et al., 2008).

Hemoglobin A1c (HbA1c) reflects long-term glycemic control over the past 2–3 months, while glycated albumin (GA) reflects shorter-term glycemic excursions over 2–3 weeks. Both have been increasingly studied for their role in cardiovascular prognosis. Elevated HbA1c and GA levels have been associated with poor outcomes in acute coronary syndrome (ACS) and post-MI patients in various global cohorts (Zhang et al., 2024; Kim et al., 2021). However, Indian data in this context remain sparse, despite the differing glycemic profiles, including higher postprandial glucose levels and earlier onset of complications in Indian diabetics (Unnikrishnan et al., 2014). Thus, we conducted this matched case-control study to evaluate the prognostic value of HbA1c and GA in STEMI patients, in predicting adverse cardiovascular outcomes in the post-MI period.

2 Materials and Methods

This institution-based observational study with a matched case-control design was conducted in a tertiary care hospital of Kolkata from December 2023 to January 2025. It was conducted among 260 type II diabetes mellitus patients who were presented with STEMI.

Sample size Calculation & Sampling: Sample size was calculated using the following formula,

$$n = \frac{(r+1)}{r} \frac{P(1-P)\left(Z_{1-\alpha} + Z_{1-\beta}\right)^2}{(P_1 - P_2)^2}$$

Where dyslipidaemia in diabetic patients is a risk factor for developing adverse outcomes in the post-MI period, and the proportion of dyslipidaemia among diabetic patients with & without adverse outcomes in the post-MI period was found to be 51% & 33.8 (Wei et al., 2016). Thus, with a case & control ratio of 1:1 at a 95% confidence level, 80% power, we arrived at the sample size of 130 cases & 130 controls. Systematic random sampling was used to recruit study participants using the patients' register as a sampling frame.

Data Collection: Adult individuals (18 years and above) who were presented with STEMI and had known history of diabetes for at least one year, now admitted after undergoing necessary interventions for STEMI i.e. thrombolysis or Percutaneous Coronary Intervention (PCI), were approached (or their family member in case the condition of the patient was critical) and recruited only after taking informed written consent (In case of consent given by family members, consent was also taken from the study participant after they recovered/ stabilized). They were asked about related socio-demographic information, i.e., age, sex, behavioural factors such as smoking, and co-morbidities etc. A venous blood sample was drawn for estimation of HbA1C & Glycated albumin levels under strict aseptic conditions. Among the participants, those who developed any kind of adverse event were considered cases, and other participants of the same sex, with similar age group (within a 5-year range) who didn't develop any adverse event, were recruited as matched controls.

Statistical Analysis: Data was analysed using MS Excel version 2019 & SPSS version 25 software. Continuous & categorical data were described using mean ± SD or Median (Inter-Quartile Range) as per the normality of the data & number (percentage). Normality of the data was assessed using the Shapiro-Wilk test. An appropriate test of significance was used to check for any statistical significance (a p-value less than 0.05 was considered significant). To identify the risk factors, multivariable conditional logistic regression was performed. Model fitness was assessed using the likelihood ratio test statistic. The Receiver Operating Characteristic (ROC) curve was used to predict the adverse outcome in the post-MI period by HbA1C & Glycated albumin levels.

Ethical Statement: This study was approved by the institutional ethics committee (ref No. 1746/ NOV/2022-'23) and all ethical principles as per the Declaration of Helsinki were strictly adhered to during the study procedure.

3 Results and Discussions

3.1 Results

The mean age of the study participants was 53.4 ± 8.6 years and 55.6 ± 6.9 years among the cases & controls, respectively. Among the cases, the most common post-MI complication observed was arrhythmia (59.4%), mostly atrial fibrillation, followed by repeat MI (22.5%), stroke (17.6%), and heart failure (10.7%). Only three people died among the cases. In comparison to controls, cases had a statistically significantly higher proportion of smoking (40% v/s 52.3%, p-value 0.046), hypertension (66.1% v/s 86.1%, p-value 0.001), and Dyslipidaemia (50.7% v/s 70.7%, p-value < 0.001). Among the study participants, though cases had a higher mean duration of diabetes, it was not statistically significant (p-value 0.05). [Table 1].

Among them, cases had a statistically significantly higher proportion of raised HbA1C levels (93% v/s 70.7%, p-value 0.007) in comparison to controls, and similar findings were noticed in the case of raised glycated albumin levels (98.4% v/s 42.3%, p-value < 0.001). Multivariable conditional logistic regression showed that participants with dyslipidaemia had 6.52 times higher odds of developing cardiovascular adverse events in the post-MI period. Participants with raised HbA1C levels & glycated albumin levels also had 5.55 times & 10.9 times higher odds of developing adverse events in the post-MI period, respectively. (Model was fit with likelihood ratio test statistic 0.459) [Table 1]

Both HbA1C & Glycated albumin levels had high sensitivity in predicting post-MI adverse events (93% & 98.4%, respectively), while glycated albumin levels are more specific to rule out any post-MI adverse events in comparison to HbA1C levels (57.6% v/s 29.2%). [Table 2]. ROC curve also showed that glycated albumin had

overall higher validity in comparison to HbA1C levels in predicting post-MI adverse events in diabetic patients. [Figure 1]

3.2 Discussion

We conducted a matched case-control study to assess the prognostic value of HbA1C and glycated albumin (GA) levels in predicting adverse cardiovascular outcomes in diabetic patients post-ST-elevation myocardial infarction (STEMI). The findings provide compelling evidence that both HbA1C and GA serve as significant predictors of post-MI complications, with GA demonstrating superior predictive validity. The mean age of the study population (53.4 ± 8.6 years among cases) aligns with the known epidemiological pattern of MI in Indian diabetics, who tend to experience cardiovascular events at a younger age compared to Western populations (Yusuf et al., 2001). The higher prevalence of atrial fibrillation (59.4%), recurrent MI (22.5%), and stroke (17.6%) among cases highlights the substantial burden of adverse events in the post-MI period among diabetics.

Among classical risk factors, hypertension, dyslipidaemia, and smoking were significantly more prevalent in cases, supporting the existing literature that these comorbidities potentiate post-MI complications (Fox et al., 2007; Huang et al., 2020). Importantly, while the mean duration of diabetes was longer among cases, it was not statistically significant, suggesting that glycaemic control, rather than duration alone, may be more critical in predicting outcomes—a hypothesis corroborated by this study's findings on glycaemic markers. Both HbA1C and GA levels were significantly elevated in cases compared to controls, and their association with adverse cardiovascular events remained significant after adjusting for confounders. Specifically, raised HbA1C and GA conferred 5.55- and 10.9-times higher odds, respectively, of developing complications post-MI. This reinforces earlier findings suggesting that chronic hyperglycaemia, as captured by HbA1C, and more acute glycaemic fluctuations, reflected by GA, contribute to adverse cardiac remodelling and poor recovery (Jiao et al., 2023; Furusyo & Hayashi, 2013).

The higher sensitivity of GA (98.4%) and better specificity (57.6%) compared to HbA1C (93% sensitivity, 29.2% specificity) in predicting complications further supports its clinical utility. GA also had a higher area under the ROC curve (0.948 vs. 0.678), suggesting superior overall accuracy. These findings align with recent studies that propose GA as a more responsive marker to glycaemic excursions and oxidative stress, which are more closely linked to cardiovascular pathology than chronic glycaemic burden alone (Kobayashi et al., 2018; Selvin et al., 2015). Several prior studies have indicated the role of HbA1C as a predictor of cardiovascular risk in diabetic patients. A meta-analysis by Cavender et al. (2015), reported that each 1% rise in HbA1C was associated with a 15–18% increase in cardiovascular events. However, recent evidence suggests that HbA1C may not fully capture short-term glycaemic variability, which can be a critical driver of acute complications post-MI (Monnier et al., 2008). Glycated albumin, with its shorter half-life (14–20 days), is more sensitive to recent glycaemic changes. In a prospective study by Selvin et al., GA showed stronger associations with coronary artery disease than HbA1C, especially in patients with renal dysfunction or anaemia, which may impair the accuracy of HbA1C readings (Selvin et al., 2015; Abbas et al., 2023). Our findings support this and extend the evidence to the Indian context, where variability in haemoglobinopathies and malnutrition can limit HbA1C reliability. The elevated cardiovascular risk associated with increased GA levels can be explained through multiple mechanisms. GA reflects rapid glycaemic fluctuations, which are closely linked to endothelial dysfunction, oxidative stress, and pro-thrombotic states—all of which are critical contributors to myocardial remodeling and post-infarct complications (Ceriello et al., 2009). On the other hand, elevated HbA1C, indicative of prolonged hyperglycaemia, promotes advanced glycation end-product (AGE) formation and low-grade chronic inflammation, exacerbating atherosclerotic progression and vascular stiffness (Forbes & Cooper, 2013).

Strengths & Limitations

Despite its strengths like matched case-control design, inclusion of both traditional (HbA1C) and emerging (i.e. glycated albumin) biomarkers and use of ROC analysis and multivariable modelling enhanced interpretability and clinical relevance, the study has several limitations, like though sample size was statistically adequate, it was limited to a single tertiary care center, potentially restricting generalizability.

Other glycaemic markers like fructosamine or continuous glucose monitoring (CGM) data were not included, which could have provided a more comprehensive assessment. Nonetheless, the study used a retrospective case-control design, which may introduce selection and recall bias. A confounding by treatment variability, like medication adherence and therapeutic regimens post-MI (e.g., statins, beta-blockers, antiplatelets), was not controlled for, which could influence outcomes. Thus, future studies might consider a prospective cohort design to establish temporal causality.

4 Conclusion

These study findings highlight glycated albumin's potential as a robust biomarker in stratifying cardiovascular risk among diabetic patients post-MI, based on which future research should explore options like integration of glycated albumin in risk prediction models like TIMI or GRACE scores., evaluation of glycated albumin-guided glycaemic control strategies in post-MI period, and lastly the role of glycated albumin in predicting other microvascular and macrovascular complications. From a clinical standpoint, the study supports the dual use of HbA1C and glycated albumin in diabetic patients recovering from MI to better individualize risk and treatment plans, especially in the Indian context where HbA1C accuracy may be compromised by anaemia or haemoglobinopathies.

Author Contribution:
All three authors had contributed to Conceptualization, data collection & analysis, manuscript writing & editing, supervision, and Guarantor

Conflict of Interest:
The Author declared that there was no conflict of interest.

Ethical statement:
This study was approved by the institutional ethics committee (ref No. 1746/ NOV/2022-'23), and all ethical principles as per the Declaration of Helsinki were strictly adhered to during the study procedure. Written informed consent was taken from the study participants or their family member, whichever is applicable.

Data Availability Statement:
Data related to this study will be available upon request to the corresponding author.

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Appendix

Table 1
Distribution & comparison of the study participants as per various parameters (N = 260)

Parameters	Number (%)		p-value	Matched aOR (95% CI)
	Case (n = 130)	Control (n = 130)		
Age (Years)	53.4 ± 8.6**	55.6 ± 6.9**	0.988#	-
Sex				
Male	87 (66.9)	87 (66.9)	-	-
Female	43 (33.1)	43 (33.1)		
Smoking				
Yes	68 (52.3)	52 (40)	**0.046***	1.76 (0.1 – 3.59)
No	62 (47.7)	78 (60)		1 (Reference)
Hypertension				
Yes	112 (86.1)	86 (66.1)	**0.001***	3.69 (0.9 – 7.45)
No	18 (13.9)	44 (33.9)		1 (Reference)
Dyslipidaemia				
Yes	92 (70.7)	66 (50.7)	**< 0.001***	**6.52 (2.29 – 14.8)**
No	38 (29.3)	64 (49.3)		1 (Reference)
Duration of Diabetes (Years)	10.7 ± 2.1**	7.6 ± 3.1**	0.05#	2.01 (0.2 – 4.47)
HbA1C level (%)				
Raised (> 6.5)	121 (93)	92 (70.7)	**0.007***	**5.55 (4.32 – 10.96)**
Normal (≤ 6.5)	9 (7)	38 (29.3)		1 (Reference)
Glycated Albumin level (%)				
Raised (> 14.3)	128 (98.4)	55 (42.3)	**< 0.001***	**10.9 (8.42 – 12.22)**
Normal (≤ 14.3)	2 (1.6)	75 (57.7)		1 (Reference)
Total	130 (100)	130 (100)		

Paired t-test *McNamara's Chi-square test ** Mean ± SD
aOR(95% CI): Adjusted Odds Ratio (95% Confidence Level), Likelihood ratio statistic 0.459

Table 2
Validity of HbA1C & glycated albumin level in predicting adverse events post-MI (N = 260)

Predictors	Number (%)		ROC AUC (95% CI)	p-value	Sensitivity	Specificity
	Case (n = 130)	Control (n = 130)				
HbA1C level (%) *	9.96 ± 2.7	6.71 ± 1.3	0.678 (0.559 – 0.797)	**0.005**	93%	29.2%
Raised (> 6.5)	121 (93)	92 (70.7)				
Normal (≤ 6.5)	9 (7)	38 (29.3)				
Glycated albumin level (%) *	15.6 ± 9.2	9.79 ± 3.7	0.948 (0.948 – 0.99)	**< 0.01**	98.4%	57.6%
Raised (> 14.3)	128 (98.4)	55 (42.3)				
Normal (≤ 14.3)	2 (1.6)	75 (57.7)				
Total	130 (100)	130 (100)				

* Mean ± SD AUC: Area Under the Curve

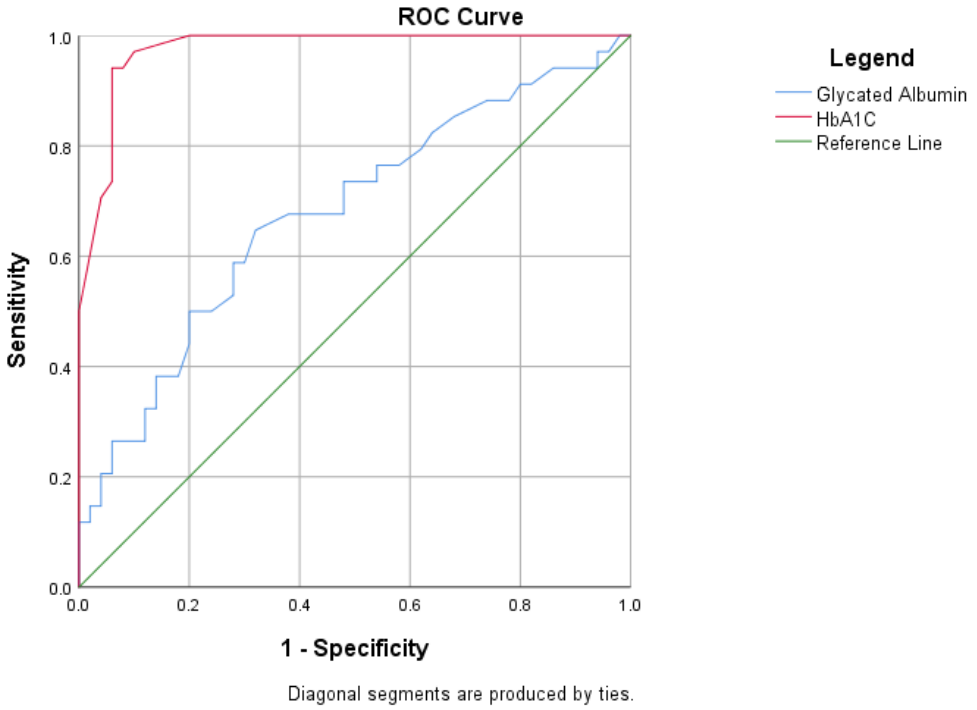
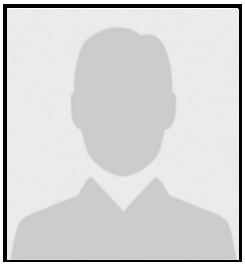


Figure 1. Receiver Operating Characteristics (ROC) curve showing the validity of the parameters in predicting adverse events post-MI (N = 260)

Biography of Authors



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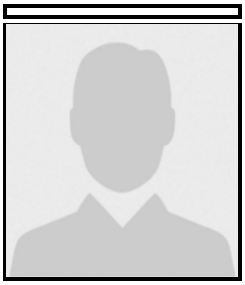

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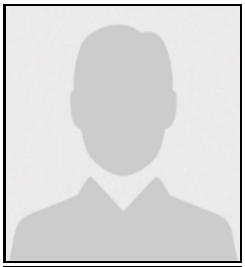

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