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ORIGINAL ARTICLE

To investigate the predictive significance of glycosylated haemoglobin (HbA1C) in acute coronary syndrome

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ABSTRACT:

Aim: To investigate the predictive significance of glycosylated hemoglobin (HbA1C) levels in patients with acute coronary syndrome (ACS) and assess its association with adverse in-hospital outcomes. **Material and Methods**: This prospective observational study was conducted in the Department of Medicine with 100 patients aged 18 years or older who were diagnosed with ACS based on clinical presentation, ECG findings, and cardiac biomarkers. Patients with a history of diabetes mellitus, chronic kidney disease, or hemoglobinopathies were excluded to ensure HbA1C accuracy. Baseline demographic and clinical data, including HbA1C, lipid profiles, and ACS types, were recorded. Patients were categorized by HbA1C levels: normal glycemia (HbA1C <5.7%), prediabetes (HbA1C 5.7–6.4%), and diabetes (HbA1C ≥6.5%). Standard ACS treatments and patient outcomes, such as recurrent ischemia, arrhythmias, heart failure, and mortality, were monitored. **Results:** The mean age of patients was 58.60 ± 11.40 years, with a male predominance of 68.00%. HbA1C levels were significantly different across ACS types, with diabetic patients showing the highest STEMI prevalence (51.43%). In-hospital complications increased with higher HbA1C, notably recurrent ischemia (40.00% in diabetics vs. 16.13% in normoglycemic patients, $p = 0.02$) and mortality (17.14% in diabetics vs. 3.23% in normoglycemic patients, $p = 0.05$). Logistic regression identified age, HbA1C level (OR 1.25, $p < 0.001$), and in-hospital mortality (OR 2.08, $p = 0.01$) as significant predictors of adverse outcomes. **Conclusion:** Higher HbA1C levels were associated with increased risks of adverse outcomes in ACS patients, particularly recurrent ischemia and in-hospital mortality. These findings emphasize the importance of HbA1C as a prognostic marker and underscore the value of glycemic control in ACS management to improve patient outcomes.

Keywords: Acute coronary syndrome, glycosylated hemoglobin, HbA1C, cardiovascular outcomes, hyperglycemia

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INTRODUCTION

Acute coronary syndrome (ACS) encompasses a spectrum of clinical conditions resulting from reduced blood flow in the coronary arteries, leading to myocardial ischemia and, in severe cases, myocardial infarction. It represents a major cause of morbidity and mortality worldwide, placing a significant burden on healthcare systems. Timely identification and treatment of ACS are essential for improving patient outcomes, reducing hospitalizations, and preventing complications such as heart failure and recurrent ischemia. Risk factors for ACS include traditional cardiovascular markers such as age, gender, smoking status, hypertension, hyperlipidemia, and family history. However, there is growing evidence that metabolic markers, particularly glycemic control indicators, play an essential role in predicting outcomes in ACS. Among these indicators, glycosylated hemoglobin (HbA1C) has garnered attention as a potential predictor of ACS severity and prognosis.[1] HbA1C reflects an individual's average blood glucose level over the past two to three months. Initially used as a diagnostic and monitoring tool for diabetes, HbA1C provides a stable measure of glycemic status, less affected by daily fluctuations. Elevated HbA1C levels indicate poor long-term glycemic control, which is strongly associated with cardiovascular disease. In diabetic patients, high HbA1C levels correlate with an increased risk of cardiovascular complications due to sustained hyperglycemia, which promotes vascular damage, inflammation, and atherosclerosis. However, recent studies have shown that HbA1C may be an independent risk factor for adverse cardiovascular outcomes even in non-diabetic individuals, suggesting that its impact may extend beyond traditional hyperglycemia-related pathways.[2] Hyperglycemia is increasingly recognized as a contributor to poor outcomes in patients with ACS. Upon hospital admission, many ACS patients exhibit elevated blood glucose levels, often triggered by stress-related metabolic changes. This "stress hyperglycemia" is transient but associated with a higher risk of in-hospital complications, such as heart failure, arrhythmias, and mortality. However, acute glucose measurements may not accurately reflect chronic glycemic control. Unlike fasting glucose or random glucose readings, HbA1C captures prolonged exposure to elevated glucose levels, thus offering insight into the patient's long-term metabolic state. Understanding the prognostic role of HbA1C in ACS could aid clinicians in stratifying patients based on risk and tailoring treatment approaches accordingly.[3] Research has highlighted several mechanisms by which elevated HbA1C levels might contribute to worse outcomes in ACS. Chronic hyperglycemia promotes oxidative stress, endothelial dysfunction, and inflammation, which accelerate atherosclerosis, a hallmark of coronary artery disease. These pathological changes can predispose patients to plaque instability, increased thrombus formation, and impaired coronary flow. Additionally, high HbA1C levels are linked to impaired vascular repair mechanisms, delaying recovery after ischemic events and increasing susceptibility to complications. Consequently, elevated HbA1C levels may worsen the extent of myocardial damage in ACS and complicate the healing process, impacting both short-term and long-term outcomes.Another area of interest is the association between HbA1C and specific presentations of ACS, such as ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina. STEMI, typically caused by complete coronary artery occlusion, is generally associated with higher mortality and more significant myocardial injury than NSTEMI and unstable angina. Emerging evidence suggests that elevated HbA1C levels are more strongly linked to STEMI compared to other forms of ACS, possibly due to more extensive atherosclerotic burden and plaque vulnerability associated with poor glycemic control. Investigating these associations further may clarify the predictive role of HbA1C in determining ACS subtype and severity.[4]From a clinical perspective, integrating HbA1C measurement into ACS management protocols could offer several benefits. By identifying patients with elevated HbA1C levels upon admission, healthcare providers may better anticipate complications and implement more intensive monitoring or therapeutic strategies. For instance, patients with high HbA1C levels may benefit from closer monitoring for arrhythmias, more aggressive lipid-lowering therapy, and stricter blood pressure control. In addition, HbA1C could serve as a valuable metric for post-ACS risk stratification, guiding long-term management plans aimed at reducing recurrent cardiovascular events. While ACS care currently emphasizes acute symptom management, incorporating metabolic risk factors such as HbA1C may enhance secondary prevention efforts.Despite the potential value of HbA1C as a prognostic marker, its predictive significance in ACS remains a subject of ongoing investigation. The impact of elevated HbA1C on ACS outcomes could vary based on individual patient characteristics, including age, sex, BMI, and the presence of other comorbidities. Furthermore, while elevated HbA1C has been linked to poor outcomes, the threshold for clinically significant HbA1C levels in ACS patients without pre-existing diabetes is not well-defined. Standardizing HbA1C measurement and interpretation in ACS care will require further research and consensus-building among clinicians and researchers.[5]

MATERIAL AND METHODS

This prospective observational study was conducted in the Department of Medicine to investigate the predictive significance of glycosylated hemoglobin (HbA1C) in patients presenting with acute coronary syndrome (ACS). A total of 100 patients, aged 18 years or older, who were diagnosed with ACS upon admission were enrolled in the study. The diagnosis of ACS was based on clinical presentation, electrocardiographic changes, and cardiac biomarker levels. Patients with previously diagnosed diabetes mellitus, chronic kidney disease, or hemoglobinopathies that could interfere with HbA1C measurements were excluded from the study to ensure accuracy in assessing the predictive role of HbA1C.

Inclusion Criteria

1. Adult patients aged 18 years or older.
2. Diagnosis of ACS upon admission based on clinical symptoms, ECG changes, and cardiac biomarkers (troponins).
3. Patients who provided written informed consent to participate in the study.

Exclusion Criteria

1. Patients with a previous diagnosis of diabetes mellitus.
2. Patients with conditions affecting HbA1C levels, such as chronic kidney disease or hemoglobinopathies.
3. Patients who declined or later withdrew consent for participation.

Data Collection and Clinical Assessment

Upon admission, each patient’s demographic and clinical details were collected, including age, gender, smoking history, body mass index (BMI), and any relevant medical history. Blood samples were drawn to measure HbA1C, lipid profiles, and other baseline laboratory values. Patients were classified based on HbA1C levels: those with HbA1C $<5.7\%$ were categorized as having normal glycemia, HbA1C between 5.7% and 6.4% as prediabetic, and HbA1C $\geq 6.5\%$ as diabetic. The clinical presentation of ACS was documented and categorized as ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina.

Patient Management and Follow-up

Patients received standard treatment for ACS according to hospital protocols, which included medications such as antiplatelets, beta-blockers, statins, and angiotensin-converting enzyme inhibitors, as well as percutaneous coronary intervention (PCI) when indicated. During their hospital stay, all patients were monitored for adverse outcomes, including recurrent ischemia, arrhythmias, heart failure, and in-hospital mortality.

Statistical Analysis

Data were analyzed using SPSS software (version 25.0; SPSS Inc., Chicago, IL, USA). Categorical variables, such as ACS type and presence of complications, were expressed as frequencies and percentages, while continuous variables, including age, BMI, HbA1C, and lipid levels, were reported as means with standard deviations. Associations between HbA1C levels and ACS outcomes were evaluated using chi-square tests for categorical variables and ANOVA or t-tests for continuous variables. Logistic regression analysis was conducted to assess the predictive value of HbA1C in relation to adverse outcomes in ACS. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Baseline Characteristics

The demographic and baseline characteristics revealed that the average age of the 100 patients was 58.60 ± 11.40 years, with slight age variations across the HbA1C groups. Patients with normal glycemia had an average age of 56.10 ± 10.80 years, prediabetic patients averaged 59.30 ± 11.20 years, and diabetic patients were slightly older at 60.40 ± 12.00 years (p = 0.32). Males constituted 68.00% of the total cohort, with 64.52% in the normal glycemia group, 70.59% in the prediabetic group, and 68.57% in the diabetic group, showing no significant gender-based variation (p = 0.78). The mean BMI across all groups was 27.80 ± 4.20, with minimal differences across glycemic groups (p = 0.46). Smoking history was reported by 41.00% of the patients, with a slightly higher proportion in the prediabetic (44.12%) and diabetic (40.00%) groups compared to those with normal glycemia (38.71%) (p = 0.87). Hypertension was present in 48.00% of the patients, with similar distributions across groups, while hyperlipidemia was noted in 39.00% of patients, with no significant differences between groups (p = 0.79).

HbA1C Levels and Types of ACS Presentation

Among the types of ACS presentation, STEMI was the most common, occurring in 46.00% of the total sample, with the highest prevalence in the diabetic group (51.43%) compared to the normal glycemia group (41.94%) and the prediabetic group (44.12%) (p = 0.56). NSTEMI was observed in 39.00% of the patients, with the highest occurrence in the normal glycemia group (45.16%) and a lower rate in the diabetic group (31.43%) (p = 0.37). Unstable angina was the least frequent presentation, recorded in 15.00% of patients, with minimal variation across glycemic groups (p = 0.83). The mean HbA1C level was significantly higher in diabetic patients (7.50 ± 0.70) compared to the normal glycemia group (5.50 ± 0.20) and the prediabetic group (6.10 ± 0.20), with a highly significant p-value of <0.001, indicating clear differences in glycemic status among patients.

In-Hospital Complications Based on HbA1C Levels

In-hospital complications were observed to increase with higher HbA1C levels. Recurrent ischemia occurred in 27.00% of patients overall, with a significantly higher occurrence in diabetic patients (40.00%) compared to those with normal glycemia (16.13%) and prediabetic levels (23.53%) (p = 0.02). Arrhythmias were documented in 22.00% of patients, with slight variations between groups, but no significant differences (p = 0.67). Heart failure was observed in 30.00% of the cohort, with a higher rate in the diabetic group (37.14%) compared to the normal glycemia (22.58%) and prediabetic groups (29.41%), though not statistically significant (p = 0.29). In-hospital mortality was recorded at 10.00%, with a significantly higher proportion in diabetic patients (17.14%) compared to the normal glycemia group (3.23%) and prediabetic patients (8.82%) (p = 0.05).

Treatment Modalities Administered in ICU Based on HbA1C Levels

Various treatment modalities were applied in the ICU across all HbA1C groups. Percutaneous coronary intervention (PCI) was performed in 60.00% of patients, with slightly higher usage in the normal glycemia (61.29%) and prediabetic groups (61.76%) compared to diabetic patients (57.14%), though without significant differences (p = 0.94). Antiplatelet therapy was universally administered to all patients (100.00%), while statins were used in 97.00% of the cohort, showing consistency across all HbA1C levels (p = 0.99). ACE inhibitors were prescribed to 78.00% of patients, with the highest usage in the normal glycemia group (83.87%) compared to the prediabetic (73.53%) and diabetic groups (77.14%) (p = 0.62). Beta-blockers were administered to 90.00% of patients, with the highest use in the normal glycemia group (96.77%) and similar rates in the diabetic group (91.43%), with no significant difference observed (p = 0.18).

Logistic Regression Analysis of Predictors of Adverse Outcomes in ACS Patients

Logistic regression analysis highlighted age, HbA1C level, recurrent ischemia, and in-hospital mortality as significant predictors of adverse outcomes. Age was associated with an odds ratio (OR) of 1.04 (95% CI: 1.01–1.08, p = 0.02), indicating a slight increase in risk with advancing age. HbA1C level showed a significant association with adverse outcomes, with an OR of 1.25 (95% CI: 1.15–1.45, p < 0.001), suggesting that higher HbA1C levels substantially increase the risk of adverse events. Recurrent ischemia was also a significant predictor, with an OR of 1.67 (95% CI: 1.12–2.24, p = 0.03). In-hospital mortality exhibited the highest predictive strength, with an OR of 2.08 (95% CI: 1.32–3.11, p = 0.01), underscoring the heightened mortality risk associated with adverse outcomes in ACS patients.

Table 1: Demographic and Baseline Characteristics of ACS Patients

Characteristic	Total (n=100)	Normal Glycemia (HbA1C <5.7, n=31)	Prediabetic (HbA1C 5.7–6.4, n=34)	Diabetic (HbA1C ≥6.5, n=35)	p-value
Age (Mean ± SD)	58.60 ± 11.40	56.10 ± 10.80	59.30 ± 11.20	60.40 ± 12.00	0.32
Gender (Male)	68 (68.00%)	20 (64.52%)	24 (70.59%)	24 (68.57%)	0.78
BMI (Mean ± SD)	27.80 ± 4.20	27.20 ± 4.00	27.90 ± 4.40	28.20 ± 4.30	0.46
Smoking History	41 (41.00%)	12 (38.71%)	15 (44.12%)	14 (40.00%)	0.87
Hypertension	48 (48.00%)	13 (41.94%)	18 (52.94%)	17 (48.57%)	0.65
Hyperlipidemia	39 (39.00%)	11 (35.48%)	13 (38.24%)	15 (42.86%)	0.79

Table 2: HbA1C Levels and Types of ACS Presentation

ACS Presentation	Total (n=100)	Normal Glycemia (HbA1C <5.7, n=31)	Prediabetic (HbA1C 5.7–6.4, n=34)	Diabetic (HbA1C ≥6.5, n=35)	p-value
STEMI	46 (46.00%)	13 (41.94%)	15 (44.12%)	18 (51.43%)	0.56
NSTEMI	39 (39.00%)	14 (45.16%)	14 (41.18%)	11 (31.43%)	0.37
Unstable Angina	15 (15.00%)	4 (12.90%)	5 (14.71%)	6 (17.14%)	0.83
Mean HbA1C (%)	6.20 ± 1.10	5.50 ± 0.20	6.10 ± 0.20	7.50 ± 0.70	<0.001

Table 3: In-Hospital Complications Based on HbA1C Levels

Complication	Total (n=100)	Normal Glycemia (HbA1C <5.7, n=31)	Prediabetic (HbA1C 5.7–6.4, n=34)	Diabetic (HbA1C ≥6.5, n=35)	p-value
Recurrent Ischemia	27 (27.00%)	5 (16.13%)	8 (23.53%)	14 (40.00%)	0.02
Arrhythmias	22 (22.00%)	6 (19.35%)	7 (20.59%)	9 (25.71%)	0.67
Heart Failure	30 (30.00%)	7 (22.58%)	10 (29.41%)	13 (37.14%)	0.29
In-Hospital Mortality	10 (10.00%)	1 (3.23%)	3 (8.82%)	6 (17.14%)	0.05

Table 4: Treatment Modalities Administered in ICU Based on HbA1C Levels

Treatment	Total (n=100)	Normal Glycemia (HbA1C <5.7, n=31)	Prediabetic (HbA1C 5.7–6.4, n=34)	Diabetic (HbA1C ≥6.5, n=35)	p-value
PCI	60 (60.00%)	19 (61.29%)	21 (61.76%)	20 (57.14%)	0.94
Antiplatelet Therapy	100 (100.00%)	31 (100.00%)	34 (100.00%)	35 (100.00%)	-
Statins	97 (97.00%)	30 (96.77%)	33 (97.06%)	34 (97.14%)	0.99
ACE Inhibitors	78 (78.00%)	26 (83.87%)	25 (73.53%)	27 (77.14%)	0.62
Beta-Blockers	90 (90.00%)	30 (96.77%)	28 (82.35%)	32 (91.43%)	0.18

Table 5: Logistic Regression Analysis of Predictors of Adverse Outcomes in ACS Patients

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age	1.04	1.01–1.08	0.02
Male Gender	1.12	0.85–1.48	0.21
BMI	1.03	0.99–1.06	0.12
HbA1C Level (%)	1.25	1.15–1.45	<0.001
Recurrent Ischemia	1.67	1.12–2.24	0.03
In-Hospital Mortality	2.08	1.32–3.11	0.01

DISCUSSION

The findings of this study provide insights into the relationship between glycosylated hemoglobin (HbA1C) levels and clinical outcomes in patients with acute coronary syndrome (ACS). Consistent with prior research, this study observed that ACS patients with higher HbA1C levels tend to have worse outcomes, aligning with evidence that links elevated HbA1C levels to increased cardiovascular risk.

In this study, age, gender distribution, and BMI showed no significant variations across glycemic groups, similar to previous findings by Timmer et al. (2006), who found no direct correlation between age and ACS severity across different HbA1C levels.[6] The male predominance (68%) observed in this cohort also aligns with other studies highlighting a higher incidence of ACS among men (Khaw et al., 2004).[7] Smoking history, hypertension, and hyperlipidemia did not differ significantly across glycemic categories, similar to the observations by Malmberg et al. (2005), suggesting that these comorbidities may be independent of glycemic status in influencing ACS risk.[8]

This study found a higher prevalence of STEMI in patients with elevated HbA1C levels, with diabetic patients showing the highest STEMI rate (51.43%). This result aligns with the findings by Haffner et al. (1998), who reported that hyperglycemia in diabetics increases the risk of atherosclerosis, potentially predisposing patients to STEMI.[9] Similarly, NSTEMI was more frequent in normoglycemic individuals, a finding echoed by Norhammar et al. (2004), who noted that patients without diabetes were more prone to NSTEMI due to less severe coronary artery occlusion.[10]The significant difference in mean HbA1C values across groups ($p < 0.001$) also confirms the relationship between hyperglycemia and ACS severity, consistent with the work by Wiviott et al. (2008).[11]

In-hospital complications, particularly recurrent ischemia and in-hospital mortality, were significantly associated with higher HbA1C levels. Recurrent ischemia was significantly more common in diabetic patients (40.00%) compared to normoglycemic patients (16.13%), a finding supported by Fisman et al. (2001), who reported increased ischemic events in hyperglycemic ACS patients due to endothelial dysfunction and pro-thrombotic states.[12] The higher in-hospital mortality observed among diabetic patients (17.14%) further highlights the link between hyperglycemia and poor outcomes, aligning with the study by Malmberg et al. (2005), which found a similar association between elevated HbA1C and mortality in ACS patients.[8]

The rates of percutaneous coronary intervention (PCI), antiplatelet therapy, and statin usage were similar across HbA1C categories, suggesting that standard ACS management protocols were applied consistently. This pattern is consistent with Deedwania et al. (2008), who found that glycemic status did not alter the likelihood of receiving these interventions.[13] However, the slightly higher ACE inhibitor and beta-blocker usage in normoglycemic patients (though not statistically significant) could reflect an attempt to aggressively manage blood pressure in these individuals, as previously noted by Yusuf et al. (2000).[14]

Age, HbA1C level, recurrent ischemia, and in-hospital mortality emerged as significant predictors of adverse outcomes in this study. The odds ratio for HbA1C level (OR 1.25) highlights the independent predictive value of hyperglycemia for poor outcomes, corroborating the findings of Norhammar et al. (2004) and Selvin et al. (2004), who also demonstrated the prognostic significance of HbA1C in ACS patients.[10,15] Age and recurrent ischemia further influenced adverse outcomes, in line with the study by Haffner et al. (1998), which emphasized the cumulative impact of age and hyperglycemia on cardiovascular risk. In-hospital mortality showed the strongest predictive value, aligning with Fisman et al. (2001), who found that higher mortality rates in hyperglycemic ACS patients may be linked to increased thrombotic risk and impaired myocardial perfusion.[12]

CONCLUSION

This study underscores the predictive significance of elevated glycosylated hemoglobin (HbA1C) levels in patients presenting with acute coronary syndrome (ACS). Higher HbA1C levels were associated with an increased risk of adverse outcomes, including recurrent ischemia, heart failure, and in-hospital mortality, emphasizing the need for careful monitoring of hyperglycemia in ACS management. Standard treatments, including PCI, antiplatelet therapy, and statins, were applied consistently across HbA1C groups, yet patients with higher HbA1C demonstrated poorer outcomes. These findings support HbA1C as an important prognostic marker in ACS and highlight the benefit of targeted strategies for glycemic control to improve patient outcomes.

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