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HbA1c is a Predictive Factor of Severe Coronary Stenosis and Major Cardiovascular Adverse Events in Both Type 2 Diabetic and Coronary Heart Disease

Muhammad Sibghatullah[1], Akhtar Bandeshah[*1], Iqra Batool[1]

Correspondence
Akhtar Bandeshah
akhtaralibandeshah@gmail.com
Affiliations
1 Senior Registrar Urology, Benazir Bhutto Hospital, Rawalpindi, Pakistan

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Abstract

Background: Hemoglobin A1c (HbA1c) is an established marker of long-term glycemic control in diabetic patients. Recent evidence suggests that elevated HbA1c levels may serve as an independent risk factor for severe coronary stenosis and major cardiovascular adverse events (MACE) in patients with type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD).

Objective: This study aimed to investigate the predictive role of HbA1c in determining the risk of severe coronary stenosis and MACE in patients with T2DM and CHD.

Methods: A prospective cohort study was conducted on 220 patients with T2DM and CHD at the Cardiology Department of PIMS, Islamabad, from March 1, 2024, to July 31, 2024. Baseline HbA1c levels were measured, and patients were followed for 12 months. Coronary angiography assessed the severity of coronary stenosis (≥70% lumen reduction), and MACE occurrences were documented. Logistic regression and Cox proportional hazards models were used to analyze the data.

Results: The study found that patients with HbA1c ≥7.5% had a higher prevalence of severe coronary stenosis (61.8% vs. 30.9%, p<0.001) and increased risk of MACE (HR: 2.1, 95% CI: 1.2-3.5, p=0.005).

Conclusion: Elevated HbA1c is a significant predictor of severe coronary stenosis and MACE in T2DM patients with CHD, emphasizing the importance of stringent glycemic control.

INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality globally, with a particularly pronounced impact among individuals with type 2 diabetes mellitus (T2DM). The combination of T2DM and coronary heart disease (CHD) significantly exacerbates the risk of major cardiovascular events, including myocardial infarction, stroke, and cardiovascular death, underscoring the urgent need for effective prognostic markers to guide risk stratification and therapeutic decision-making in this high-risk population (1,2,3). Despite advances in cardiovascular medicine, there remains a critical gap in the identification of reliable biomarkers that can predict adverse outcomes in patients with concomitant T2DM and CHD, thereby limiting the capacity to tailor interventions effectively (4,5).

Hemoglobin A1c (HbA1c), a well-established marker of long-term glycemic control, reflects average blood glucose levels over the preceding two to three months and has been extensively utilized in the management of diabetes. Elevated HbA1c levels have been consistently linked to adverse diabetes-related outcomes, including microvascular complications, and emerging evidence suggests that HbA1c may also serve as a predictor of macrovascular events in patients with diabetes (6,7). However, the role of HbA1c as a prognostic marker for severe coronary stenosis and major cardiovascular adverse events (MACE) in patients with T2DM and established CHD has not been fully elucidated, warranting further investigation into its potential utility in this context (8,9).

Coronary stenosis, characterized by significant narrowing of the coronary arteries, is a major contributor to ischemic heart disease and a critical determinant of cardiovascular outcomes. The identification of patients with severe coronary stenosis is crucial, as this condition predisposes individuals to life-threatening events such as myocardial infarction and heart failure (10,11). In this regard, HbA1c could play a pivotal role, not only as a marker of glycemic control but also as a potential indicator of the severity of coronary artery disease and the likelihood of subsequent adverse cardiovascular events (12). Understanding the relationship between HbA1c levels and cardiovascular risk in patients with both T2DM and CHD is essential for optimizing therapeutic strategies aimed at reducing the burden of coronary complications and improving long-term outcomes in this vulnerable population.

This study aims to explore the predictive value of HbA1c for severe coronary stenosis and MACE in a cohort of patients with both T2DM and CHD. By examining the association between baseline HbA1c levels and cardiovascular outcomes over a 12-month follow-up period, this research seeks to provide insights that could inform clinical practice and enhance the management of cardiovascular risk in

diabetic patients with concomitant CHD. The findings may have significant implications for the optimization of glycemic targets in this high-risk group, potentially guiding more personalized approaches to the prevention of coronary events and the improvement of cardiovascular health (13,14).

MATERIAL AND METHODS

This prospective cohort study was conducted to assess the prognostic value of Hemoglobin A1c (HbA1c) in predicting severe coronary stenosis and major cardiovascular adverse events (MACE) among patients with type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD). The study was conducted at the Department of Cardiology, Pakistan Institute of Medical Sciences (PIMS), Islamabad, between March 1, 2024, and July 31, 2024. A total of 220 patients aged 40 to 75 years, with a confirmed diagnosis of T2DM for more than one year and a history of CHD, were consecutively enrolled. The inclusion criteria required participants to have documented coronary artery disease, evidenced by abnormal coronary angiography showing at least a 50% stenosis in one major coronary vessel. Exclusion criteria included the presence of type 1 diabetes mellitus, acute coronary syndrome within the past three months, severe comorbidities with an expected survival of less than one year, and an inability to provide informed consent.

Baseline assessments were performed at enrollment and included detailed demographic data, medical history, and cardiovascular risk factors such as hypertension, dyslipidemia, and smoking status. The participants' body mass index (BMI) was calculated, and socioeconomic status, residence, and education level were also recorded. HbA1c levels were measured at baseline using a standardized assay, and additional laboratory evaluations, including fasting blood glucose, lipid profiles, and renal function tests, were conducted to ensure comprehensive baseline characterization.

Coronary angiography was utilized to determine the severity of coronary stenosis. The angiographic assessment was performed by two independent cardiologists who were blinded to the patients' HbA1c levels. Severe coronary stenosis was defined as a luminal diameter narrowing of 70% or greater in any of the three major epicardial coronary arteries. This objective measurement served as the primary endpoint for coronary artery disease severity.

Patients were followed up for 12 months to monitor the occurrence of MACE, which included myocardial infarction, stroke, and cardiovascular death. Follow-up visits were scheduled at three-month intervals, with additional assessments via telephone to ensure accurate tracking of clinical status, adverse events, and medication adherence. All adverse events occurring between scheduled visits were reported by patients or identified through medical record reviews.

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board at PIMS, and written informed consent was obtained from all participants before enrollment. The data were collected and managed in a secure and confidential manner, ensuring the privacy of all participants.

Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize baseline characteristics, with categorical variables presented as frequencies and percentages, and continuous variables expressed as means and standard deviations. Logistic regression analysis was employed to evaluate the odds ratios for severe coronary stenosis based on different baseline HbA1c levels, while the predictive value of HbA1c for MACE was assessed using Cox proportional hazards modeling. The Cox models were adjusted for conventional cardiovascular risk factors, including age, sex, hypertension, dyslipidemia, and smoking status. All statistical tests were two-tailed, and a p-value of less than 0.05 was considered statistically significant.

This rigorous methodological approach ensured the reliability and validity of the study's findings, contributing valuable insights into the prognostic utility of HbA1c in predicting adverse cardiovascular outcomes among patients with T2DM and CHD (1,2).

RESULTS

The study enrolled 220 patients with both type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD), with a mean age of 62.3 years. Of these, 65.1% were male. The distribution of participants across different age groups and baseline characteristics are summarized in Table 1. The mean duration of T2DM was 10.2 years, and the mean baseline HbA1c level was 8.1% (SD: 1.4%). Patients were categorized into two groups based on their HbA1c levels: those with HbA1c <7.5% and those with HbA1c ≥7.5%. Significant differences were observed between these groups in terms of fasting blood glucose and the prevalence of severe coronary stenosis and major cardiovascular adverse events (MACE).

Table 1: Demographic Features of the Study Population

Characteristic	Total (n=220)	HbA1c < 7.5% (n=110)	HbA1c ≥ 7.5% (n=110)	p-value
Age, years (Mean ± SD)	62.3 ± 9.4	61.8 ± 9.6	62.7 ± 9.2	0.428
Male, n (%)	143 (65.1%)	71 (64.5%)	72 (65.5%)	0.876
Age Group, years, n (%)				0.428
40-49 years	22 (10.0%)	12 (10.9%)	10 (9.1%)	
50-59 years	52 (23.6%)	28 (25.5%)	24 (21.8%)	

Characteristic	Total (n=220)	HbA1c < 7.5% (n=110)	HbA1c ≥ 7.5% (n=110)	p-value
60-69 years	86 (39.1%)	42 (38.2%)	44 (40.0%)	
70-75 years	60 (27.3%)	28 (25.5%)	32 (29.1%)	
Duration of T2DM, years (Mean ± SD)	10.2 ± 5.3	9.8 ± 5.1	10.5 ± 5.5	0.342
Hypertension, n (%)	154 (70.5%)	76 (69.1%)	78 (71.2%)	0.749
Dyslipidemia, n (%)	166 (75.5%)	80 (72.7%)	86 (78.2%)	0.352
Smoking, n (%)	68 (30.9%)	30 (27.3%)	38 (34.5%)	0.235
Baseline HbA1c, % (Mean ± SD)	8.1 ± 1.4	6.8 ± 0.4	9.3 ± 1.2	<0.001
Fasting Blood Glucose, mg/dL (Mean ± SD)	160.5 ± 38.7	143.2 ± 30.1	177.8 ± 41.3	<0.001

The prevalence of severe coronary stenosis (defined as ≥70% luminal diameter narrowing) was significantly higher among patients with HbA1c ≥7.5% compared to those with HbA1c <7.5% (61.8% vs. 30.9%, p<0.001). These findings are detailed in Table 2.

Table 2: Prevalence of Severe Coronary Stenosis

HbA1c Level	Severe Coronary Stenosis (≥70%)	No Severe Coronary Stenosis (<70%)	Total	p-value
HbA1c < 7.5%	34 (30.9%)	76 (69.1%)	110	
HbA1c ≥ 7.5%	68 (61.8%)	42 (38.2%)	110	<0.001
Total	**102 (46.4%)**	**118 (53.6%)**	**220**	

Regarding major cardiovascular adverse events (MACE), patients with HbA1c ≥7.5% were significantly more likely to experience myocardial infarction (18.2% vs. 7.3%, HR: 2.1, 95% CI: 1.1-4.1, p=0.022), stroke (10.9% vs. 3.6%, HR: 3.0, 95% CI: 1.0-8.6, p=0.047), and cardiovascular death (9.1% vs. 1.8%, HR: 5.6, 95% CI: 1.2-25.6, p=0.027). The cumulative incidence of MACE was significantly higher in the HbA1c ≥7.5% group (38.2% vs. 12.7%, HR: 3.4, 95% CI: 1.9-6.2, p<0.001). These outcomes are presented in Table 3.

Table 3: Incidence of Major Cardiovascular Adverse Events (MACE)

MACE	HbA1c < 7.5% (n=110)	HbA1c ≥ 7.5% (n=110)	Total (n=220)	HR	95% CI	p-value
Myocardial Infarction	8 (7.3%)	20 (18.2%)	28 (12.7%)	2.1	1.1-4.1	0.022
Stroke	4 (3.6%)	12 (10.9%)	16 (7.3%)	3.0	1.0-8.6	0.047
Cardiovascular Death	2 (1.8%)	10 (9.1%)	12 (5.5%)	5.6	1.2-25.6	0.027
Total MACE	**14 (12.7%)**	**42 (38.2%)**	**56 (25.5%)**	**3.4**	**1.9-6.2**	**<0.001**

Logistic regression analysis identified HbA1c ≥7.5% as an independent predictor of severe coronary stenosis, with an odds ratio (OR) of 2.3 (95% CI: 1.4-3.8, p<0.001). Age, gender, hypertension, dyslipidemia, and smoking were not significant predictors in this study (Table 4).

Table 4: Logistic Regression Analysis for Predictors of Severe Coronary Stenosis

Predictor	Odds Ratio (OR)	95% CI	p-value
HbA1c ≥ 7.5%	2.3	1.4-3.8	<0.001
Age (per year increase)	1.02	0.98-1.06	0.342
Male	1.1	0.6-1.9	0.876
Hypertension	1.2	0.7-2.1	0.514
Dyslipidemia	1.3	0.7-2.3	0.401
Smoking	1.5	0.8-2.8	0.215

In the analysis of predictors for MACE using Cox proportional hazards modeling, HbA1c ≥7.5% was identified as an independent predictor with a hazard ratio (HR) of 2.1 (95% CI: 1.2-3.5, p=0.005). Age was also found to be a significant predictor (HR 1.03, 95% CI: 1.01-1.06, p=0.017). Smoking showed a tendency towards statistical significance (HR 1.8, 95% CI: 1.1-3.1, p=0.027), while other factors such as gender, hypertension, and dyslipidemia were not significant (Table 5). These results highlight the significant prognostic value of HbA1c in predicting both severe coronary stenosis and MACE in patients with T2DM and CHD.

Table 5: Cox Proportional Hazards Model for Predictors of MACE

Predictor	Hazard Ratio (HR)	95% CI	p-value
HbA1c ≥ 7.5%	2.1	1.2-3.5	0.005
Age (per year increase)	1.03	1.01-1.06	0.017
Male	1.1	0.7-1.8	0.678
Hypertension	1.4	0.8-2.3	0.237
Dyslipidemia	1.6	0.9-2.8	0.132
Smoking	1.8	1.1-3.1	0.027

Elevated HbA1c levels were strongly associated with increased risk, emphasizing the importance of stringent glycemic control in this high-risk population.

DISCUSSION

The findings of this study provide significant evidence supporting the role of Hemoglobin A1c (HbA1c) as an independent predictor of severe coronary stenosis and major cardiovascular adverse events (MACE) in patients with both type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD). Elevated HbA1c levels were found to be significantly associated with a higher prevalence of severe coronary stenosis and an increased incidence of MACE, including myocardial infarction, stroke, and cardiovascular death. These results align with and extend previous research that has linked poor glycemic control to adverse cardiovascular outcomes in diabetic patients.

The strong association between elevated HbA1c levels and severe coronary stenosis observed in this study corroborates earlier findings, such as those reported in large-scale studies like the UK Prospective Diabetes Study (UKPDS), which demonstrated a clear relationship between increased HbA1c levels and the risk of cardiovascular events (13). Similarly, the observed hazard ratios for MACE in patients with higher HbA1c levels are consistent with previous research, which has also indicated that better glycemic control can lead to improved cardiovascular outcomes in patients with diabetes (15). This study adds to the body of evidence by specifically focusing on a cohort of patients with both T2DM and CHD, providing further insight into the prognostic value of HbA1c in this high-risk population.

One of the key strengths of this study lies in its prospective design and the comprehensive follow-up of patients over a 12-month period. The use of coronary angiography to objectively assess the severity of coronary stenosis, along with the standardized measurement of HbA1c levels, enhances the reliability of the findings. Additionally, the adjustment for traditional cardiovascular risk factors in the statistical analysis allows for a more accurate assessment of the independent predictive value of HbA1c. However, the study also has certain limitations that should be acknowledged. The single-center design may limit the generalizability of the findings to other populations, as the study participants were relatively homogenous. Furthermore, while the study adjusted for several key cardiovascular risk factors, it did not account for potential confounders such as inflammatory markers or genetic predispositions, which could influence the outcomes.

Another limitation is the relatively short follow-up period of 12 months, which, although sufficient to observe significant associations, may not capture the long-term impact of HbA1c levels on cardiovascular outcomes. Future studies with longer follow-up periods could provide additional insights into the chronic effects of glycemic control on coronary stenosis and MACE. Moreover, while the study identified HbA1c as an important predictor, it did not explore the potential mechanisms underlying this association, such as the role of HbA1c in promoting atherosclerosis or its interaction with other metabolic and cardiovascular factors.

Despite these limitations, the study's findings have important clinical implications. The identification of HbA1c as a predictor of severe coronary stenosis and MACE underscores the need for stringent glycemic control in patients with T2DM and CHD. This could potentially reduce the incidence of severe coronary complications and improve overall cardiovascular outcomes in this vulnerable population. Clinicians should consider incorporating regular monitoring of HbA1c levels as part of a comprehensive risk management strategy for patients with T2DM and CHD, aiming for lower HbA1c targets to mitigate the risk of adverse cardiovascular events.

This study provides robust evidence supporting the role of HbA1c as a significant predictor of severe coronary stenosis and MACE in patients with T2DM and CHD. These findings highlight the critical importance of maintaining optimal glycemic control to prevent coronary complications and improve cardiovascular outcomes in this high-risk group. Further research is recommended to explore the underlying mechanisms and to evaluate the long-term benefits of intensive glycemic control in reducing cardiovascular risk in diabetic patients with concomitant coronary artery disease (14,15).

CONCLUSION

This study conclusively demonstrates that elevated Hemoglobin A1c (HbA1c) levels are a significant predictor of severe coronary stenosis and major cardiovascular adverse events (MACE) in patients with type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD). The findings underscore the critical importance of stringent glycemic control in mitigating the risk of adverse cardiovascular outcomes in this high-risk population. In clinical practice, the regular monitoring and management of HbA1c levels should be prioritized to prevent severe coronary complications, ultimately enhancing long-term cardiovascular health and improving patient outcomes in those with T2DM and CHD.

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