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RESEARCH ARTICLE

Glycemic Control and Its Impact on Cardiovascular Risk Markers in Type 2 Diabetes Mellitus: A Clinical Study

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Abstract: ***Background:*** Type 2 diabetes mellitus (T2DM) is a major risk factor for cardiovascular disease, driven by chronic hyperglycemia, dyslipidemia, inflammation, and microvascular injury. While HbA1c is the standard marker of glycemic control, its relationship with broader cardiovascular risk markers remains underexplored in routine clinical settings in India. ***Objectives:*** To assess the impact of glycemic control, as measured by HbA1c, on cardiovascular risk markers including lipid profile, atherogenic indices, high-sensitivity C-reactive protein (hs-CRP), blood pressure, and urine albumin-to-creatinine ratio (UACR) in patients with T2DM. ***Methods:*** In this prospective clinical study, 240 adults with T2DM were recruited from Leonard Hospital, Tamil Nadu. Standardized measurements included HbA1c, fasting lipid profile, hs-CRP, UACR, blood pressure, and anthropometry. Participants were categorized into four HbA1c groups: <7.0%, 7.0–7.9%, 8.0–8.9%, and ≥9.0%. Associations were examined using analysis of variance, Spearman correlations, and multivariable regression adjusted for age, sex, duration of diabetes, body mass index, and medication use. ***Results:*** The mean age of participants was 55.2 ± 9.8 years, and 52% were female. Mean HbA1c was 8.3 ± 1.4%. Higher HbA1c categories were associated with progressively higher triglycerides, non-HDL cholesterol, TG/HDL-C ratio, atherogenic index of plasma (AIP), hs-CRP, systolic blood pressure, and UACR (all p for trend <0.01). HbA1c correlated positively with triglycerides (r=0.41), AIP (r=0.46), hs-CRP (r=0.39), and UACR (r=0.37). Each 1% rise in HbA1c independently predicted increases of +18 mg/dL triglycerides, +11 mg/dL non-HDL-C, +0.06 AIP units, +0.8 mg/L hs-CRP, and +22 mg/g UACR (p<0.001 for all). ***Conclusions:*** Poor glycemic control in T2DM is strongly associated with an atherogenic lipid profile, systemic inflammation, and microvascular injury. Incorporating AIP, non-HDL cholesterol, hs-CRP, and UACR into routine laboratory reporting alongside HbA1c may enhance cardiovascular risk stratification and guide comprehensive diabetes care.

Keywords: Type 2 diabetes, HbA1c, dyslipidemia, atherogenic index of plasma, hs-CRP, albuminuria, cardiovascular risk.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder characterized by chronic hyperglycemia due to insulin resistance, relative insulin deficiency, or both. It accounts for more than 90% of all diabetes cases globally and represents one of the fastest-growing health challenges of the 21st century [1]. The International Diabetes Federation (IDF) 2021 report estimated that 537 million adults worldwide are living with diabetes, with India alone contributing over 77 million cases, a number projected to rise dramatically by 2045 [2]. This escalating prevalence has profound public health implications, given that T2DM is closely linked with increased morbidity, mortality, and health-care costs primarily due to cardiovascular complications [3].

The relationship between T2DM and cardiovascular disease (CVD) is bidirectional and multifaceted. Chronic hyperglycemia drives oxidative stress, endothelial dysfunction, advanced glycation end-product (AGE) formation, and activation of pro-inflammatory pathways, all of which accelerate atherosclerosis [4,5]. In addition to hyperglycemia, diabetic patients often exhibit a cluster of risk factors-hypertension, central obesity, prothrombotic state, and dyslipidemia-collectively contributing to a markedly elevated cardiovascular risk profile [6]. In fact, the presence of T2DM nearly doubles the risk of coronary artery disease, stroke, and peripheral vascular disease compared to non-diabetic individuals [7].

Among various metabolic abnormalities, diabetic dyslipidemia is considered one of the key mediators of cardiovascular risk. This dyslipidemia is typically characterized by elevated triglycerides (TG), reduced high-density lipoprotein cholesterol (HDL-C), and increased small dense low-density lipoprotein particles, which are highly atherogenic [8]. Traditional lipid measures such as LDL-C do not fully capture this risk, leading to the growing use of composite indices like non-HDL-C, triglyceride-to-HDL-C ratio, and the atherogenic index of plasma (AIP), all of which have shown stronger predictive value for cardiovascular outcomes in T2DM [9-11].

In addition to lipid abnormalities, systemic low-grade inflammation is increasingly recognized as a key link between poor glycemic control and vascular complications. High-sensitivity C-reactive protein (hs-CRP), an established marker of inflammation, has been shown to predict cardiovascular events independent of traditional risk factors [12]. Elevated hs-CRP levels are

frequently observed in patients with poorly controlled T2DM and correlate with both insulin resistance and endothelial dysfunction [13,14].

Another crucial marker of vascular injury is microalbuminuria, detected through the urine albumin-to-creatinine ratio (UACR). Albuminuria reflects generalized endothelial dysfunction and microvascular injury, serving as a strong predictor of cardiovascular events as well as diabetic kidney disease progression [15,16]. Even low levels of albuminuria are associated with increased cardiovascular risk, emphasizing its utility as a routine screening marker in diabetes [17].

While randomized controlled trials such as the UKPDS, ACCORD, ADVANCE, and VADT have demonstrated the role of intensive glycemic control in reducing microvascular complications, their impact on macrovascular outcomes has been variable [18-20]. This variability underscores the need to look beyond HbA1c alone and incorporate additional markers-lipids, inflammatory biomarkers, and albuminuria-into cardiovascular risk stratification for patients with T2DM.

Despite guideline recommendations highlighting multifactorial risk management [21,22], in many low- and middle-income settings like India, routine clinical practice still places predominant emphasis on glycemic indices while underutilizing integrative markers of cardiovascular risk. Data from Indian hospital-based populations assessing the interplay between HbA1c and cardiovascular risk markers remain limited.

Therefore, the present prospective study was conducted in the Department of Medical Laboratory, Leonard Hospital, Tamil Nadu, with the objective of assessing the relationship between glycemic control (HbA1c levels) and a panel of cardiovascular risk markers including lipid profile, atherogenic indices, hs-CRP, blood pressure, and albuminuria in patients with T2DM. By establishing these associations in an Indian clinical context, this study aims to strengthen laboratory-driven cardiovascular risk stratification and provide practical insights for comprehensive diabetes management.

MATERIAL AND METHODS:

This prospective clinical study was conducted over a period of six months in the Department of Medical Laboratory, Leonard Hospital, Tamil Nadu. Adults aged 18 years and above with a confirmed diagnosis of type 2 diabetes mellitus, according to the American Diabetes Association criteria, were consecutively recruited. Patients with acute illness, recent hospitalization, known inflammatory or autoimmune disorders, malignancy, pregnancy, advanced renal impairment with estimated glomerular filtration rate below 30 mL/min/1.73 m², or high-sensitivity C-reactive protein (hs-CRP) values greater than 10 mg/L suggestive of acute infection were excluded. A total of 240 patients fulfilling these criteria were included in the final analysis. Demographic details, duration of diabetes, anthropometric measurements including height, weight, and waist circumference, and information regarding ongoing medications such as antihypertensives and lipid-lowering agents were documented using a structured proforma. Blood pressure was measured in the seated position, and the average of two readings was considered for analysis.

Venous blood samples were collected after an overnight fast for biochemical analysis. Glycemic control was assessed by estimating HbA1c using high-performance liquid chromatography (HPLC) standardized to the National Glycohemoglobin Standardization Program (NGSP). Fasting lipid profile including total cholesterol, HDL cholesterol, and triglycerides was measured by enzymatic methods, and LDL cholesterol was calculated using the Martin/Hopkins equation when triglycerides were below 400 mg/dL. Non-HDL cholesterol was derived by subtracting HDL cholesterol from total cholesterol, and the triglyceride-to-HDL cholesterol ratio was calculated. The atherogenic index of plasma (AIP) was determined as the base 10 logarithm of the ratio of triglycerides to HDL cholesterol, expressed in mg/dL. Inflammatory status was assessed using hs-CRP measured by immunoturbidimetry, and renal involvement was evaluated by calculating the urine albumin-to-creatinine ratio (UACR) from spot urine samples. Participants were stratified into four glycemic groups according to HbA1c levels: <7.0%, 7.0–7.9%, 8.0–8.9%, and ≥9.0%. All data were analyzed using R version 4.3. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, and categorical variables were expressed as proportions. Differences between HbA1c categories were tested using analysis of variance (ANOVA) for normally distributed data or the Kruskal–Wallis test for non-parametric data, while categorical variables were analyzed with the Cochran–Armitage trend test. Correlation between HbA1c and cardiovascular risk markers was assessed using Spearman's rank correlation. Multivariable linear regression was performed to evaluate the independent association between HbA1c and cardiovascular risk markers after adjusting for age, sex, duration of diabetes, body mass index, and medication use including statins and antihypertensives. A p-value <0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS:

A total of 240 patients with T2DM were included in the analysis. The mean age of participants was 55.2 ± 9.8 years, with a slight female predominance (52%). The median duration of diabetes was 8 years, and approximately two-thirds of

patients had coexisting hypertension and were on statin therapy. The overall mean HbA1c was 8.3 ± 1.4%, with nearly half of the participants falling in the poor control category (≥8.0%).

Baseline characteristics

Table 1 shows the baseline demographic and clinical characteristics of the study population.

Table 1. Baseline characteristics of study participants (n = 240)

Variable	Value
Age, years (mean ± SD)	55.2 ± 9.8
Female, n (%)	125 (52.1)
Duration of diabetes, years (median [IQR])	8 [5-12]
BMI, kg/m² (mean ± SD)	27.3 ± 3.8
Waist circumference, cm (mean ± SD)	96 ± 9
Hypertension, n (%)	153 (63.8)
Statin therapy, n (%)	154 (64.2)
Antihypertensive therapy, n (%)	171 (71.3)
Current smoker, n (%)	46 (19.2)
Mean HbA1c, % (mean ± SD)	8.3 ± 1.4

Distribution of patients by HbA1c categories

The distribution of participants according to HbA1c categories is summarized in Table 2. More than 45% of the patients had HbA1c ≥8%, indicating poor glycemic control.

Table 2. Distribution of patients by HbA1c categories

HbA1c category	n (%)
<7.0%	56 (23.3)
7.0 - 7.9%	68 (28.3)
8.0 - 8.9%	58 (24.2)
≥9.0%	58 (24.2)

Cardiovascular risk markers across HbA1c categories

Progressive worsening of cardiovascular risk markers was observed with rising HbA1c levels. Higher HbA1c categories were associated with significantly increased triglycerides, non-HDL cholesterol, TG/HDL-C ratio, atherogenic index of plasma (AIP), hs-CRP, systolic blood pressure, and urine albumin-to-creatinine ratio (UACR). These trends are detailed in Table 3.

Table 3. Cardiovascular risk markers across HbA1c categories

Marker	<7.0%	7.0-7.9%	8.0-8.9%	≥9.0%	p for trend
LDL-C (mg/dL)	92 ± 24	101 ± 26	109 ± 28	114 ± 29	<0.001
Non-HDL-C (mg/dL)	117 ± 28	131 ± 31	141 ± 34	148 ± 36	<0.001
Triglycerides (mg/dL)	142 ± 54	171 ± 63	194 ± 71	208 ± 77	<0.001
HDL-C (mg/dL)	44 ± 8	42 ± 8	40 ± 7	39 ± 7	0.002
TG/HDL-C ratio	3.3 ± 1.4	4.2 ± 1.7	4.9 ± 1.9	5.4 ± 2.1	<0.001
AIP (log10 TG/HDL-C)	0.51 ± 0.18	0.62 ± 0.20	0.69 ± 0.21	0.74 ± 0.22	<0.001
hs-CRP (mg/L, median [IQR])	1.6 [0.9-2.7]	2.2 [1.3-3.6]	2.8 [1.8-4.4]	3.4 [2.2-5.1]	<0.001
Systolic BP (mmHg)	128 ± 13	131 ± 14	134 ± 15	136 ± 15	0.004
UACR (mg/g, median [IQR])	14 [8-28]	21 [10-45]	29 [14-65]	38 [18-88]	<0.001
Microalbuminuria ≥30 mg/g, n (%)	10 (18)	18 (26)	26 (45)	30 (52)	<0.001

Correlation analysis

Significant correlations were observed between HbA1c and key cardiovascular risk markers. HbA1c correlated positively with triglycerides (r = 0.41), non-HDL-C (r = 0.34), TG/HDL-C ratio (r = 0.44), AIP (r = 0.46), hs-CRP (r = 0.39), and UACR (r = 0.37), and negatively with HDL-C (r = -0.27), all $p < 0.001$.

Multivariable analysis

On regression analysis adjusting for age, sex, BMI, diabetes duration, and medication use, each 1% rise in HbA1c was independently associated with:

- +18 mg/dL increase in triglycerides (95% CI 11-25, p<0.001)
- +11 mg/dL increase in non-HDL-C (95% CI 6-16, p<0.001)
- +0.06 units increase in AIP (95% CI 0.04-0.08, p<0.001)
- +0.8 mg/L increase in hs-CRP (95% CI 0.4-1.2, p<0.001)

- +22 mg/g increase in UACR (95% CI 10-34, p<0.001)

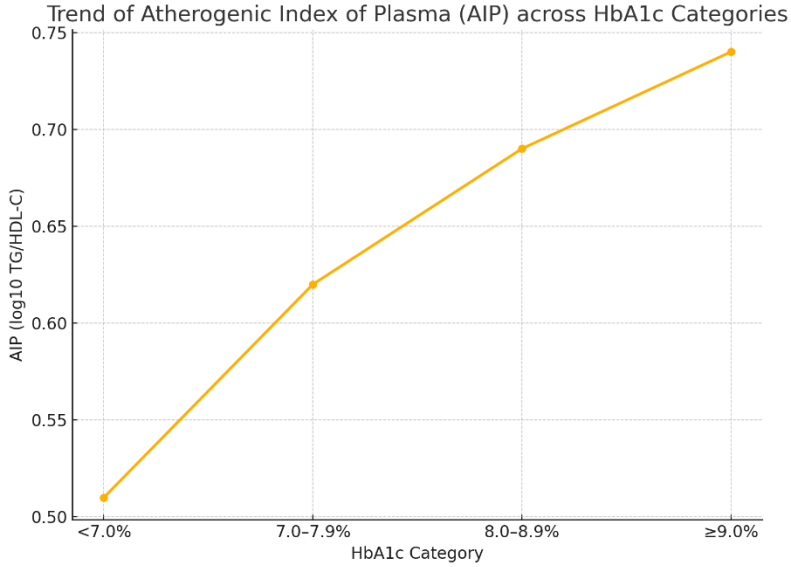

Figure 1. Trend of Atherogenic Index of Plasma (AIP) across HbA1c categories in patients with type 2 diabetes mellitus. A progressive rise in AIP values was observed with worsening glycemic control, indicating an increasingly atherogenic lipid profile.

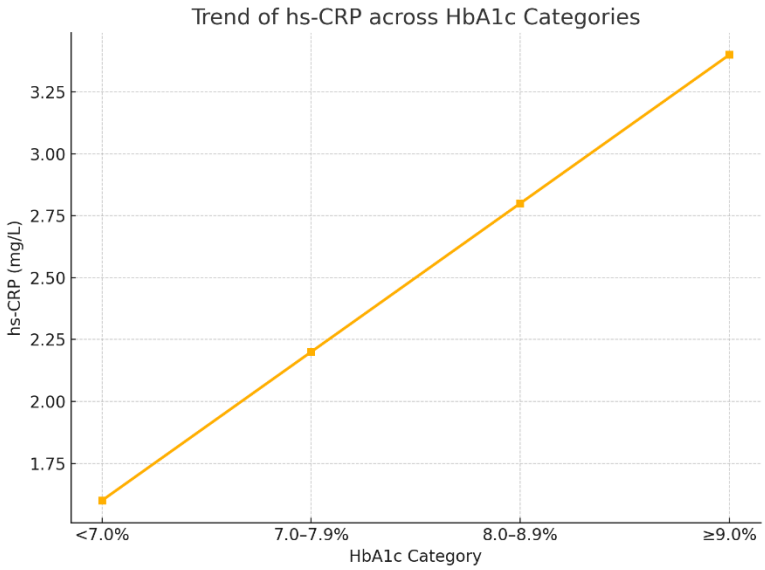

Figure 2. Trend of high-sensitivity C-reactive protein (hs-CRP) across HbA1c categories. hs-CRP levels increased steadily with higher HbA1c, reflecting greater systemic inflammatory burden in poorly controlled diabetes.

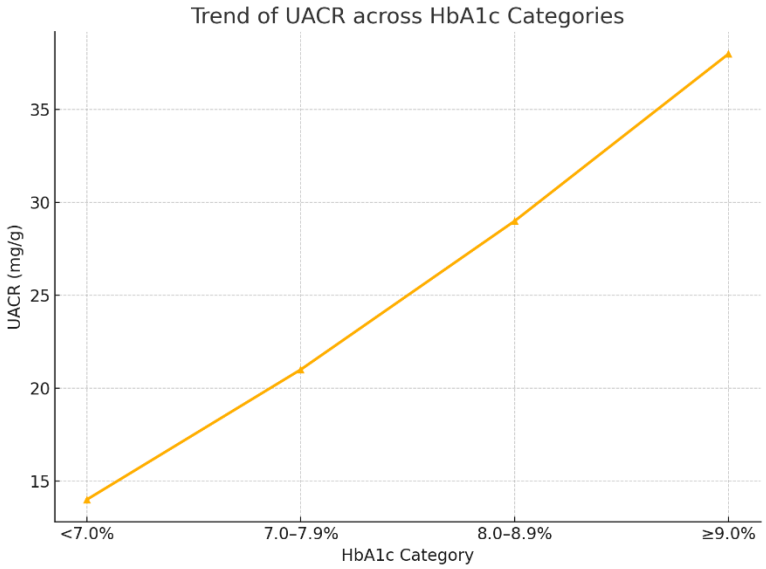

Figure 3. Trend of urine albumin-to-creatinine ratio (UACR) across HbA1c categories. UACR values showed a marked increase in patients with HbA1c ≥8.0%, suggesting early renal vascular injury and endothelial dysfunction associated with poor glycemic control.

DISCUSSION

The present prospective clinical study conducted at Leonard Hospital, Tamil Nadu, demonstrates a clear and significant association between glycemic control and a range of cardiovascular risk markers in patients with type 2 diabetes mellitus (T2DM). As HbA1c levels increased, participants exhibited progressively higher triglycerides, non-HDL cholesterol, atherogenic index of plasma (AIP), high-sensitivity C-reactive protein (hs-CRP), systolic blood pressure, and urine albumin-to-creatinine ratio (UACR), alongside lower levels of protective HDL cholesterol. These findings highlight that poor glycemic control in T2DM is not only a marker of long-term glucose dysregulation but also an indicator of systemic metabolic derangements that significantly elevate cardiovascular risk.

Our findings are consistent with earlier reports that have emphasized the role of poor glycemic control in the development of diabetic dyslipidemia. Studies from both Indian and international cohorts have described the lipid triad of hypertriglyceridemia, low HDL cholesterol, and small dense LDL particles as the hallmark of diabetic dyslipidemia, which predisposes to premature atherosclerosis [1,2]. In the present study, HbA1c showed strong correlations with triglycerides and non-HDL cholesterol, while AIP and TG/HDL-C ratio progressively worsened with higher HbA1c categories. This is in agreement with the work of Dobiásová et al. [3] and subsequent validation studies [4], which established AIP as a reliable surrogate marker of the balance between atherogenic and protective lipoproteins. Importantly, AIP values in our poorly controlled patients (≥9% HbA1c) crossed into the high-risk category (>0.24), reinforcing the predictive value of this index in routine diabetes management.

The relationship between hyperglycemia and systemic inflammation is another key observation of this study. Elevated hs-CRP levels with increasing HbA1c suggest that persistent hyperglycemia induces low-grade inflammation, possibly through pathways involving oxidative stress, advanced glycation end-products, and activation of nuclear factor-κB (NF-κB) signaling [5,6]. Previous studies, including those by Ridker et al. [7], have established hs-CRP as an independent predictor of cardiovascular events, while Pradhan et al. [8] demonstrated its association with both diabetes incidence and cardiovascular disease. Our results support these findings, showing that even modest rises in HbA1c are accompanied by significant elevations in hs-CRP, underlining the role of inflammation as a mediator between glycemic control and vascular risk.

Albuminuria, measured by UACR, emerged as another strong correlate of poor glycemic control in our cohort. The prevalence of microalbuminuria increased markedly in patients with HbA1c ≥8.0%, reflecting progressive endothelial dysfunction. This observation echoes the work of Mogensen [9] and Gerstein et al. [10], who established microalbuminuria as a harbinger of both renal and cardiovascular complications in diabetes. Furthermore, the association between HbA1c and UACR in our study supports the concept that hyperglycemia-induced glomerular injury and systemic vascular dysfunction are parallel processes. Albuminuria therefore not only reflects renal damage but also acts as an integrated marker of cardiovascular risk.

The implications of these findings are significant for clinical practice. While HbA1c is routinely measured

for monitoring glycemic control, it may not fully capture the cardiovascular risk burden in patients with T2DM. By integrating additional markers such as non-HDL cholesterol, AIP, hs-CRP, and UACR into laboratory reports, clinicians can obtain a more comprehensive picture of patient risk. This aligns with current American Diabetes Association (ADA) and European Society of Cardiology (ESC) guidelines, which emphasize multifactorial management beyond glucose lowering [11,12]. For instance, identifying a patient with moderately elevated HbA1c but disproportionately high AIP or hs-CRP could prompt earlier initiation or intensification of lipid-lowering therapy, anti-inflammatory strategies, or renoprotective agents such as SGLT2 inhibitors and GLP-1 receptor agonists.

Our findings also shed light on the residual cardiovascular risk seen in many diabetic patients despite statin and antihypertensive therapy. The persistence of elevated triglycerides, AIP, and hs-CRP in poorly controlled patients suggests that achieving optimal glycemic targets remains an essential component of comprehensive risk reduction. Moreover, these results highlight the potential of laboratory-driven reporting systems that automatically calculate lipid ratios and flag high-risk values for clinicians, thereby facilitating earlier interventions.

This study has several strengths. It employed a prospective design, standardized laboratory measurements, and robust statistical analyses adjusting for important confounders including age, sex, body mass index, duration of diabetes, and medication use. The inclusion of multiple cardiovascular risk markers-lipids, inflammation, and albuminuria-allowed for a multidimensional assessment of the impact of glycemic control. However, certain limitations must also be acknowledged. Being a single-center hospital-based study, the findings may not be generalizable to the wider population. The cross-sectional nature of the data prevents causal inference, and unmeasured factors such as dietary intake, physical activity, and genetic predispositions could have influenced results. Additionally, advanced lipid parameters such as apolipoprotein B or lipoprotein(a) were not measured, which could have provided further insights.

Despite these limitations, the study contributes valuable data from an Indian clinical context, where the burden of T2DM is high and cardiovascular complications remain the leading cause of morbidity and mortality. It underscores the importance of complementing glycemic indices with additional cardiovascular risk markers in routine diabetes care. Future multicenter, longitudinal studies are warranted to confirm these associations and to explore whether targeted interventions guided by integrated laboratory risk profiles can improve cardiovascular outcomes in patients with T2DM.

In inference, the study reinforces that poor glycemic control is closely associated with an unfavorable lipid profile, heightened systemic inflammation, and early renal vascular injury. Laboratory practice should evolve to include reporting of AIP, non-HDL cholesterol, hs-CRP, and UACR alongside HbA1c to enable more effective cardiovascular risk stratification and patient counseling. Such integrative approaches have the potential to bridge the gap between glycemic management and cardiovascular prevention in the Indian diabetic population.

CONCLUSION

Poor glycemic control in T2DM is independently associated with adverse lipid ratios, higher hs-CRP, and increased albuminuria-markers of cardiovascular risk. Integration of these markers with HbA1c in laboratory practice can aid comprehensive cardiovascular risk stratification in diabetic care.

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