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Association Between Glycaemic Control And Systemic Inflammatory-Haematological Markers In Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Abstract

Background: Chronic hyperglycaemia in Type 2 Diabetes Mellitus (T2DM) precipitates systemic inflammation and oxidative stress, which may be reflected in alterations of routine haematological parameters. The relationship between glycaemic control and these inexpensive, readily available markers warrants further investigation in diverse populations.
Objectives: This study aimed to evaluate the association between HbA1c levels and a panel of haematological and biochemical parameters in Indian patients with T2DM.
Methods: A cross-sectional study was conducted at a tertiary care centre from September 2022 to June 2024. Consecutively enrolled adults with T2DM (n=154) were stratified into good (HbA1c <7%) and poor (HbA1c ≥7%) glycaemic control groups. Fasting blood samples were analysed for complete blood count (CBC), lipid profile, renal and liver function tests using standard automated methods. Data were analysed using independent t-tests, Mann-Whitney U, Chi-square tests, Pearson's correlation, and multivariate linear regression.
Results: The cohort's mean age was 52.4±12.1 years, with 59.1% males. Poor glycaemic control was highly prevalent (73.4%). It was significantly associated with elevated Red Cell Distribution Width (RDW) (13.37% vs. 11.99%, p<0.001), Mean Platelet Volume (MPV) (9.41 fL vs. 8.99 fL, p=0.010), total cholesterol (161.27 mg/dL vs. 125.12 mg/dL, p<0.001), LDL-cholesterol (95.61 mg/dL vs. 70.78 mg/dL, p<0.001), serum creatinine (1.27 mg/dL vs. 0.92 mg/dL, p=0.009), and proteinuria (33.6% vs. 17.1%, p=0.046). HbA1c showed a strong positive correlation with RDW (r=0.686, p=0.002). On multivariate analysis, HbA1c remained a significant independent predictor of RDW (β=0.62, p<0.001), LDL (β=20.15, p<0.001), and total cholesterol (β=29.87, p<0.001) after adjusting for age, sex, and hypertension.
Conclusion: Poor glycaemic control is independently correlated with adverse changes in haematological indices and lipids. Monitoring RDW and MPV could provide a holistic, cost-effective approach for risk stratification and managing T2DM complications.

Keywords: Type 2 Diabetes Mellitus, HbA1c, Red Cell Distribution Width, Mean Platelet Volume, Dyslipidaemia, Diabetic Nephropathy.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is a global pandemic characterized by chronic hyperglycaemia resulting from insulin resistance and progressive β-cell dysfunction [1]. Its significant morbidity and mortality are primarily driven by devastating microvascular and macrovascular complications [2], making early detection and effective management imperative. Beyond its well-established microvascular and macrovascular complications, T2DM is also frequently complicated by other endocrine disorders, such as a high prevalence of thyroid dysfunction, which is increasingly recognized as a significant comorbidity that can influence overall metabolic health [3].

Beyond dysglycaemia, T2DM is a state of chronic, low-grade inflammation and heightened oxidative stress [4]. This systemic milieu can manifest in alterations of routine haematological parameters. Red Cell Distribution Width (RDW), a measure of erythrocyte size variability, is increasingly recognized as a biomarker of underlying inflammation and oxidative stress [5]. Similarly, Mean Platelet Volume (MPV) indicates platelet size and reactivity, reflecting a pro-thrombotic state that amplifies cardiovascular risk in diabetes [6]. Concurrently, the characteristic biochemical dysregulation of T2DM—including atherogenic dyslipidaemia and incipient renal dysfunction—interacts with these haematological changes, creating a vicious cycle that accelerates end-organ damage [7].

While the individual links between hyperglycaemia, dyslipidaemia, and nephropathy are well-established, a comprehensive analysis of their relationship with underutilized haematological markers like RDW and MPV within a single cohort is lacking, particularly in Indian populations. This study aimed to bridge this gap by conducting a holistic assessment of the correlation between glycaemic control and a broad spectrum of haematological and biochemical parameters in patients with T2DM. The findings could identify simple, cost-effective biomarkers for better risk stratification and more integrated management strategies.

2. Patients and Methods

2.1. Study Design and Setting

This hospital based cross-sectional study was conducted at the Department of General Medicine in tertiary care hospital & reseach centre from western india from September 2022 to June 2024. The study protocol was approved by the Institutional Ethics Committee of our hospital and it was conducted in accordance with the Declaration of Helsinki. The study is reported following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

2.2. Study Participants

A total of 154 adult patients (>18 years) with a known diagnosis of T2DM, as per the American Diabetes Association (ADA) 2022 criteria [2], were consecutively enrolled from the outpatient and inpatient departments. Written informed consent was obtained from all participants.

2.3. Inclusion and Exclusion Criteria

Inclusion criteria were: (1) Diagnosis of T2DM; (2) Age >18 years; (3) Provision of informed consent.
Exclusion criteria were: (1) Type 1 diabetes; (2) Pregnancy or lactation; (3) Acute infections, active inflammatory conditions, known haematological disorders, or advanced liver disease; (4) Use of medications known to significantly alter haematological parameters (e.g., corticosteroids, immunosuppressants) in the preceding three months.

2.4. Data Collection and Laboratory Methods

Demographic and clinical data were collected using a pre-designed proforma. Following an overnight fast, venous blood samples were drawn for:

- **Glycaemic Control:** HbA1c was measured by High-Performance Liquid Chromatography (HPLC).
- **Haematological Parameters:** A complete blood count (CBC), including Haemoglobin, RBC indices, RDW, MPV, and platelet count, was analysed using a Beckman Coulter DxH 900 automated analyser.

Biochemical Parameters: Lipid profile (Total Cholesterol, Triglycerides, HDL, LDL), renal function test s (serum creatinine, urea, Urine Albumin-to-Creatinine Ratio - UACR), liver function tests (SGOT/AST, S GPT/ALT, albumin), and electrolytes were analysed using standard spectrophotometric techniques on aut omated clinical chemistry analysers. All laboratory analyses were performed in the institutional central lab oratory following standardized protocols. Quality control measures were maintained throughout the study period

2.5. Statistical Analysis

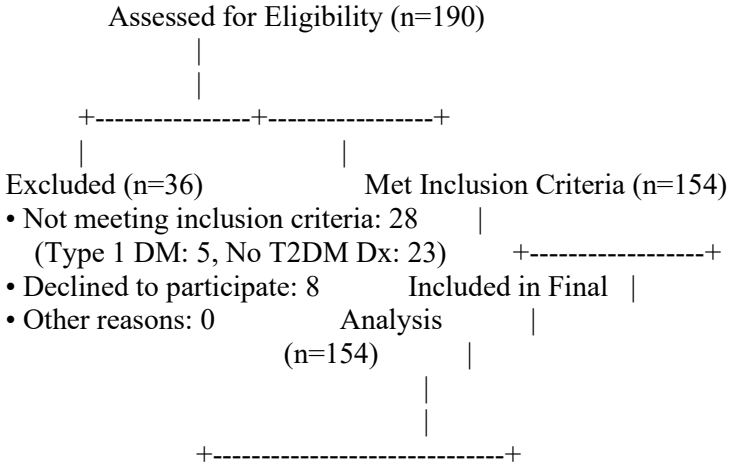
Data were analysed using IBM SPSS Statistics (version 26.0). Continuous variables were expressed as mean ± standard deviation (SD) if normally distributed, and categorical variables as frequencies (%). The Kolmogorov-Smirnov test was used to assess normality. Differences between groups (HbA1c <7% vs. ≥7%) were analysed using the independent samples t-test (for normally distributed data), Mann-Whitney U test (for non-normal data), and Chi-square test (for categorical variables). Pearson's correlation coefficient was used to assess the relationship between HbA1c and other continuous variables. To determine the independent association between HbA1c and key outcome variables, multivariate linear regression models were constructed, adjusting for age, sex, and hypertension status. The results are presented as adjusted beta coefficients (β) with 95% confidence intervals (CI). A two-tailed p-value of <0.05 was considered statistically significant.

3. Results

3.1. Participant Flow and Baseline Characteristics

The flow of participants through the study is detailed in Figure 1 ,Of 190 patients assessed, 36 were exclu ded (28 did not meet inclusion criteria, 8 declined participation). The final analysis included 154 patients. The final analysis cohort consisted of 154 T2DM patients with a mean age of 52.4 ± 12.1 years. The cohor t consisted of 91 (59.1%) males and 63 (40.9%) females. The baseline demographic characteristics are pre sented in Table 1.

Figure 1: STROBE Flow Diagram of Participant Selection



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Analyzed for Haematological
and Biochemical Parameters
(n=154)

Table 1: Baseline Demographic Characteristics of the Study Participants (N=154)

Age Group (Years)	Male, n (%)	Female, n (%)	Total, n (%)
< 30	6 (6.6)	0 (0.0)	6 (3.9)
31-40	18 (19.8)	5 (7.9)	23 (14.9)
41-50	14 (15.4)	12 (19.0)	26 (16.9)
51-60	27 (29.7)	25 (39.7)	52 (33.8)
>60	26 (28.6)	21 (33.3)	47 (30.5)
Total	**91 (100)**	**63 (100)**	**154 (100)**

3.2. Glycaemic Control and Diabetes Duration

A high prevalence of poor glycaemic control (HbA1c ≥7%) was observed, affecting 113 patients (73.4%). The mean HbA1c of the cohort was 8.4 ± 1.9%. Hypertension was present in 45.5% (n=70) of participants . The association between diabetes duration and glycaemic control is shown in Table 2. A higher proportio n of patients with longer disease duration had poor control, though this trend was not statistically significa nt (p=0.063).

Table 2: Association between Duration of T2DM and Glycaemic Control

Duration of T2DM	HbA1c <7%, n (%)	HbA1c ≥7%, n (%)	Total, n (%)
< 1 Year	18 (43.9)	29 (25.7)	47 (30.5)
1 - 5 Years	10 (24.4)	46 (40.7)	56 (36.4)
> 5 Years	13 (31.7)	38 (33.6)	51 (33.1)
Total	**41 (100)**	**113 (100)**	**154 (100)**

3.3. Haematological Parameters

Comparative analysis revealed significant differences in key haematological indices. Patients with poor glycaemic control had significantly higher RDW (13.37 ± 1.37% vs. 11.99 ± 0.52%, p<0.001) and MPV (9.41 ± 1.75 fL vs. 8.99 ± 1.26 fL, p=0.010). No other haematological parameters showed significant differences (Table 3).

Table 3: Comparison of Haematological Parameters by Glycaemic Control Status

Parameter	HbA1c <7% (n=41), Mean ± SD	HbA1c ≥7% (n=113), Mean ± SD	p-value
RDW (%)	11.99 ± 0.52	13.37 ± 1.37	**<0.001**
MPV (fL)	8.99 ± 1.26	9.41 ± 1.75	**0.010**
Haemoglobin (g/dL)	11.58 ± 1.87	11.81 ± 2.41	0.582
Platelets (x10^3/µL)	234 ± 134	261 ± 157	0.318

3.4. Biochemical Parameters

Lipid Profile: Poor glycaemic control was strongly associated with dyslipidaemia. The poor control group had significantly higher total cholesterol (161.27 ± 59.98 mg/dL vs. 125.12 ± 43.52 mg/dL, p<0.001) and LDL-cholesterol (95.61 ± 24.74 mg/dL vs. 70.78 ± 21.80 mg/dL, p<0.001). Triglyceride and HDL levels were not significantly different (Table 4).

Table 4: Comparison of Lipid Profile by Glycaemic Control Status

Parameter	HbA1c <7% (n=41), Mean ± SD	HbA1c ≥7% (n=113), Mean ± SD	p-value
Total Cholesterol (mg/dL)	125.12 ± 43.52	161.27 ± 59.98	**<0.001**
LDL (mg/dL)	70.78 ± 21.80	95.61 ± 24.74	**<0.001**
HDL (mg/dL)	34.51 ± 16.49	33.56 ± 12.31	0.699

Renal Function: Markers of renal impairment were significantly worse in the poor control group. Serum creatinine was higher (1.27 ± 0.81 mg/dL vs. 0.92 ± 0.43 mg/dL, p=0.009), and the prevalence of proteinuria was significantly greater (33.6% vs. 17.1%, p=0.046) (Tables 5 & 6).

Table 5: Association between Proteinuria and Glycaemic Control

HbA1c	Proteinuria Absent, n (%)	Proteinuria Present, n (%)	Total
<7%	34 (82.9)	7 (17.1)	41
≥7%	75 (66.4)	38 (33.6)	113

HbA1c	Proteinuria Absent, n (%)	Proteinuria Present, n (%)	Total
Total	**109**	**45**	**154**

Table 6: Comparison of Renal Function Parameters

Parameter	HbA1c <7% (n=41), Mean ± SD	HbA1c ≥7% (n=113), Mean ± SD	p-value
Creatinine (mg/dL)	0.92 ± 0.43	1.27 ± 0.81	**0.009**
UACR (mg/g)	28.27 ± 32.89	43.70 ± 49.62	0.067

Liver Function Tests: No significant differences were observed in any liver function parameters between the two groups.

3.5. Correlation and Multivariate Regression Analysis

Pearson correlation analysis demonstrated a strong positive correlation between HbA1c and RDW (r=0.68 6, p=0.002). Moderate positive correlations were observed with total cholesterol (r=0.502, p<0.001) and L DL-cholesterol (r=0.581, p<0.001). Weak but significant positive correlations were found with serum crea tinine (r=0.251, p=0.002) and UACR (r=0.229, p=0.004). The prevalence of poor glycemic control (HbA1 c ≥7%) was 73.4% (113/154).

To ascertain the independent relationship, multivariate linear regression models were employed, adjusting for age, sex, and hypertension status. As shown in Table 7, HbA1c remained a statistically significant inde pendent predictor for Red Cell Distribution Width (RDW), LDL-cholesterol, and Total Cholesterol. The a ssociation between HbA1c and serum creatinine was attenuated and was no longer statistically significant after multivariate adjustment.

Table 7: Multivariate Linear Regression Analysis of HbA1c Association with Key Parameters*

Dependent Variable	Adjusted Beta Coefficient (β)	95% Confidence Interval	p-value
Red Cell Distribution Width (RDW)	0.62	0.48 to 0.76	**<0.001**
LDL-Cholesterol	20.15	14.22 to 26.08	**<0.001**
Total Cholesterol	29.87	18.45 to 41.29	**<0.001**
Serum Creatinine	0.12	-0.04 to 0.28	0.139

All models are adjusted for age, sex, and hypertension status.

4. Discussion

This cross-sectional study provides a comprehensive analysis of the systemic correlates of glycaemic control in an Indian T2DM cohort. Our principal findings confirm that poor glycaemic control is significantly associated with a adverse alterations in specific, easily measurable haematological and biochemical parameters. The most salient findings are the strong, independent associations between HbA1c and Red Cell Distribution Width (RDW), Mean Platelet Volume (MPV), and atherogenic lipids, even after adjusting for key confounders. These results underscore the profound systemic impact of chronic hyperglycaemia and highlight the potential utility of routine parameters in the holistic risk assessment of T2DM patients.

The significant elevation of RDW and MPV in patients with poor glycaemic control is a cornerstone of our findings. RDW, a measure of anisocytosis, is no longer viewed merely as a haematological curiosity but is increasingly recognized as a biomarker of systemic inflammation and oxidative stress [5, 8]. The state of chronic, low-grade inflammation inherent in T2DM disrupts erythropoiesis and reduces red blood cell survival, leading to a greater heterogeneity in erythrocyte size [8]. Our finding of a strong positive correlation ($r=0.686$) and, more importantly, a robust independent association on multivariate analysis, solidifies the link between hyperglycaemia-driven inflammation and this haematological aberration. Similarly, elevated MPV indicates larger, hyper-reactive platelets, which are more prone to aggregation and contribute to the pro-thrombotic state that characterizes T2DM and underlies its devastating macrovascular complications [6, 9]. The fact that these changes occurred in the absence of significant anaemia or thrombocytopenia underscores their specificity as sensitive indicators of the diabetic milieu rather than overt haematological disease.

The demonstrated association between poor glycaemic control and atherogenic dyslipidaemia—characterized by significantly elevated LDL and total cholesterol—reinforces a well-established yet critically important pathophysiological synergy [10, 11]. Hyperglycaemia promotes dyslipidaemia through multiple mechanisms, including increased free fatty acid flux, oxidative stress, and glycation of LDL particles, making them more atherogenic. Our multivariate analysis confirming HbA1c as an independent predictor of LDL and total cholesterol levels underscores that this relationship is not merely a consequence of shared risk factors like age or hypertension but is directly driven by the glycaemic state itself. This reinforces the non-negotiable clinical imperative of managing both hyperglycaemia and dyslipidaemia in tandem to mitigate the accelerated atherosclerotic risk in this population.

A nuanced and insightful finding emerged from our analysis of renal parameters. While bivariate analysis showed the expected significant association between higher HbA1c and elevated serum creatinine and proteinuria, this relationship was attenuated and lost statistical significance after adjustment for age, sex, and hypertension. This suggests that the link between glycaemic control and renal dysfunction, as measured by creatinine, may be more complex and indirectly mediated by other factors, notably hypertension. Hypertension is a common companion in T2DM and a potent driver of renal damage itself; its pathophysiological pathways often intertwine with those of hyperglycaemia-induced nephropathy [12, 13]. This finding does not diminish the importance of glycaemic control for renal protection but highlights that renal function in our cohort may be more immediately sensitive to haemodynamic factors, or that the impact of glycaemia manifests over a longer timeframe or through more specific markers like UACR, which showed a positive trend.

Conversely, the lack of a significant association between HbA1c and liver enzymes is a valuable negative finding. It suggests that in a cohort without pre-existing advanced liver disease, glycaemic control is not a primary determinant of hepatic injury within the cross-sectional snapshot of our study. This indicates that discovering elevated liver enzymes in a T2DM patient should prompt a thorough investigation into other aetiologies, such as non-alcoholic fatty liver disease (NAFLD), viral hepatitis, or drug-induced toxicity, rather than being automatically attributed to poor diabetes control alone [14].

In conclusion, our study paints a detailed picture of the systemic repercussions of suboptimal glycaemic control, weaving together haematological inflammation, pro-thrombotic tendencies, and lipid metabolism dysregulation. The major strength of this study lies in its holistic approach and the use of multivariate analysis to demonstrate independent associations, providing a deeper level of evidence than simple correlations. However, the limitations of a cross-sectional design, which precludes causal inference, and a single-centre cohort, which may affect generalizability, must be acknowledged. Furthermore, residual confounding from unmeasured variables, such as detailed dietary habits, physical activity levels, and specific medication use (e.g., SGLT2 inhibitors, GLP-1 RAs, or statins), cannot be entirely ruled out.

4.2. Conclusion and Clinical Implications

Notwithstanding these limitations, our findings carry significant clinical implications. They advocate for a paradigm shift towards a more integrated, holistic monitoring approach in T2DM.
We recommend:

1. **Clinical Integration:** Routinely available and inexpensive parameters like RDW and MPV should be actively monitored and interpreted as indirect, yet valuable, indicators of poor glycaemic control and heightened inflammatory-thrombotic risk.
2. **Holistic Management:** Treatment strategies must be multifaceted, simultaneously addressing hyperglycaemia, dyslipidaemia, and hypertension to effectively disrupt the interconnected pathways leading to complications.
3. **Vigilant Screening:** The established link with renal markers mandates the continued rigorous screening for nephropathy using both serum creatinine and UACR in all T2DM patients. Adopting this integrative approach can facilitate earlier identification of high-risk patients, allow for timely intervention, and ultimately improve long-term outcomes in the management of this complex metabolic disorder.

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