Original Article

The Association of Red Blood Cell Indices with Glycosylated Hemoglobin and Microalbuminuria in Patients with Type 2 Diabetes Mellitus in a Tertiary Care Hospital – A Prospective Cross-sectional Study

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a major global health concern, often presenting asymptomatically and diagnosed only after complications arise. Poor glycemic control is linked to increased morbidity, including diabetic nephropathy. This study investigates the association between red blood cell (RBC) indices, glycosylated hemoglobin (HbA1c), and urinary albumin-to-creatinine ratio (UACR) to explore their potential in predicting early diabetic complications.

Methods: A prospective cross-sectional study was conducted in a tertiary care hospital after institutional ethical clearance. Relevant clinical and laboratory data—including hemoglobin, MCV, MCH, MCHC, RDW, HbA1c, and UACR—were collected from patients with T2DM. Statistical analysis was performed using SPSS and EZR software. Normality was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Associations were analyzed using Spearman's correlation and the Mann–Whitney U test, with $p < 0.05$ considered statistically significant.

Results: A weak, though statistically non-significant, positive correlation was observed between RDW and HbA1c ($p = 0.50$). No significant association was found between HbA1c and other RBC indices. A statistically significant positive correlation was observed between HbA1c and UACR, suggesting that poor glycemic control is associated with early renal impairment.

Conclusion: RDW may serve as a useful indicator for early hematologic alterations in T2DM, while elevated UACR reflects early nephropathy associated with poor glycemic control. These markers could aid in the timely detection and prevention of diabetic complications.

Keywords: type 2 diabetes mellitus; erythrocyte indices; glycated hemoglobin a; microalbuminuria

Introduction

Type 2 Diabetes Mellitus (T2DM) has emerged as a significant global health challenge over recent decades[1], driven by lifestyle factors and characterized by insulin deficiency or resistance[2]. This metabolic disorder leads to hyperglycemia, triggering oxidative stress via oxygen-derived free radicals, which damages multiple organ systems[3]. In India, the prevalence of T2DM is alarmingly high, with approximately 77 million individuals affected in 2019[4]. Poor glycemic control exacerbates complications such as microangiopathy, neuropathy, nephropathy, retinopathy, and cardiovascular diseases, contributing to substantial morbidity and mortality[5]. Early diagnosis and management are critical to reducing these adverse outcomes and associated healthcare costs[6].

Glycosylated hemoglobin (HbA1c) is a cornerstone for diagnosing and monitoring T2DM due to its stability and low variability[7]. Elevated HbA1c levels may alter hemoglobin structure and function, potentially affecting red blood cell (RBC) indices, including RBC count, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW)[8]. These changes could influence RBC deformability and blood viscosity, contributing to microvascular and macrovascular complications[9]. Additionally, microalbuminuria (MAU), an early marker of diabetic nephropathy, is linked to hyperglycemia[10]. Given the scarcity of data exploring these interrelationships, the present study aims to evaluate the association between RBC indices and HbA1c levels in patients with T2DM, and to examine the relationship between variability in RBC indices and the presence of microalbuminuria in this population at a tertiary care hospital.

Materials and Methods

This prospective cross-sectional study was conducted over a two-month period in the Department of Pathology, Central Laboratory, and Medical Records Department of a tertiary care teaching hospital. Approval was obtained from the Institutional Review Board (IRB) and Institutional Ethics Committee (IEC) (MOSC/ IEC/ 647 /2022), with a waiver of informed consent granted as the study involved the use of de-identified retrospective data from hospital records. The study was designed to test the null hypothesis (H_0) that there is no significant association between glycemic control (as measured by HbA1c), red blood cell (RBC) indices, and the presence of microalbuminuria (MAU) in patients with type 2 diabetes mellitus (T2DM), against the alternative hypothesis (H_1) that such an association is present.

A total of 141 patients were included, with the sample size determined using the formula for comparing two means to ensure adequate statistical power. Eligible participants were adults aged 18 years or older with a confirmed diagnosis of T2DM and receiving oral hypoglycemic agents and/or insulin. Patients with anemia, hematological disorders, malignancy, chronic kidney disease, a history of blood transfusion within the preceding three months, or pregnancy at the time of data extraction were excluded. The sample size was determined using the formula for comparing two means: $n = (Z_{\alpha/2} + Z_{\beta})^2 \times 2\sigma^2 / d^2$, with $Z_{\alpha/2} = 1.96$, $Z_{\beta} = 0.84$, $\sigma = 1.2$, and $d = 0.4$, yielding $n = 141$. The data were prospectively obtained from the electronic medical records system. The variables collected included hematological parameters (hemoglobin, RBC count, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and red cell distribution width) and biochemical parameters (fasting blood glucose, HbA1c, blood urea, serum creatinine, and urine albumin-to-creatinine ratio [UACR]). Blood samples collected in EDTA tubes were analyzed using an automated hematology analyzer, while UACR, urea, and creatinine values were generated by the VITROS 5600 integrated system reported in mg/g of creatinine. Microalbuminuria was defined as a UACR value between 30 and 300 mg/g of creatinine. All data were entered into Microsoft Excel and analyzed using SPSS software and EZR (a graphical interface for R). Categorical variables were summarized as frequencies and percentages. Normality of continuous variables was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests; non-normally distributed variables were described using medians and interquartile ranges. Associations between variables were evaluated using Spearman's rank correlation coefficient and the Mann–Whitney U test, with a p-value <0.05 considered statistically significant.

Results

Characteristics of the Study PopulationA total of 141 patients with type 2 diabetes mellitus were included in the study. The gender distribution of the participants is presented in Table 1, while the overall baseline characteristics of the study cohort, including key demographic, hematological, and biochemical variables, are summarized in Table 2. Descriptive statistics for these parameters were generated, and the distribution of continuous data was assessed for normality, which informed the use of non-parametric tests where normality assumptions were not met. The profile depicted in Tables 1 and 2 reflects typical features of individuals with established diabetes, providing a suitable foundation for examining the relationship between glycemic control, hematological indices, and early renal dysfunction.

Association of Red Blood Cell Indices with HbA1c Spearman's rank correlation analysis revealed differential degrees of association between HbA1c levels and individual red blood cell indices. Weak inverse correlations were observed between

Table 1: Gender distribution of the study population included in the analysis (n = 141), showing the number and percentage of male and female participants.

Gender	Frequency	Percentage
Male	95	67.4%
Female	46	32.6%
Total	141	100%

Table 2: Baseline characteristics of the study population (n = 141).

Parameter	Median (IQR)	Units
Age	60 (49–66)	years
Hemoglobin	14.2 (13.4–15.0)	g/dL
RBC Count	4.78 (4.30–5.31)	$\times 10^6/\mu$L
PCV	41.0 (38.0–44.4)	%
MCV	84.5 (81.4–90.2)	fL
MCH	29.5 (28.0–31.4)	pg
MCHC	34.3 (33.2–36.7)	g/dL
Fasting Blood Glucose	164 (136–199)	mg/dL
HbA1c	8.3 (7.35–9.4)	%
Serum Urea	29 (24–34.25)	mg/dL
Serum Creatinine	0.9 (0.7–1.5)	mg/dL
UP/UC	0.19 (0.06–0.76)	mg/g creatinine

HbA1c and hemoglobin (r = –0.08, p = 0.32) and hematocrit (r = –0.06, p = 0.41), suggesting that poorer glycemic control may be associated with reduced erythrocyte indices. Meanwhile, RDW showed a weak positive correlation with HbA1c (r = 0.12, p = 0.50), indicating increased anisocytosis among individuals with higher glycemic levels. These trends highlight the potential impact of chronic hyperglycemia on erythrocyte morphology and turnover. Scatter plots illustrating the direction and magnitude of these correlations are presented in Figure 1 to enhance visual interpretation of findings.

Association of RBC Indices with Microalbuminuria To assess whether RBC parameters may reflect early renal involvement, correlations were examined between hematological indices and markers of renal function, including serum urea, serum creatinine, and the urine protein-to-creatinine (UP/UC) ratio. Overall, the examination of RBC indices in relation to renal markers showed mostly weak associations. A statistically significant positive correlation was seen between HbA1c and UACR (r = 0.31, p = 0.02), indicating that alterations in RBC indices are likely influenced primarily by glycemic status rather than early nephropathy. However, subtle trends—such as a mild inverse relationship between hemoglobin and UP/UC ratio—suggest that declining renal function may contribute to early reductions in oxygen-carrying capacity. Selected scatter plots provided in Figure 2 further visualize these patterns. Correlation strengths were interpreted based on established criteria, with coefficients ranging between 0–0.3 considered weak, 0.3–0.69 moderate, and $\geq$ 0.70 strong, with positive or negative signs indicating the direction of association.

Discussion

In the present study, we evaluated the relationship between glycemic control, as measured by HbA1c, and various RBC indices including RBC count, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW) in patients with T2DM. Among these variables, RDW demonstrated a linear but statistically non-significant correlation with HbA1c (p = 0.50). Although not significant, this pattern is comparable to the trend reported by Suryavanshi et al.[11], who also observed a positive but weak association. Our findings therefore suggest that variability in erythrocyte size may increase with poorer glycemic control, potentially reflecting early hematologic alterations in T2DM. Importantly, this study adds evidence from a South Indian tertiary-care cohort, a population for which published data remain limited.

In contrast to the RDW trend, we observed no significant correlations between HbA1c and MCV, MCH, or MCHC. This result aligns with Suryavanshi et al.[11] but differs from the observations of Hardikar et al.[12], who reported inverse correlations between HbA1c and MCV, MCH, and MCHC in non-diabetic individuals. Their hypothesis—that reduced hemoglobin content may increase the proportion of glycated hemoglobin—did not appear applicable to our diabetic cohort. Waggiallah et al.[13] also reported significant reductions in hemoglobin concentration, RBC count, MCH, and MCHC in diabetic subjects compared with non-diabetic controls. Such variations across studies may reflect differences in population characteristics, nutritional status, disease duration, or coexisting anemia. Additionally, Glesby et al.[14] observed an inverse association between HbA1c and MCV in HIV-infected diabetic women, attributing this to increased erythrocyte turnover. By contrast, Alamri et al.[15] reported a positive correlation between MCV, MCH, and HbA1c, underscoring the heterogeneity

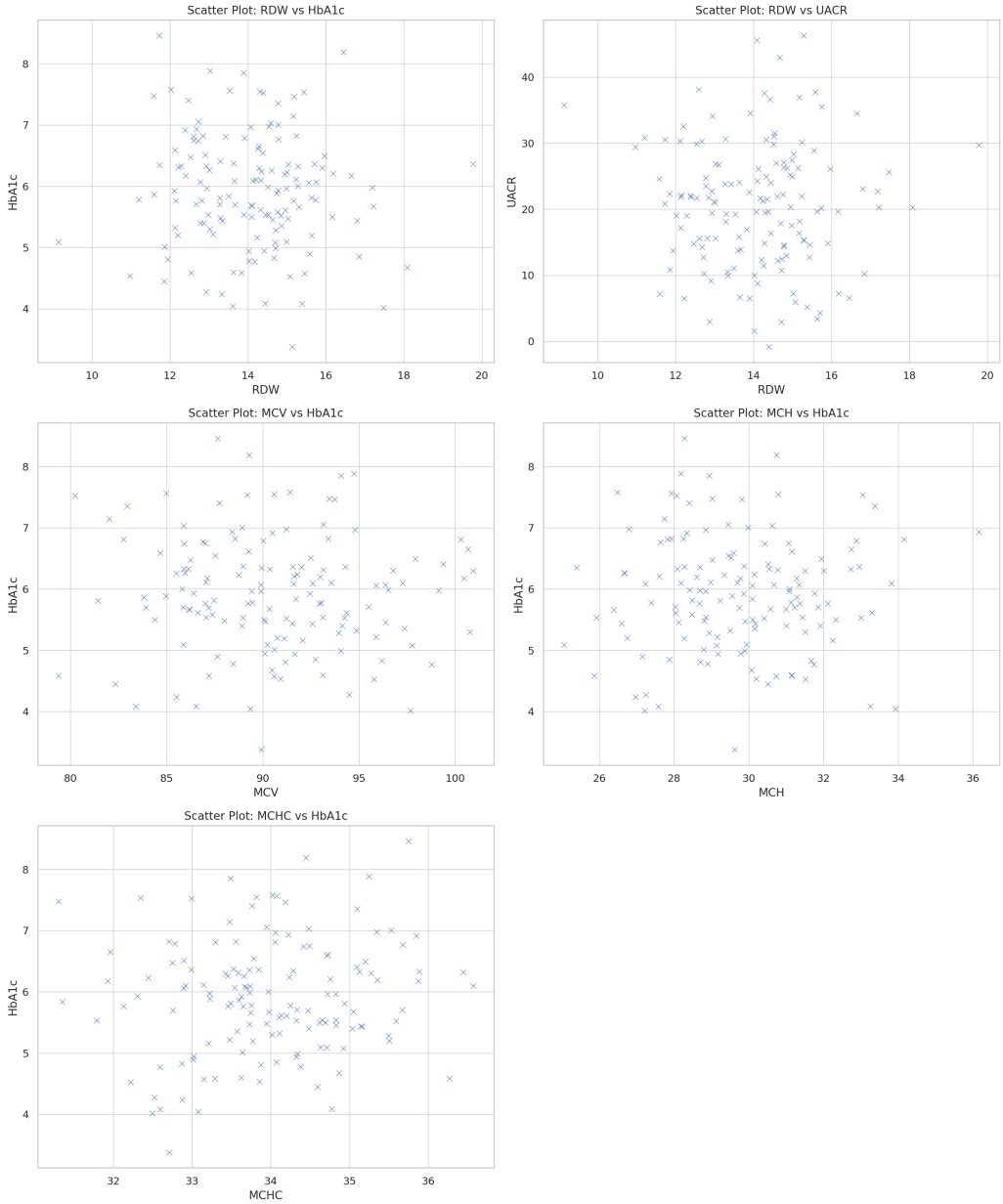

Figure 1: Scatter plots demonstrating the correlations between HbA1c levels and red blood cell indices, including RDW, MCV, MCH, and MCHC, as well as the relationship between RDW and urinary albumin-to-creatinine ratio (UACR). Each plot illustrates the distribution of data points for the respective variable pairs.

of RBC behavior in different clinical settings. Our findings contribute to this evolving evidence base by demonstrating that, within our cohort, RBC indices—other than RDW—were not meaningfully associated with glycemic control.

We also examined the relationship between HbA1c and UACR. A statistically significant positive correlation was observed, indicating that higher HbA1c levels were associated with greater urinary albumin excretion. This supports the concept that persistent hyperglycemia drives early renal injury through mechanisms such as increased formation of advanced glycation end-products and heightened oxidative stress. Our findings are consistent with the work of Haque et al.[16] and Sheikh et al.[17], both of whom demonstrated a similar association in T2DM cohorts. The present study reinforces this relationship and provides additional evidence from a region where data remain sparse.

This study provides population-specific evidence from a South Indian tertiary-care setting, thereby expanding the geographic diversity of research on hematologic and renal associations with HbA1c. Our findings suggest that RBC indices other than RDW may have limited usefulness as markers of glycemic control in T2DM patients within this demographic. Additionally, the study reinforces existing evidence of a direct association between poor glycemic control and early renal dysfunction, underscoring the value of UACR as a practical adjunct marker in routine diabetes care.This work is limited by its cross-sectional nature, which restricts interpretation of causality. A single-center study design and the absence of nutritional and inflammatory status indicators may also have influenced hematological correlations. A larger sample with longitudinal

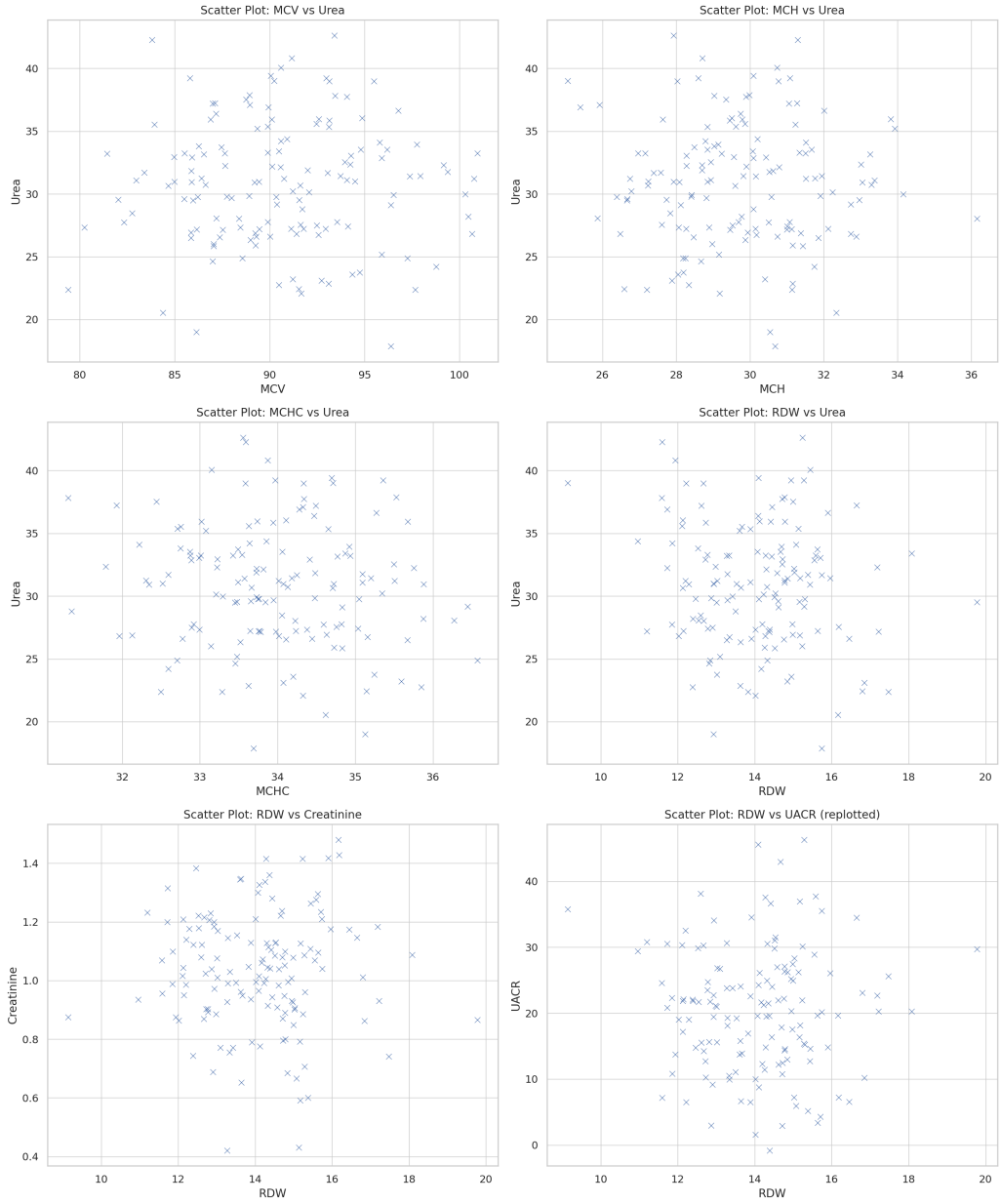

Figure 2: Scatter plots showing the correlations of RBC indices (MCV, MCH, MCHC, and RDW) with renal function markers, including serum urea, serum creatinine, and urinary albumin-to-creatinine ratio (UACR), demonstrating the variability of data points across the study population.

follow-up could better clarify the temporal relationships observed.

Clinical Implications and Future Directions RDW, a routinely available parameter, may serve as a supportive marker for early hematological disturbance in diabetes, especially where resource limitations hinder frequent biochemical monitoring. Future studies should explore whether integrating RDW with renal biomarkers enhances predictive accuracy for microvascular complications.

Conclusion

The present study found that although RDW did not show a statistically significant correlation with HbA1c, the observed linear trend suggests a potential link between red cell variability and glycemic control. In contrast, UACR demonstrated a significant positive association with HbA1c, reaffirming its role as a sensitive marker of early diabetic nephropathy. Together, these readily available and inexpensive parameters could enhance routine monitoring, enabling earlier detection and prevention of hematologic and renal complications in T2DM. These findings warrant validation through larger, multi-center studies to establish their utility in clinical practice.

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