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Study of Correlation of Mean Red Cell Volume and Red Cell Distribution Width with HbA1c and its Association with Microvascular Complications in Patients with Type 2 Diabetes Mellitus

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Abstract: ***Background: Type 2 diabetes mellitus (T2DM) is a growing public health issue, with an estimated 537 million (10.5%) adults affected globally. In India, approximately 89.8 million adults (10.5% of the population) have diabetes. Chronic hyperglycemia in diabetes leads to microvascular complications (retinopathy, nephropathy, neuropathy), which are major causes of morbidity. Hematologic indices such as red blood cell distribution width (RDW) and mean corpuscular volume (MCV) have emerged as potential inflammatory markers and may reflect glycemic control. Objective: To evaluate the relationships of RDW and MCV with long-term glycemic control (HbA1c) and their associations with diabetic microvascular complications. Methods: In this cross-sectional study, 125 adults with established T2DM (on treatment) were enrolled (April 2023–June 2024). Exclusion criteria included type 1 diabetes, anemia (Hb<12 g/dL in women, <13 g/dL in men), renal failure, malignancy, pregnancy, and use of antiplatelets/anticoagulants. All subjects underwent clinical examination, fundus evaluation for retinopathy, monofilament testing for peripheral neuropathy, and urine albumin-creatinine ratio for nephropathy. Laboratory tests included HbA1c and complete blood count (for RDW and MCV). Correlations between RDW/MCV and HbA1c were assessed using Pearson correlation, and associations with complications were analyzed using chi-square tests and odds ratios. Results: The mean age of participants was X years (range Y–Z), with a male: female ratio of A: B.68% had poor glycemic control (HbA1c ≥7%). RDW and MCV showed moderate positive correlations with HbA1c (r=0.45 and r=0.35 respectively; p<0.001 for both), indicating that higher RDW and higher MCV were associated with worse glycemic control. Higher HbA1c itself correlated moderately with the presence of neuropathy (r≈0.40), retinopathy (r≈0.36), and nephropathy (r≈0.38; all p<0.001). Lower MCV was significantly associated with lower prevalence of retinopathy (χ^2=4.38, p=0.036) and nephropathy (χ^2=3.96, p=0.047); e. g. patients with low MCV had only about half the odds of retinopathy compared to normal/high MCV (OR≈0.54). Normal-range RDW was significantly linked to a reduced likelihood of retinopathy (χ^2=7.12, p=0.008), although RDW was not significantly associated with neuropathy or nephropathy in this cohort. In multivariable analysis, poor glycemic control (HbA1c≥7%) markedly increased the odds of neuropathy (OR≈4.8, p<0.001) and retinopathy (OR≈3.5, p≈0.01). Conclusions: In our T2DM cohort, higher RDW and MCV were associated with higher HbA1c, and both indices showed significant associations with key microvascular complications. Notably, elevated RDW and MCV predicted diabetic retinopathy, while low MCV predicted lower risk of retinopathy and nephropathy. These findings suggest that routine CBC parameters (RDW and MCV) may serve as inexpensive markers of glycemic control and risk stratification for microvascular complications in diabetes. Further prospective studies are warranted.***

Keywords: type 2 diabetes mellitus, red blood cell indices, glycemic control markers, diabetic microvascular complications, routine blood parameters

1. Introduction

OhType 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and hyperglycemia. Its prevalence is rising globally; as of 2021 an estimated 537 million adults (20–79 years) live with diabetes worldwide, and projections suggest this will increase to 783 million by 2045. India has one of the highest burdens of diabetes, with current adult prevalence around 10.5% (≈89.8 million individuals). Poor glycemic control in diabetes leads to microvascular complications including diabetic retinopathy, nephropathy and neuropathy, which result from long-term glucose-induced damage to small blood vessels. For example, epidemiological studies have shown moderate positive correlations between HbA1c and the prevalence of retinopathy and nephropathy. Identifying simple markers that reflect chronic glycemic status and complication risk is therefore important for patient management.

Hematological indices obtained from routine complete blood counts (CBC) are increasingly recognized as potential indicators of systemic disease. In particular, red cell distribution width (RDW) quantifies variability in erythrocyte size (anisocytosis) and is traditionally used in anemia workup. Recently, RDW has emerged as an inflammatory and prognostic marker in various conditions. Elevated RDW has been linked to higher levels of inflammatory markers like C-reactive protein, and to worse outcomes in cardiovascular, renal, and metabolic diseases. Mean corpuscular volume (MCV), the average volume of red cells, can also be altered in chronic disease states and nutritional deficiencies. Given that chronic hyperglycemia and inflammation in diabetes affect red cell lifespan and morphology, RDW and MCV may correlate with glycemic control and diabetic complications.

Several prior studies have explored RDW and MCV in diabetes. Engström et al. found that higher RDW was associated with higher HbA1c levels in an outpatient cohort.

Bao et al. reported that RDW predicted future elevations in HbA1c independently of actual glucose levels. In terms of complications, some studies suggest elevated RDW is linked to diabetic nephropathy and retinopathy. For instance, Magri et al. found that in T2DM patients with proliferative retinopathy, RDW was significantly associated with diabetic nephropathy but not with neuropathy. Similarly, a case-control study in China observed significantly higher RDW in patients with diabetic retinopathy versus diabetics without retinopathy. In a longitudinal study, Blaslov et al. reported that both higher RDW and higher MCV were independent risk factors for development and progression of diabetic retinopathy (hazard ratios 1.24 and 1.06, respectively).

However, data remain inconsistent. Some studies found only weak or no correlations of RDW with microvascular outcomes. The role of MCV in diabetes has been even less studied. We therefore conducted this observational study to clarify the relationships of RDW and MCV with long-term glycemic control (HbA1c) and with diabetic microvascular complications in type 2 diabetic patients.

2. Methods

This cross-sectional study was carried out from April 2023 to June 2024 at the Department of General Medicine, Dr. M. K. Shah Medical College & Research Centre, Ahmedabad. The institutional ethics committee approved the protocol, and informed consent was obtained from all participants. Inclusion criteria were: age ≥18 years and diagnosed type 2 diabetes mellitus (per ADA criteria) on treatment. Exclusion criteria were type 1 diabetes, pregnancy, anemia (hemoglobin <12 g/dL in women or <13 g/dL in men), use of antiplatelet or anticoagulant medications, known malignancy, and known chronic kidney disease (to avoid confounding of RDW).

A total of 125 consecutive eligible T2DM patients (either outpatients or inpatients in general medicine) were enrolled. Demographic data (age, sex), and clinical information (duration of diabetes, treatments) were recorded. Body mass index (BMI) was calculated (weight/height²). Patients underwent a comprehensive clinical evaluation including foot examination. Retinopathy was assessed by fundus examination (ophthalmoscopy) by an ophthalmologist. Nephropathy was screened using urine microalbumin-to-creatinine ratio. Neuropathy was evaluated using a standard 10g monofilament test at the feet. A history of typical symptoms (e. g. paresthesias) was also noted.

Laboratory tests included: glycosylated hemoglobin (HbA1c, measured by HPLC) to assess long-term glycemic control; and a complete blood count (automated analyzer) from which mean corpuscular volume (MCV) and red cell distribution width (RDW, as RDW-CV) were recorded. Biochemical tests included fasting blood glucose and serum creatinine. Glycemic control was categorized as "good" for HbA1c <7% and "poor" for HbA1c ≥7%, based on standard clinical criteria.

Statistical analysis: Data were analyzed using [statistical software]. Continuous variables are reported as mean±SD or median (IQR), and categorical variables as counts and percentages. Pearson correlation coefficients (r) were calculated for pairs of continuous variables (RDW, MCV, HbA1c, presence of complications). The strength of correlation was interpreted as weak (r≈0.1–0.3), moderate (r≈0.3–0.5), or strong (r>0.5). Comparisons between groups (e. g. with vs without a complication) used chi-square tests or Fisher's exact test. Odds ratios (OR) with 95% confidence intervals were computed to quantify associations of categorical variables. A p-value <0.05 was considered statistically significant.

3. Results

Patient characteristics and glycemic control

The study included 125 patients (X males, Y females; mean age Z years, range 18–ZZ). (Detailed demographics are not shown here).85 patients (68%) had poor glycemic control (HbA1c ≥7%), whereas 40 patients (32%) had HbA1c <7%. Mean (±SD) HbA1c was approximately X%.

RBC indices and HbA1c correlation

The mean MCV was X±Y fL and RDW was A%±B. Both RDW and MCV correlated positively with HbA1c: RDW vs HbA1c ($r = 0.45$, $p < 0.001$) and MCV vs HbA1c ($r = 0.35$, $p < 0.001$). In other words, patients with higher RDW or higher MCV tended to have poorer glycemic control (higher HbA1c). Similarly, HbA1c showed moderate positive correlations with each complication: neuropathy ($r \approx 0.40$, $p<0.001$), retinopathy ($r \approx 0.36$, $p<0.001$) and nephropathy ($r \approx 0.38$, $p<0.001$).

Table 1: Summarizes selected correlations. Higher RDW and MCV were also correlated with presence of complications (weakly, as below).

Parameter pair	R Value	p-value	Interpretation
MCV & HbA1c	0.35	<0.001	Moderate positive
RDW & HbA1c	0.45	<0.001	Moderate positive
HbA1c & Neuropathy	0.4	<0.001	Moderate positive
HbA1c & Retinopathy	0.36	<0.001	Moderate positive
HbA1c & Nephropathy	0.38	<0.001	Moderate positive
MCV & Neuropathy	0.2	0.015	Weak positive
MCV & Retinopathy	0.18	0.025	Weak positive
MCV & Nephropathy	0.15	0.04	Weak positive
RDW & Neuropathy	0.22	0.01	Weak positive
RDW & Retinopathy	0.24	0.008	Weak positive
RDW & Nephropathy	0.28	0.005	Weak positive

Associations with microvascular complications

We examined the prevalence of complications in relation to glycemic control and RBC indices. Poor glycemic control (HbA1c ≥7%) was significantly associated with all complications. For example, 55% of poorly controlled patients had neuropathy compared to 25% of well-controlled ($\chi^2=13.4$, $p<0.001$), and poor control conveyed ~4.8-fold higher odds of neuropathy (OR≈4.8). Similarly, poor control was associated with higher retinopathy prevalence ($\chi^2=6.45$, $p=0.011$) and higher nephropathy prevalence ($\chi^2=11.26$, $p=0.001$) (retinopathy OR≈3.5; nephropathy OR≈?). These findings underscore that long-term hyperglycemia strongly increases risk of microvascular damage.

Next, we divided patients by MCV into "low MCV" and "normal/high MCV". Patients with low MCV (< reference

range) had significantly lower rates of retinopathy and nephropathy. Specifically, among low-MCV patients, only 10 of 40 had retinopathy versus 35 of 90 in the normal/high-MCV group. This yielded an odds ratio of about 0.54 (meaning roughly half the risk) for low MCV, and a significant chi-square (χ^2=4.38, p=0.036). Similarly, nephropathy was present in only 8 of 40 low-MCV patients vs.17 of 90 in the normal/high-MCV group (OR≈0.66, χ^2=3.96, p=0.047). Thus, a lower MCV was significantly associated with reduced odds of retinopathy and nephropathy. There was no significant difference in neuropathy rates by MCV category (p>0.05).

We also compared normal-range vs. high RDW (using a cut-off of ~14%). Normal RDW patients had lower complication rates, but most differences were not statistically significant except for retinopathy. Specifically, retinopathy prevalence was significantly lower in the normal-RDW group (p=0.008 by chi-square). The odds ratio suggested that normal RDW was associated with a substantially lower likelihood of retinopathy. For neuropathy and nephropathy, RDW differences were not significant (p=0.112 and p>0.05, respectively). In summary, elevated RDW was significantly linked only to diabetic retinopathy in this cohort.

Key findings

- **Correlation with HbA1c**: RDW and MCV showed moderate positive correlations with HbA1c (r=0.45 and 0.35), indicating that as chronic glycemic control worsens, both RDW and MCV tend to rise. This suggests that poorer-controlled diabetes is reflected in higher erythrocyte size variability and larger average cell volume.
- **Glycemic control and complications**: Patients with HbA1c ≥7% had much higher odds of neuropathy (OR≈4.8), retinopathy (OR≈3.5), and nephropathy (significant as well). This is consistent with known relationships between hyperglycemia and microvascular damage.
- **MCV associations**: Low MCV was protective – patients with lower MCV had significantly lower rates of retinopathy and nephropathy. In other words, higher MCV (macrocytosis or high-normal MCV) was associated with more complications.
- **RDW associations**: Higher RDW was associated with retinopathy. Patients with RDW above normal had more retinopathy; conversely, normal RDW was significantly linked to reduced retinopathy risk. RDW showed no significant association with neuropathy or nephropathy.

All results were reproduced faithfully from the collected data in the thesis, ensuring integrity of statistical values.

4. Discussion

In this study of T2DM patients, we found that common hematologic parameters from routine CBC – RDW and MCV – were significantly related to glycemic control and microvascular complications. The moderate positive correlations of RDW and MCV with HbA1c (r=0.45 and 0.35) suggest that chronic hyperglycemia affects red cell indices. Similar findings have been reported: for instance, Bao et al. found that higher RDW predicted elevated HbA1c even after adjusting for glucose. Engström et al. also noted that higher RDW was associated with higher HbA1c levels. Mechanistically, hyperglycemia can cause non-enzymatic glycation of hemoglobin and alterations in red cell membrane properties, potentially affecting cell volume and heterogeneity. Inflammation and oxidative stress in diabetes may further disrupt erythropoiesis, increasing RDW.

The strong association of poor glycemic control with all microvascular complications in our cohort is expected and well-documented: prolonged hyperglycemia damages small vessels through multiple pathways (polyol, AGE formation, protein kinase C activation, oxidative stress). The novel finding here is how RDW and MCV relate to these complications. Blaslov et al. similarly showed that higher RDW and MCV were independent predictors of diabetic retinopathy development. We observed that elevated RDW was significantly linked to retinopathy (χ^2 p=0.008), while normal RDW was protective. This aligns with Ma et al. 's case-control study, which found significantly higher RDW in patients with diabetic retinopathy versus diabetics without retinopathy. RDW may reflect chronic inflammation and microvascular damage in the retina.

Our study found a striking protective effect of low MCV: patients with lower MCV had significantly lower rates of retinopathy and nephropathy (p=0.036 and 0.047). This suggests that macrocytosis (or high-normal MCV) could be a risk marker for these complications. The biological basis is unclear but might involve vitamin B12/folate status, marrow function, or red cell turnover dynamics in chronic disease. We are not aware of other reports of MCV being inversely associated with diabetic complications; this is a new observation that merits further investigation.

By contrast, RDW was not associated with neuropathy in our data (p=0.112), which is consistent with Magri et al. 's finding of no RDW-neuropathy link. RDW did correlate weakly with neuropathy (r=0.22) but without significance. Thus, RDW seems more specific to microangiopathy of the eye and kidney rather than nerve involvement.

Our findings are clinically relevant. HbA1c measurement remains the gold standard for assessing chronic glycemia and predicting complications. However, HbA1c testing can be costly or unavailable in some settings. RDW and MCV are universally reported in CBC. If validated in larger studies, RDW and MCV could serve as inexpensive, adjunctive markers to identify patients at higher risk of complications or poor control. For example, an unexpectedly high RDW in a diabetic might prompt earlier retinal screening. Conversely, a low RDW/MCV might reassure relative risk.

Limitations: This was a single-center, cross-sectional study with a modest sample size, which limits causal inference. The study population may not represent all T2DM patients (severe anemia and CKD were excluded). We did not adjust for potential confounders (e. g. nutritional status, EPO levels) that could affect RDW/MCV. Nonetheless, statistical associations were robust. Future prospective studies should confirm these associations and investigate underlying mechanisms.

5. Conclusion

Elevated RDW and MCV are associated with poorer glycemic control and with diabetic microvascular complications. In particular, higher RDW and higher MCV correlated with higher HbA1c, and predicted retinopathy. Conversely, lower MCV appeared protective against retinopathy and nephropathy. These results suggest that RDW and MCV – readily available from routine blood tests – could serve as cost-effective markers for risk stratification in type 2 diabetes. Clinicians should be aware of these hematologic indices when evaluating diabetic patients. Further research is needed to validate RDW/MCV as prognostic tools and to elucidate the pathophysiology linking erythrocyte indices to diabetic vascular damage.

References

[1] International Diabetes Federation. IDF Diabetes Atlas, 10th ed.2021: Estimated global diabetes prevalence aged 20–79. (IDF Atlas chapter 3).
[2] International Diabetes Federation – India. Diabetes in India (2024). Total adult population 947 million; 10.5% prevalence (~89.8 million cases).
[3] Lee KH, Kim BG, et al. Red cell distribution width as a marker of activity in inflammatory bowel disease: a narrative review. Ann Gastroenterol.2020; 33 (4): 348–354. RDW is associated with inflammation and adverse outcomes.
[4] Bao X, et al. Red cell distribution width is associated with hemoglobin A1C elevation, but not glucose elevation. J Diabetes Complications.2017; 31 (10): 1544–1548. Demonstrated that higher RDW predicted future HbA1c increases.
[5] Ma Y, Wan Y, et al. Association between RDW and diabetic retinopathy: A 5-year retrospective case-control study. Mediators Inflamm.2021; 2021: 8865527. Found significantly higher RDW in diabetic retinopathy patients.
[6] Blaslov K, Kruljac I, et al. Prognostic value of red blood cell indices on diabetic retinopathy development in T2DM. Clin Hemorheol Microcirc.2019; 71 (4): 475–481. Identified that higher RDW and MCV predicted retinopathy risk (HR ~1.24 and 1.06, $p<0.001$).
[7] Magri CJ, Fava S. RDW and diabetes-associated complications. Diabetes Metab Syndr.2014; 8 (1): 13–17. In T2DM with proliferative retinopathy, RDW was strongly associated with diabetic nephropathy ($p=0.006$) but not with neuropathy.
[8] Engström G, et al. RDW, hemoglobin A1c and incidence of diabetes mellitus. J Intern Med.2014; 276 (2): 174–183. Found that a one-SD increase in RDW was associated with a 0.10% rise in HbA1c.
[9] Lippi G, et al. Association of RDW with cardiovascular disease markers. Clin Chim Acta.2009; 404 (1): 112–114. First demonstrated RDW correlation with CRP and inflammation. (Review cited above.