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Association Between Red Cell Distribution Width and Microvascular–Macrovascular Dysfunction in Type 2 Diabetes Mellitus: A Prognostic Perspective

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Abstract

Type 2 Diabetes Mellitus (T2DM) is associated with progressive microvascular and macrovascular dysfunction and identifying simple prognostic markers remains a clinical challenge. This cross-sectional observational study, conducted on 160 subjects at Mahatma Gandhi Memorial Medical College and M.Y. Hospital, Indore, evaluated the association between Red Cell Distribution Width (RDW) and vascular complications in T2DM. Participants were categorized into four groups: health controls, diabetics without complications, and those with microvascular or macrovascular dysfunction. RDW levels increased progressively with vascular severity (12.6% to 16.2%; $p < 0.001$) and showed strong correlations with HbA1c ($r = 0.482$), urine ACR ($r = 0.521$), and disease duration, while inversely correlating with eGFR ($r = -0.449$). Logistic regression revealed RDW as an independent predictor of vascular dysfunction (OR = 2.10, $p = 0.001$). The findings highlight RDW as a cost-effective, routinely available biomarker with significant prognostic value for early detection and risk assessment of diabetic vascular complications.

Keywords: Type 2 Diabetes Mellitus, Red Cell Distribution Width, Microvascular Complications, Macrovascular Dysfunction, Prognostic Biomarker, Vascular Dysfunction Severity Index.

INTRODUCTION

T2DM is defined as chronic hyperglycemia, insulin One of the most common chronic metabolic conditions in the world is Type 2 Diabetes Mellitus (T2DM), which is the insulin resistance, dysfunction of the β-cells, and persistent hyperglycemia [1]. Persistent hyperglycemia has harmful impact on both the microvascular and macrovascular systems resulting in a multitude of complications that cause most morbidity and mortality due to diabetes [2]. Although the disease is being better diagnosed and managed, the cost of diabetic vascular complications is still high, particularly in developing countries like India which also currently hold the position of the country with one of the highest counts of diabetic patients in the world [3].

1.1. Microvascular and Macrovascular complications of T2DM

Vascular complications of diabetes are widely divided into the microvascular (including small blood vessels, e.g. capillaries, arterioles, and venules) and macrovascular (e.g. larger arteries and veins).

- **Microvascular complications** are diabetic nephropathy, retinopathy, and neuropathy. These are due to thickening of capillary basement membrane, dysfunction of endothelia and loss of pericytes resulting in tissue hypoxia and ischemic injury [4].
- **Macrovascular complications** include coronary artery disease (CAD), cerebrovascular disease (CVD), and peripheral arterial disease (PAD), and are caused by increased rates of atherosclerosis, endothelial dysfunction, and persistent inflammation [5].

These two types of vascular injury are interconnected, and they usually co-exist in one individual, indicating a vascular continuum between microvascular and macrovascular pathology. The key processes that connect these processes include endothelial damage and oxidative stress, and therefore diagnosis of vascular dysfunction in its initial stages remains the key to disease progression prevention.

1.2. Need for reliable and cost-effective biomarkers

The existing methods of evaluating diabetic vascular risk including microalbuminuria, HbA1c, lipid profile and imaging based endothelial evaluation are useful but can be constrained by high costs and complexity as well as slowness in discoveries [6]. Therefore, emphasis is being put more on identifying simple, cost-effective and routinely obtainable biomarkers that can be utilized in detecting an early change in vascularity before it is too late [7].

The Red Cell Distribution Width (RDW) is one such emerging biomarker which is a part of the normal complete blood count (CBC) [8]. RDW, which is used traditionally as a measure of the variability of red blood cell (RBC) volume (anisocytosis), is used to distinguish the types of anemia [9]. Within recent years, however, RDW has been identified as a possible sign of whole-body inflammation, oxidative stress, and vascular damage, all of which are typical of diabetic complications.

1.3. Pathophysiological Relationship of RDW and Vascular Dysfunction

There are several biological processes through which the correlation between RDW and vascular dysfunction may be explained:

a. Inflammation and oxidative stress:

High RDW is indicative of augmented oxidative strain and cytokine action (it involves interleukin-6, tumor necrosis factor-a) that dampen erythropoiesis and concise RBC breaking down period. The same inflammatory mediators play a role in endothelial dysfunction, stiffness of the arteries, and remodeling of the vessels [10].

b. Erythropoietin and iron metabolism:

Chronic inflammation inhibits erythropoietin response and disturbs iron metabolism, causes heterogeneous production of RBCs and high RDW. Erythropoietin deficiency itself is also associated with vascular endothelial damage and nitric oxide loss of production [11].

c. RBC Deformability and microcirculation:

High RDW means that there is a distortion in the size of RBCs; this may lower deformability and interfere with microcirculation. Poor microcirculation also adds to tissue hypoxia, which leads to exacerbation of microvascular and macrovascular disease [12].

d. Renal Dysfunction:

The reduced production of erythropoietin and uremic toxin in diabetic nephropathy affects RBC survival, making the RDW higher. RDW is increasingly sensitive to kidney functioning and vascular disease as the condition of impaired renal functions develops [13].

Collectively, all these mechanisms make RDW the kind of an integrative biomarker- one that does not only indicate physiological well-being but the overall metabolic and vascular environment of diabetic patients [14].

1.4. Gaps and Rationale of Current Study

Although previous literature highlights the existence of a relationship between RDW and vascular events, there are several limitations:

I. Most of the studies have focused on microvascular or macrovascular complications separately, instead of looking at the collective vascular burden (micro + macro) in diabetes.
II. RDW as a predictor of the severity or progression of vascular dysfunction has limited information, particularly in non-end-stage groups of T2DM.
III. Not many studies have stratified diabetic patients based on vascular burden or developed composite indices of vascular dysfunction in respect to RDW.
IV. Numerous studies have been conducted in the populations of the West or non-Indians; there is little local information in Indian locations (with unique epidemiology, genetic and environmental determinants).
V. RDW is already routinely measured by normal labs as a component of the complete blood count but its clinical value in vascular risk stratification of T2DM is less well-understood.

This study uses a hospital-based sample of T2DM patients (complicated and not) and healthy controls to resolve the discussed issues. This study discusses RDW with reference to microvascular (nephropathy, retinopathy) and macrovascular (coronary artery disease, peripheral artery disease) dysfunction. This study also develops an index of Vascular Dysfunction Severity Index (VDSI) to represent the range of the vascular burden, with no complications, micro vascular complications, macrovascular complications and both microvascular and macrovascular complications. In this context by examining RDW, this study evaluates its prognostic outlook, i.e. does an increase in RDW indicate an increase in vascular burden, and does RDW remain predictive regardless of more traditional risk factors.

1.5. The Conceptual Framework Overview

This paper therefore establishes RDW as a connection between systemic inflammation, oxidative stress, and vascular dysfunction in T2DM. The study focusses on identifying the potential of RDW to be used as a holistic measure of vascular health in diabetes by examining its relationship with microvascular and macrovascular complications. The final objective is to determine whether RDW may be incorporated in the current risk assessment models to enhance the prevention and early diagnosis of diabetic vascular complications.

1.6. Aim and objectives of the study

1.6.1. Aim

To examine the relationship between Red Cell Distribution Width (RDW) and the occurrence and

intensity of microvascular and macrovascular dysfunction in Type 2 Diabetes Mellitus (T2DM) patients and the feasibility of vascular complication prognosis using RDW as a prognostic biomarker.

1.6.2. Objectives

a. To compare the RDW levels of T2DM patients with and without microvascular and macrovascular complications and non-diabetic controls.

b. To evaluate the prognostic value of RDW concerning the indicators of vascular dysfunction (HbA1c, serum creatinine, albumin-creatinine ratio, eGFR, duration of diabetes) and to derive the predictive cut-off value of RDW to identify diabetic vascular complications.

2. Review of literature

Red Cell Distribution Width (RDW), an ordinary value given in complete blood counts, a measure of the variability in erythrocyte size (anisocytosis), has been actively explored as a systemic biomarker in addition to anemia diagnosis [15]. RDW has been associated with inflammation, oxidative stress, dysfunctional erythropoiesis, and unfavorable outcomes in cardiovascular, renal, and metabolic diseases during the past 10 years [16]. With the use of RDW, research has been accumulating since 2015 in patients with Type 2 Diabetes Mellitus (T2DM) on the association between RDW and microvascular complications (nephropathy, retinopathy) and macrovascular disease (coronary disease, peripheral artery disease, stroke), and whether RDW predicts vascular burden [17].

2.1. RDW and Diabetic Nephropathy (microvascular kidney)

A number of novel research findings suggest that RDW is elevated in patients of T2DM with renal involvement (microalbuminuria, lowered eGFR, progressive nephropathy) and is associated with progression. Zhang et al., (2015, 2018) assessed new T2DM cohorts and larger clinical series and found high RDW in patients with microalbuminuria and more advanced diabetic kidney disease; RDW was associated with urine albumin excretion and negatively correlated with eGFR [18]. These associations remained after the control of commonplace confounds in numerous studies, indicating that RDW indicates renal-related pathophysiology including diminished erythropoietin, inflammation, and uremic milieu.

Xiong et al., (2017) presented more convincing data with a fairly large cohort of patients with T2D (n=809 T2DM) and categorized them into quartiles of RDW and showed that higher RDW quartiles were associated with increased prevalence of proteinuria and increasing creatinine and diabetic nephropathy; multivariate analysis revealed RDW to be an independent correlation of nephropathy and poor renal indices. The authors were talking about the potential mechanisms such as oxidative stress, shortened RBC life and impairment of marrow response in diabetic renal disease [19].

This was later followed up by other studies that associated RDW (and RDW-based ratios) with CKD progression in diabetics and demonstrating prognostic correlations with both renal progression and poor renal outcomes. Combined, the renal literature makes RDW a replicable predictor of diabetic nephropathy severity and the risk of advancement in T2DM [20].

2.2. RDW Diabetic Retinopathy (microvascular retina)

A number of current cross-sectional and case-control studies have indicated the increased RDW in patients with diabetic retinopathy (DR) in comparison with patients with no retinopathy and healthy controls. Kurtul et al., (2017) found that there is a strong correlation between high RDW and DR; RDW persistently correlated with retinopathy in the cases of HbA1c and years of diabete [21]. The same results were discovered by Ma et al., (2021) who noted that RDW was more prevalent among DR patients and correlated with the occurrence of DR in adjusted analyses. These works suggest the biological mediator of RDW and retinal microvascular damage to be inflammatory and hypoxic processes (neurovascular unit impairment, oxidative stress) [22].

Even though most DR studies are cross-sectional, and cannot be used to establish causation, the evidence that RDW is consistent in DR across settings confirms the hypothesis that RDW is a marker of systemic processes (inflammation/oxidative stress) that accompany retinal microvascular damage. Prospective studies are required in the future to find out whether RDW is a predictor of development or development of retinopathy overall [22].

2.3. RDW and macrovascular disease (CAD, PAD, stroke)

In addition to microvascular complications, RDW has been linked to macrovascular projections among diabetics and the general populations. On a large cohort level and disease-specialized research, increased RDW is associated with cardiovascular events, atherosclerotic volume, and death. The investigators, Pan et al., (2023) conducted a follow-up (long-term follow-up) study (Malmquist Diet and Cancer Study) which investigated RDW and RDW polygenic scores and found that RDW is associated with the onset of cardiovascular disease, heart failure, stroke, chronic kidney disease and mortality- results that are applicable to causal and prognostic relationships linking RDW to cardiometabolic outcomes. Even though the study is not diabetes-specific, it shows RDW has extensive prognostic ability in vascular outcomes [23].

Higher RDW quartiles in diabetic-focused analyses have been associated with increased odds of myocardial infarction, heart failure and cerebrovascular events in

national surveys-based and hospital cohorts and this association was independent of hemoglobin and conventional cardiovascular risk factors in most studies, which suggests that RDW provides additional prognostic information on top of anemia. Moreover, recent studies have investigated the association of RDW and peripheral artery disease (PAD) and suggested RDW-to-albumin ratio (RAR) as a more effective predictor of PAD risk in diabetics [24].

2.4. RDW, Glycemic Control and Metabolic Correlates

RDW is not linearly correlated with glycaemic markers. Certain cohort evidence suggests that the predictive value of RDW of future increases in HbA1c without glucose variations suggests non-glycemic etiology (e.g. inflammatory regulation of hemoglobin glycation pathways, erythrocyte turnover) [25]. Correlations between RDW and HbA1c, disease duration, and dyslipidaemia are observed to be positive in diabetic cohorts in other cross-sectional studies. These associations agree with the idea that RDW increases with combative metabolic stress [26].

2.5. Mechanistic Insights

The main lines of research, primary research, and translational research highlight several of such mechanistic pathways: chronic inflammation (IL-6, TNF-a) diets erythropoiesis and iron homeostasis, when oxidative stress shortens RBCs, size variation increases, including erythropoietin deficiency in kidney impairment wasting adds to anisocytosis and altered RBC deformability degrades microcirculation flow- a situation that may enhance tissue hypoxia and endothelial dysfunction [27]. Most of the mechanistic descriptions are inductive in clinical studies, however convergent observations in kidney, retina and cardiovascular cohorts provide biological plausibility to the role of RDW as a systemic vascular health indicator [28].

2.6. Prognostic performance and Cut-offs

RDW discriminative power has been evaluated by a few investigators through ROC analysis and quartile risk stratification. The recommended cut-offs in published cohorts would tend to be in the 14-15 percent (against analyzer and lab reference ranges) area with an increasing proportion of RDW quartiles showing a much higher incidence of vascular training [29]. Several studies (kidney, retina, combined vascular outcomes) using multivariate logistic models demonstrate that RDW is an independent predictive factor upon age, sex, HbA1c, blood pressure and renal indices- supporting the usefulness of RDW as a risk stratification tool. However, the lack of heterogeneity among the studies (methodology, RDW type of measurement RDW-CV vs RDW-SD, lab ranges) makes it difficult to adopt universal cut-off [30].

MATERIALS AND METHODS

It was a cross-sectional observational study that was done in a hospital in the Department of Pathology in conjunction with the Department of Medicine, Mahatma Gandhi memorial medical college and Maharaya Yeshwant Rao Holkar Hospital, Indore, Madhya Pradesh, India. The research was carried out between January 2023 and June 2024. The population of the study was 160 patients who had type 2 diabetes mellitus (T2DM) with and without complications as well as a group of individuals who were healthy non-diabetics. The patients with diabetes were enlisted in outpatient and inpatient units of the hospital with clinical assessment and lab assessment to confirm the presence of diabetes as used in WHO criteria of diabetes diagnosis.

2.7. Grouping Study Subjects

The subjects were divided into four groups according to the vascular complications: The presence or absence of vascular complications.

- **Group I:** Healthy control (non-diabetic).
- **Group II:** T2DM without complications.
- **Group III:** T2DM having micro vascular complications (nephropathy and/or retinopathy).
- **Group IV:** T2DM containing macrovascular complications (coronary artery disease, peripheral artery disease, or cerebrovascular disease).

To conduct the prognostic analysis, the occurrence of any vascular complication was treated as a composite outcome variable, and further stratification was performed in terms of the severity and the presence of multiple complications.

2.8. Inclusion Criteria

- Adults with Type 2 Diabetes Mellitus who were 18 years old and above.
- Diabetic patients who have or do not have microvascular or macro vascular complications.
- People who can make an informed written consent.
- The controls are healthy volunteers.

2.9. Exclusion Criteria

- Gestational diabetes or type 1 diabetes.
- The previous hematological disorders, liver disease, malignancy, or HIV / AIDS.
- The patients are acute infected patients with chronic inflammatory disease, or erythropoietin treatment.
- Women that are pregnant or patients having some systemic disease that affects erythropoiesis.

2.10. Sample Size

One hundred and sixty participants were enrolled:

- 45 healthy controls,
- 50 diabetic patients free of complications, and
- 65 that had diabetics and vascular complications.

The sample size was determined by the standard statistical formulae in a 95% level of confidence, the anticipated prevalence of the vascular complications

with T2DM in previous research, and the margin of error of 5%.

2.11. Data Collection Procedur

A structured proforma was used to gather demographic, clinical, biochemical and hematological data.

- **Clinical parameters included:**

Effects inclination Age, sex, BMI, duration of diabetes, blood pressure and treatment history.

- **Biochemical parameters included:**

Serum creatinine, lipid profile, urine albumin-to-creatinine ratio (ACR), and fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c).

- **Hematological parameters included:**

Complete blood count (CBC) including Red Cell Distribution Width (RDW), hemoglobin, mean corpuscular volume (MCV), total leukocyte count, and platelet count.

2.12. Diagnostic evaluation included:

- Fundoscopy and optical coherence tomography (OCT) of diabetic retinopathy.
- eGRP and urine ACR of nephropathy.
- Peripheral vascular disease or other dysfunctions of the microvasculature should be assessed by ankle-brachial Index (ABI) or Doppler ultrasonography.

2.13. Laboratory Analysis

- The blood samples were collected after an overnight fasting period.
- Automated hematology analyzer (Sysmex XN-1000) was used to analyze CBC.
- RDW has been given as RDW-CV (% which was automatically calculated by the analyzer using the formula:

$$\text{RDW (\%)} = \frac{\text{SD of MCV}}{\text{Mean MCV}} \times 100$$

- A Beckman Coulter AU480 analyzer was used to determine biochemical parameters (glucose, creatinine, lipid profile, HbA1c).
- Microalbuminuria was measured through immunoturbidimetric assay, and the value was given in mg/g creatinine.

2.14. Assessment of Vascular dysfunction.

1. Microvascular Dysfunction:

Patients diagnosed with sections of diabetic nephropathy (microalbuminuria and/or lost eGFR) and/or diabetic retinopathy (fundoscopic / OCT alternations).

2. Macrovascular Dysfunction:

Characterized by clinical/Doppler manifestations of coronary artery disease and peripheral/ABI 0.9 and less artery disease or cerebrovascular disease.

3. Composite Vascular Dysfunction Score:

An index of prognostic Vascular Dysfunction Severity (VDSI) was derived:

- **0** = No complications
- **1** = Microvascular only
- **2** = Macrovascular only
- **3** = Micro-vascular and macrovascular involvement

3.11. Statistical Analysis

The data were processed by SPSS version 26.0 and Microsoft Excel version 2019.

- Mean SD was used to represent continuous variables and frequency used to represent categorical data in terms of frequency percentage.
- The ANOVA or Student t-test of continuous variables, and Chi-square test of categorical variables were used in comparison between groups.
- The relationship between RDW and clinical parameters (HbA1c, ACR, eGFR) was tested using Pearson correlation analysis.
- Multivariate logistic regression analysis was used to determine the independent predictors of vascular dysfunction.
- The optimal cut-off value of RDW that predicts microvascular-macrovascular dysfunction was determined by studying Receiver Operating Characteristic (ROC) curves. A p-value that was less than 0.05 was taken to be statistically significant.

3.12. Ethical Consideration

The Institutional Ethics Committee of Mahatma Gandhi Medical College and M.Y. Hospital, Indore (Approval No: EC/MGM/aug-22/35) gave ethical approval. All participants were informed about it before any data collection was done by signing a written informed consent document. The research was done according to the Declaration of Helsinki (2013).

RESULTS

4.1 Demographic and Clinical Characteristics

A total of 160 subjects participated in this study. They were divided into four groups:

- **Group I:** Healthy controls (n = 45)
- **Group II:** T2DM without complications (n = 50)
- **Group III:** T2DM with microvascular complications (n = 35)
- **Group IV:** T2DM with macrovascular complications (n = 30)

The average age of participants was 53.42 ± 9.56 years, with more males (57.5%). The average duration of diabetes in diabetic subjects was 8.2 ± 3.7 years. Body Mass Index (BMI) significantly increased among T2DM groups compared to

controls ($p < 0.001$). Systolic and diastolic blood pressure readings were notably higher in the complication groups, especially in macrovascular cases ($p < 0.01$).

Table 1. Demographic and clinical characteristics of study subjects

Parameter	Control (n=45)	T2DM without Comp. (n=50)	Microvascular (n=35)	Macrovascular (n=30)	p-value
Age (years)	49.12 ± 8.45	52.26 ± 9.12	54.80 ± 8.75	57.43 ± 9.63	0.021*
Male (%)	55.6	56.0	60.0	60.3	0.82
Duration of diabetes (years)	–	6.45 ± 3.18	8.84 ± 3.92	9.60 ± 4.02	<0.001**
BMI (kg/m²)	23.9 ± 2.4	25.1 ± 3.2	26.2 ± 3.6	27.0 ± 3.8	0.002**
SBP (mmHg)	118.3 ± 7.6	126.2 ± 8.9	134.4 ± 10.2	138.8 ± 12.3	<0.001**
DBP (mmHg)	74.6 ± 6.2	78.8 ± 7.1	84.1 ± 8.6	86.5 ± 8.9	<0.001**

Interpretation: Table 1 shows the demographics and clinical characteristics of the exploratory players in the four well-controlled cohorts, T2DM free of complications, T2DM with microvascular and macrovascular complications. The average epoch of the patient with macrovascular complications was increased from control to patient. This implies vascular dysfunction in aged diabetic human beings (phosphorus = 0.021). The proportion of males was similar in all teams, meaning there was no significant difference in identity ($p = 0.82$). The duration of diabetes was significantly longer in patients with microvascular and macrovascular complications compared to those who did not have any complications (p 0.001). That confirms the extended effects of chronic high blood sugar on vascular health. Furthermore, BMI, systolic blood pressure (SBP), and diastolic bp (DBP) overall show steady increases from control to macrovascular scenarios, with very significant differences (p 0.01). The current course indicates that the development of vascular complications in the middle of the T2DM patient requires the addition of increased body fat and increased HDL.

4.2 Biochemical and Hematological Profile

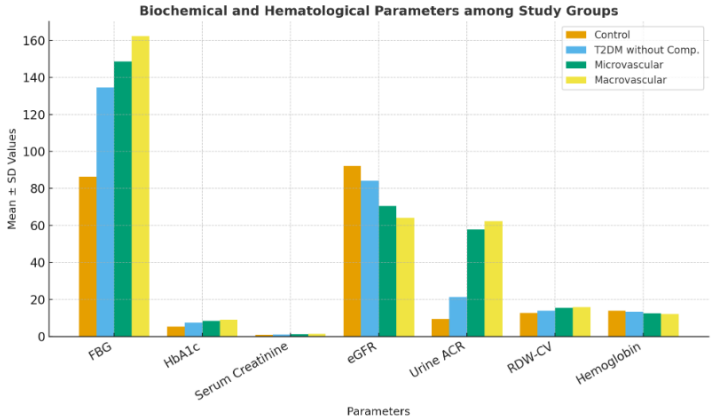
Marked differences appeared in biochemical and hematological parameters among the study groups. Mean HbA1c increased from the control group to the macrovascular group (5.2 ± 0.4 vs. 8.9 ± 1.1; $p < 0.001$). Serum creatinine and the albumin-to-creatinine ratio (ACR) were significantly higher in the microvascular and macrovascular groups.

The Red Cell Distribution Width (RDW-CV) showed a clear and statistically significant increase in the groups with vascular complications compared to those without and the controls ($p < 0.001$).

Table 2. Biochemical and Hematological parameters among study groups

Parameter	Control	T2DM without Comp.	Microvascular	Macrovascular	p-value
FBG (mg/dL)	86.4 ± 11.2	134.6 ± 23.4	148.7 ± 27.1	162.3 ± 31.5	<0.001**
HbA1c (%)	5.2 ± 0.4	7.5 ± 0.6	8.3 ± 0.9	8.9 ± 1.1	<0.001**
Serum Creatinine (mg/dL)	0.84 ± 0.12	0.95 ± 0.15	1.21 ± 0.26	1.34 ± 0.29	<0.001**
eGFR (mL/min/1.73m²)	92.3 ± 7.6	84.2 ± 9.1	70.6 ± 8.4	64.1 ± 7.8	<0.001**
Urine ACR (mg/g)	9.4 ± 3.6	21.3 ± 5.2	57.8 ± 11.5	62.4 ± 14.3	<0.001**
RDW-CV (%)	12.6 ± 0.8	13.9 ± 0.9	15.4 ± 1.1	15.9 ± 1.2	<0.001**
Hemoglobin (g/dL)	13.8 ± 1.2	13.2 ± 1.1	12.4 ± 1.3	12.1 ± 1.4	0.008**

Interpretation: Table 2 shows important variations in biochemical and hematologic components across study cohorts. From the direct group to the diabetic communities, fast glucose and HbA1c levels have steadily increased. The observed trend shows that the hardening of glycemic control occurs with worsening of the disease (p 0.001). The nephritic indicator, admire serum creatinine, and urine ACR were increasing significantly, and eGFR declined, indicating that nephritic performance in vascular complication patients decreases (p 0.001). The RDW-CV escalates sharply, with control measurements of 12.6 percent and cases involving macrovascular 15.9 percent. That change is a resonant indication of vascular dysfunction (p 0.001). Hemoglobin level decreases considerably in complicated diabetes ($p = 0.008$). All in all, the results indicate that inadequate glycemic regulation, renal lesions, and increased RDW are highly linked with vascular complications in T2DM.



Graph 1: Biochemical and Hematological Parameters Among Study Groups

Interpretation: The graphs demonstrate variations in biochemical measurements and related measurements in the various cohorts of the studies, starting with the regulated individuals to the patients with diabetic microvascular and macrovascular disease. The higher the diabetes level is transformed into a more complicated form, the higher the levels of fast blood glucose, HbA1c, serum creatinine, urine ACR, and RDW-CV. This rise is an indicator of poor blood sugar management, kidney issues, and alterations in blood parameters. During an alternative holdover period, the eGFR and hemoglobin levels slightly declined, which suggests the reduction of the renal capacity and anemia caused by diabetic complications. The disparity in total parameters is statistically significant (p 0.001), which presupposes the negative effect of it on metabolism and blood circulation. The facts provide a clear display of the evolutionary metabolic issues that develop with the advancement of diabetes and its complications.

4.3 Correlation of RDW with Clinical and Vascular Parameters

Pearson correlation analysis shows that RDW was constructively correlated with HbA1c (r = 0.482, phosphorus 0.001), ACR (r = 0.521, phosphorus 0.001), and diabetes duration (r = 0.417, phosphorus 0.001). The RDW and eGFR had a negative association (r = -0.449, phosphorus 0.001). That indicates an inverse relationship of renal function to renal function.

Table 3. Correlation of RDW with clinical and biochemical parameters

Parameter	Correlation Coefficient (r)	p-value	Interpretation
HbA1c	0.482	<0.001	Significant positive correlation
Serum Creatinine	0.389	<0.001	Moderate positive correlation
eGFR	–0.449	<0.001	Significant negative correlation
Urine ACR	0.521	<0.001	Strong positive correlation
Duration of Diabetes	0.417	<0.001	Significant positive correlation

Interpretation: Table 3 shows the association of Red Cell Circulation Width (RCW) and several clinical and biochemical signs of blood vessel problems in Type 2 diabetes Mellitus (T2DM). yonder be a robust useful association between RDW and HbA1c (r = 0.482, phosphorus 0.001) and urine ACR (r = 0.521, phosphorus 0.001). Thus, higher RDW beliefs are associated with disadvantaged blood sugar management and further kidney damage. RDW is also positively correlated with serum creatinine and diabetes duration. The current reflects the overall effect of sustained metabolic stress. A significant negative association with eGFR (r = –0.449, phosphorus 0.001) indicates that RDW increases as kidney function deteriorates. These effects collectively show that RDW is a responsive indicator of artery and metabolic decline in diabetic patients.

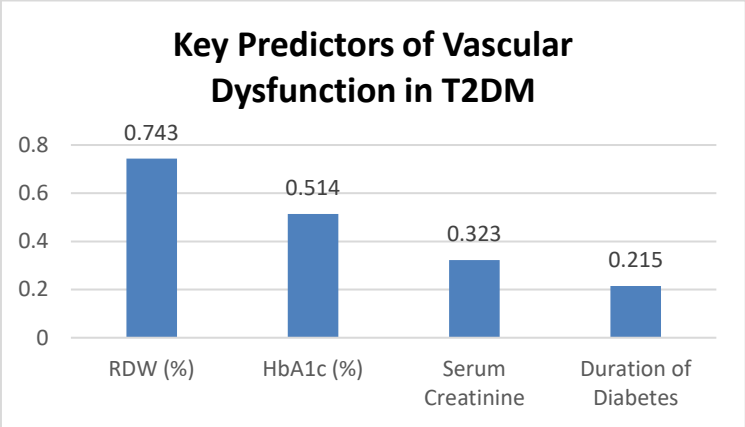
4.4 Logistic Regression Analysis

On multivariate logistic regression, RDW appeared as an independent predictor of vascular dysfunction after adjusting for age, sex, HbA1c, and serum creatinine.

Table 4. Multivariate logistic regression showing predictors of vascular dysfunction

Variable	β Coefficient	Odds Ratio (95% CI)	p-value
RDW (%)	0.743	2.10 (1.38–3.21)	0.001**
HbA1c (%)	0.514	1.67 (1.20–2.31)	0.004**
Serum Creatinine	0.323	1.45 (1.10–2.08)	0.016*
Duration of Diabetes	0.215	1.23 (1.04–1.49)	0.028*

Interpretation: Table 4 shows a multivariate logistic delayed development evaluation which identifies an independent predictor of vascular dysfunction in patients with T2DM. RDW (%) an odds ratio of 2.10 (95 % CI: 1.38, 3.21, phosphorus = 0.001). As it stands, for every 1 % increase in RDW, there is double chance of developing vascular complications. Furthermore, HbA1c (%) had a significant connection (p = 0.004) confirming that low blood sugar contributes to vascular damage. Similarly, serum creatinine and diabetes duration were important predictors (p 0.05). The current implies an additional vascular hazard due to kidney failure and a long course of disease. Overall, RDW independently predicts vascular disorders in addition to the usual blood sugar and kidney marker.



Graph 2: Key Predictors of Vascular Dysfunction in T2DM

Interpretation: The bar graph shows the β coefficients of key factors that lead to vascular problems in T2DM patients. This data comes from a multivariate logistic regression analysis. RDW (%) has the highest β coefficient at 0.743, making it the most important independent predictor of vascular complications. HbA1c (%) is next with a coefficient of 0.514, highlighting the serious effects of poor blood sugar control. Serum creatinine (0.323) and the duration of diabetes (0.215) also have positive contributions. This means that a longer disease duration and kidney issues increase vascular risk. In summary, RDW has the strongest link to vascularr dysfunction, showing it is more important than traditional metabolic and kidney markers in predicting these problems.

4.5 Comparison of RDW Across Vascular Dysfunction Severity Index (VDSI)

A graded elevation in RDW was observed with increasing VDSI categories. Patients with both micro- and macrovascular complications exhibited the highest RDW values.

Table 5. Comparison of RDW across Vascular Dysfunction Severity Index (VDSI) categories

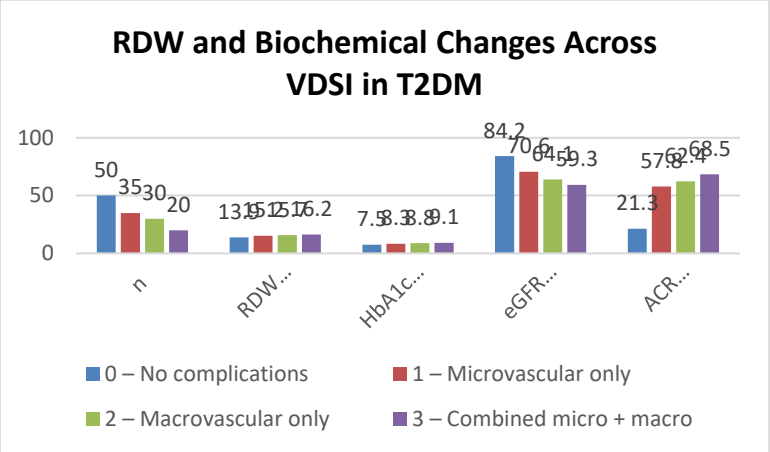
VDSI Category	n	RDW (%) ± SD	HbA1c (%) ± SD	eGFR (mL/min/1.73 m²)	ACR (mg/g)	*p*-value
0 – No complications	50	13.9 ± 0.9	7.5 ± 0.6	84.2 ± 9.1	21.3 ± 5.2	—
1 – Microvascular only	35	15.2 ± 1.0	8.3 ± 0.9	70.6 ± 8.4	57.8 ± 11.5	<0.001**
2 – Macrovascular only	30	15.7 ± 1.1	8.8 ± 1.1	64.1 ± 7.8	62.4 ± 14.3	<0.001**
3 – Combined micro + macro	20	16.2 ± 1.2	9.1 ± 1.2	59.3 ± 6.9	68.5 ± 15.2	<0.001**

Interpretation: table 5 presents the distribution of RDW and other biochemical values at various phases of the vascular dysfunction as indicated by the Vascular Dysfunction Severity Index. The RDW standards have significantly risen between a patient who has no complications (13.9 0.9%) and a patient who even has a micro- and macro-involvement (16.2 1.2%. This shows that there is a great positive relationship between RDW and vascular burden (p 0.001). In addition to that, HbA1c and ACR also rise, whereas eGFR declines. The extensive modifications above validate a declining metabolic and nephritic disease as a vascular complication. These results indicate that RDW is tightly associated with the general cause of vascular defect, and it is useful to validate its role as a biomarker that indicates the effect of diabetes-related vascular injury.

Graph 3: RDW and Biochemical Changes Across VDSI in T2DM

Interpretation: The graph indicates alterations in RDW, HbA1c, eGFR, and ACR as an addition to the VDSI groups. This implies that RDW is associated with the intensity of vascular dysfunction. Non-complicated diabetics clearly show an increase in the RDW and HbA1c stages compared to micro and macrovascular complications. This represents aggravation of glycemic condition and variability of erythropoietin. Conversely, there is a consistent decline in the eGFR principles, and this may indicate deterioration of the nephritic function. ACR escalates as the disease advances, indicating the

development of nephropathies. The figure indicates that the increased RDW must be strictly associated with the increased vascular responsibility and inevitable metabolic activity in diabetic patients. Their usefulness as a predictive index is confirmed by the present.



DISCUSSION

The current study comprehensively measures the relationship of Red Cell Dispersion Width (RDW) and the spectrum of vascular dysfunction in patients with type 2 diabetes Mellitus (T2DM). The decision shows that diabetic patients, particularly those with microvascular and macrovascular complications, have been highly honored by the RDW grade compared to those who do not have diabetes. The present addition to the RDW is strongly correlated with the HbA1c glycemic position, the renal parameters (serum creatinine, eGFR, urine ACR), and the duration of diabetes, demonstrating the role of individuals as a combined biomarker of vascular and metabolic obligations in T2DM.

Demographic analysis has shown that age, BMI, and blood pressure have shifted more from control patients to patients with vascular complications, which are not changing with the known risk profile of diabetic vasculopathy (Horton & Barrett, 2021). These clinical parameters are known to increase oxidative stress and endothelial damage, creating a proinflammatory environment that contributes to vascular dysfunction. The steady increase in HbA1c and fast blood glucose stages alongside the progression of the disease suggests that the chronic hyperglycemia–inflammation–endothelial dysfunction axis defined in the anterior assignment (Libby et al., 2018).

Hematologically, promoting RDW in diabetic patients harmonizes with previous investigations and suggests that anisocytosis is caused by systemic inflammatory reaction, impaired erythropoiesis, and oxidative stress (Arkew et al., 2022). Inflammation-driven cytokines, such as IL-6 and TNF-, can suppress erythropoietin synthesis and iron mobilization, principally for heterogeneous erythropoietin size and reduced RBC life (Marques et al., 22022) These procedures are like those which interrupt vascular dysfunction and provide a plausible pathological link between RDW and endothelial damage.

The strong useful connection between RDW and albumin–creatinine ratio (r = 0.521) and the undesirable relationship with eGFR (r = –0.449) detected here confirms that higher RDW standards are associated with progressive kidney disease and impaired nephritic clearance. Such findings are consistent with the Zhang et al report. (2018) and Roumeliotis et al. (2020), which identified RDW as a predictive indicator of nephritic function impairment in diabetics. In addition, the significant association between RDW and HbA1c (r = 0.482) indicates that chronic glycemic disturbances contribute to erythropoietin organizational adaptations and increased vascular stress.

Multivariate regression analyses showed that red blood cell distribution width (RDW) was the most important independent factor predicting vascular dysfunction (OR: 2.10, 95% CI: 1.38–3.21, p = 0.001), and it was the HbA1c and serum creatinine that were most significant. This confirms the fact that RDW is an indicator of vascular injury in the instances of high blood glucose as well as normal levels of glucose levels, which is aligned with the study conducted by Pan et al. (2023). A specific increase in RDW was demonstrated by the Vascular Dysfunction Severity Index (VDSI), which showed the increase from 13.9% in uncomplicated diabetes to 16.2% in individuals with a combination of micro- and macro-vascular complications, which suggests that RDW is a reflection of the entire vascular load and is related to microvascular injury in diabetic retinopathy and nephropathy (Kurtul et al., 2017; Ma et al., 2021). The integration of the various vascular diseases into VDSI model is a great move in understanding vascular complications because of diabetes.

From a mechanical perspective, RDW could be a reason for the damage to the vessels because it is linked to red blood cells with less deformability and worsened microcirculation which eventually leads to tissue hypoxia and endothelial stress. The interplay between anisocytosis, oxidative alteration of erythrocyte membranes, and the decline in nitric oxide availability aggravates the arterial stiffness and the progression of atherosclerosis (Poz et al., 2019). Hence, high RDW should be regarded as a factor of vascular dysfunction that actively participates in the disease process instead of being merely a bystander.

The findings of the study, along with other studies, support the idea of RDW as a cheap and easy to obtain marker which denotes the fundamental role of the metabolic–vascular interaction in T2DM. The RDW is a strong contender to the diabetes risk stratification model considering its association with nephritic and glycemic parameters, as well as its ability to indicate vascular load irrespective of the standard markers.

CONCLUSION

The research concludes that Red Cell Distribution Width (RDW) is a significant and separate diagnostic marker indicating the hypoxia of both microvascular and macrovascular systems in Type 2 Diabetes Mellitus (T2DM). RDW levels that are high indeed reflected poor glycemic control, renal failure, and long disease duration, thus indicating the accumulated burden on the vascular system. Even after being controlled for traditional risk factors such as HbA1c and serum creatinine, RDW was still able to predict the occurrence of vascular complications independently. The upward trend of RDW across the levels of the Vascular Dysfunction Severity Index (VDSI) is indicative of its prognostic value. Being a parameter that is normally available and inexpensive, RDW is very likely to be used for early identification, risk stratification, and clinical monitoring of vascular complications in diabetic patients.

REFERENCES

1. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. International journal of molecular sciences. 2020 Aug 30;21(17):6275.
2. Zakir M, Ahuja N, Surksha MA, Sachdev R, Kalariya Y, Nasir M, Kashif M, Shahzeen F, Tayyab A, moazzam Khan MS, Junejo M. Cardiovascular complications of diabetes: from microvascular to macrovascular pathways. Cureus. 2023 Sep 24;15(9).
3. Walker IF, Garbe F, Wright J, Newell I, Athiraman N, Khan N, Elsey H. The economic costs of cardiovascular disease, diabetes mellitus, and associated complications in South Asia: a systematic review. Value in health regional issues. 2018 May 1;15:12-26.
4. Horton WB, Barrett EJ. Microvascular dysfunction in diabetes mellitus and cardiometabolic disease. Endocrine reviews. 2021 Feb 1;42(1):29-55.
5. Zakir M, Ahuja N, Surksha MA, Sachdev R, Kalariya Y, Nasir M, Kashif M, Shahzeen F, Tayyab A, moazzam Khan MS, Junejo M. Cardiovascular complications of diabetes: from microvascular to macrovascular pathways. Cureus. 2023 Sep 24;15(9).
6. Raut SS, Acharya S, Deolikar V, Mahajan S. Navigating the frontier: emerging techniques for detecting microvascular complications in type 2 diabetes mellitus: a comprehensive review. Cureus. 2024 Jan 31;16(1).
7. Vasan RS. Biomarkers of cardiovascular disease: molecular basis and practical considerations. Circulation. 2006 May 16;113(19):2335-62.
8. Arkew M, Gemechu K, Haile K, Asmerom H. Red blood cell distribution width as novel biomarker in cardiovascular diseases: a literature review. Journal of blood medicine. 2022 Jan 1:413-24.
9. Buttarello M. Laboratory diagnosis of anemia: are the old and new red cell parameters useful in classification and treatment, how?. International journal of laboratory hematology. 2016 May;38:123-32.
10. Libby P, Loscalzo J, Ridker PM, Farkouh ME, Hsue PY, Fuster V, Hasan AA, Amar S. Inflammation, immunity, and infection in atherothrombosis: JACC review topic of the week. Journal of the American College of Cardiology. 2018 Oct 23;72(17):2071-81.
11. Marques O, Weiss G, Muckenthaler MU. The role of iron in chronic inflammatory diseases: from mechanisms to treatment options in anemia of inflammation. Blood, The Journal of the American Society of Hematology. 2022 Nov 10;140(19):2011-23.
12. Mathew RT. Association of Red Cell Distribution width (RDW) and RBC Adherence with the Presence and Severity of Diabetic Retinopathy (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
13. Hamza E, Metzinger L, Metzinger-Le Meuth V. Uremic toxins affect erythropoiesis during the course of chronic kidney disease: a review. Cells. 2020 Sep 6;9(9):2039.
14. Mbatha NA, Mushebenge AG, Khathi A. Identification of putative causal relationships between blood-based biomarkers and prediabetes-induced senescence: a comprehensive review. Physiologia. 2024 Apr 8;4(2):149-81.
15. Garg R. Beyond anemia: Red cell distribution width as a universal biomarker in contemporary medicine. Journal of Hematology and Allied Sciences. 2025:1-0.
16. García-Escobar A, Lázaro-García R, Goicolea-Ruigómez J, González-Casal D, Fontenla-Cerezuela A, Soto N, González-Panizo J, Datino T, Pizarro G, Moreno R, Cabrera JÁ. Red blood cell distribution

width is a biomarker of red cell dysfunction associated with high systemic inflammation and a prognostic marker in heart failure and cardiovascular disease: a potential predictor of atrial fibrillation recurrence. High Blood Pressure & Cardiovascular Prevention. 2024 Sep;31(5):437-49.
17. Roumeliotis S, Stamou A, Roumeliotis A, Theodoridis M, Leivaditis K, Panagoutsos S, Liakopoulos V. Red blood cell distribution width is associated with deterioration of renal function and cardiovascular morbidity and mortality in patients with diabetic kidney disease. Life. 2020 Nov 22;10(11):301.
18. Zhang M, Zhang Y, Li C, He L. Association between red blood cell distribution and renal function in patients with untreated type 2 diabetes mellitus. Renal failure. 2015 Apr 21;37(4):659-63.
19. Xiong XF, Yang Y, Chen X, Zhu X, Hu C, Han Y, Zhao L, Liu F, Sun L. Red cell distribution width as a significant indicator of medication and prognosis in type 2 diabetic patients. Scientific reports. 2017 Jun 2;7(1):2709.
20. Zhang J, Zhang R, Wang Y, Li H, Han Q, Wu Y, Wang S, Guo R, Wang T, Li L, Liu F. The association between the red cell distribution width and diabetic nephropathy in patients with type-2 diabetes mellitus. Renal failure. 2018 Oct 15;40(1):590-6.
21. KURTUL BE, İNAL B, ÖZER PA, KABATAŞ EU. The correlation between red cell distribution width and diabetic retinopathy in patients with type 2 diabetes mellitus. Turkiye Klinikleri Journal of Ophthalmology. 2017;26(1):19-24.
22. Ma Y, Li S, Zhang A, Ma Y, Wan Y, Han J, Cao W, Xu G. Association between red blood cell distribution width and diabetic retinopathy: a 5-year retrospective case-control study. Journal of ophthalmology. 2021;2021(1):6653969.
23. Pan J, Sun J, Goncalves I, Kessler M, Hao Y, Engström G. Red cell distribution width and its polygenic score in relation to mortality and cardiometabolic outcomes. Frontiers in Cardiovascular Medicine. 2023 Nov 20;10:1294218.
24. Li D, Long J, Zhang J, He M, Zeng Q, He Q, Zhan W, Chi Y, Zou M. Association between red cell distribution width–and–albumin ratio and the risk of peripheral artery disease in patients with diabetes. Frontiers in Endocrinology. 2024 Feb 9;15:1272573.
25. Tsilingiris D, Makrilakis K, Barmpagianni A, Dalamaga M, Tentolouris A, Kosta O, Eleftheriadou I, Liatis S. The glycemic status determines the direction of the relationship between red cell distribution width and HbA1c. Journal of Diabetes and its Complications. 2021 Oct 1;35(10):108012.
26. Mathew RT. Association of Red Cell Distribution width (RDW) and RBC Adherence with the Presence and Severity of Diabetic Retinopathy (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
27. Pirotte M. Detailed investigation of erythropoiesis and iron metabolism in the context of allogeneic hematopoietic stem cell transplantation (Doctoral dissertation, Universite de Liege (Belgium)).
28. Poz D, De Falco E, Pisano C, Madonna R, Ferdinandy P, Balistreri CR. Diagnostic and prognostic relevance of red blood cell distribution width for vascular aging and cardiovascular diseases. Rejuvenation research. 2019 Apr 1;22(2):146-62.
29. Mburu LW. Diagnostic utility of red cell indices in relation to serum iron indices for evaluation of iron deficiency in heart failure.
30. Xiong XF, Yang Y, Chen X, Zhu X, Hu C, Han Y, Zhao L, Liu F, Sun L. Red cell distribution width as a significant indicator of medication and prognosis in type 2 diabetic patients. Scientific reports. 2017 Jun 2;7(1):2709.