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Association of Red Cell Distribution Width with Early Metabolic–Renal Alterations in Patients with Type 2 Diabetes Mellitus and Preserved Renal Filtration

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ABSTRACT

Background: Renal dysfunction in individuals with type 2 diabetes mellitus (T2DM) should be detected early to allow prevention of chronic kidney disease (CKD). Yet classic renal markers tend to identify kidney impairment once significant levels of functional deterioration have taken place. Red cell distribution width (RDW), which is a regularly reported value of the complete blood count, has been linked to inflammation, oxidative stress, and unfavorable metabolic and renal consequences. Nevertheless, it has not been clearly defined how RDW can be an early predictor of metabolic renal dysfunction in diabetic patients with intact renal filtration, despite these associations. The aim of the study was to assess the association between RDW and early metabolic renal abnormalities in the person with T2DM and normal estimated glomerular filtration rate (eGFR). **Methods:** The analytical study was cross-sectional, and 250 adults with type 2 diabetes mellitus were studied in a tertiary care diabetic clinic. Participants were all in good renal filtration (eGFR ≥60 mL/min/1.73 m 2) and had never been diagnosed with chronic kidney disease. Hematological indexes such as RDW and hemoglobin were measured with the help of an automated hematology analyzer. Serum creatinine, blood urea, fasting plasma glucose, and glycated hemoglobin (HbA1c) were used as a biochemical measure. Renal functioning was assessed based on the CKD-EPI formula to determine eGFR. Participants were divided into groups of normal renal status and early renal stress depending on borderline increases in creatinine and/or urea despite a normal eGFR. Statistical tests involved group comparisons, correlation analysis, logistic regression as well as receiver operating characteristic (ROC) analysis. **Results:** Individuals that had early renal stress had higher levels of RDW than those who had normal renal status (15.1 + 1.4% vs. 13.8 + 1.1% p = 0.001). RDW had positive relationships with serum creatinine, blood urea, fasting glucose, and HbA1c and negative correlation to eGFR. The multivariate logistic regression analysis determined that RDW was an independent predictive factor of early renal stress. The ROC analysis showed that diagnostic accuracy was moderate with AUC of 0.72 with an optimal cutoff of RDW being 14.5%. **Conclusion:** Higher RDW is linked to initial metabolic and renal defects of T2DM patients even in the conditions of preserved renal filtration. RDW can be used as a low-cost and easy-to-detect biomarker of early warning against metabolic-renal dysfunction in diabetic patients.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) has become an epidemic proportion in the world and is also one of the leading causes of microvascular and macrovascular morbidity. Constantly increased glucose levels, insulin resistance, low-grade inflammatory response, and oxidative stress are the factors that accumulate end-organ damage [1-4]. Diabetic Nephropathy is the most predominant complication among these which causes chronic kidney disease (CKD) and end-stage renal disease in the world [5-8]. Despite the development of renal blockade renin-angiotensin-aldosterone system and sodium-glucose cotransporter-2, a significant percentage of T2DM patients still undergo progressive renal dysfunction [9-11].

Diabetic kidney disease traditionally is characterized by continued albuminuria and / or low estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m 2) [6,12]. Nevertheless, these indicators indicate rather sophisticated structural damage and nephron loss [13,14]. Albuminuria is not always constant and does not necessarily reflect initial renal damage whereas a fall in eGFR is not detected until a significant proportion of

functional reserve has been destroyed [12-15]. It is emerging that subclinical renal impairment can start many years before classical diagnostic charts are met [16-18]. This highlights the necessity of cheap, easy to access biomarkers that can identify early metabolic-renal stress in diabetic patients despite being shown to have preserved eGFR.

The pathogenesis of diabetic renal injury comes down to systemic inflammation and oxidative stress [3,4,19]. Chronic hyperglycemia causes the development of advanced glycation end products, activation of protein kinase C signaling, endothelial dysfunction, and inflammatory cascades of cytokines in the renal microvasculature [3,19-21]. These mechanisms cause not only glomerular damage but also a change in the erythropoiesis and red blood cell morphology [22,23]. Thus, the hematologic markers of inflammatory and oxidative stress conditions can offer indirect information on the early renal dysfunction.

Red Cell Distribution Width (RDW), which is regularly reported to us as the complete blood count, assesses the heterogeneity of circulating erythrocyte sizes. RDW, which was historically utilized in the differential diagnosis of anemia, has in the last ten years become a strong prognostic in cardiovascular disease, systemic inflammation, and CKD [22-25]. RDW is an elevated level indicating a disrupted maturation process of the erythrocyte, inefficient erythropoiesis, oxidative damage to the membrane, and disturbed iron metabolism caused by inflammation [22,26,27]. Such processes are biologically feasible in diabetes, where persistent inflammation and dysmetabolism is the rule.

Several investigations have shown that higher RDW is predictive of negative renal outcomes and fastened eGFR deterioration amid the presence of pre-existing CKD [28-30]. Another use of high RDW is that it has been associated with high mortality in patients who are under dialysis care and development of renal dysfunction in non-dialysis CKD cohorts [28,29]. RDW has been found to be associated with serum creatinine, albuminuria, and glycemic indices of fasting plasma glucose and HbA1c in patients with T2DM [31-33]. In addition, elevated levels of RDW have been linked to the existence and intensity of diabetic microvascular complications [31,34].

However, there is still a gap in literature that is critical. Most current studies deal with patients having overt CKD, macroalbuminuria, or eGFR that is significantly low [28-30]. Limited research has specifically been conducted to determine whether RDW is able to identify subtle renal impairment in patients with T2DM with preserved eGFR (60 mL/min/1.73 m 2 and above) and without classical CKD. This difference is not minor, in terms of clinical perspective. When the eGFR drops to below 60 mL/min/1.73 m 2, the nephrons have already been significantly lost [13,14]. The delays associated with conventional thresholds to be met delay the possibilities of early intervention.

The early metabolic-renal dysfunction concept is characterized by the presence of non-critical increase in both creatinine and urea levels within the upper normal range, subclinical inflammatory burden, and inadequate glycemic control, all preceding actual classification of CKD [16-18,35]. Since it is sensitive to inflammatory and oxidative stress pathways, RDW can be used as a composite surrogate endpoint with the ability to reflect these early pathophysiologic changes. Since RDW is cheap, universally calculable, and automatically identified in regular hematology laboratory reports, its potential value of translation in resource-constrained environments is significant [22,25]. Although several studies have demonstrated an association between elevated RDW and adverse renal outcomes in patients with established chronic kidney disease, limited evidence exists regarding its relationship with subtle renal alterations in individuals with type 2 diabetes who still have preserved glomerular filtration. Identifying simple hematological markers that reflect early metabolic-renal stress may improve early risk stratification.

The current study was therefore aiming at examining whether RDW is directly related with early renal stress and inadequate glycemic control among adults with T2DM and preserved eGFR. We hypothesized that high RDW would be associated with slight increases in serum creatinine and urea, indicate negative correlation with eGFR at normal range, and be independent predictors of early metabolic-renal dysfunction after controlling demographic and hematologic confounding factors.

This study will assess the potential of a hematologic parameter that has been routinely ignored in RDW and is undertaken by shifting the focus of this parameter in diabetes to earlier metabolic-renal changes as an early warning indicator of more vigorous renal protection measures.

MATERIALS AND METHODS

Study Design: The research was done in the form of cross-sectional analytical research to examine the association between red cell distribution width (RDW) and early metabolic-renal dysfunction in patients with type 2 diabetes mellitus (T2DM) and preserved renal filtration function. The objectives of the study were to find out whether RDW could be used as an early warning of some metabolic and renal abnormalities, before the onset of overt chronic kidney disease. This was a hospital-based cross-sectional analytical study.

Study Setting: This was conducted in the outpatient clinic and clinical laboratory of a tertiary care hospital where diabetes is treated. The standardized diagnostic equipment and procedures were done in the central laboratory of the hospital by using laboratory analyses.

Study Duration: The research was carried out within 12 months between June 2025 and December 2025.

Study Population: The sample population was comprised of adult patients with diabetes mellitus type 2 that visited the diabetic outpatient clinic during the period of study. The study involved only patients whose renal filtration remained intact (eGFR 60 mL/min/1.73 m 2 and above).

Sample Size: The study had 250 patients with type 2 diabetes mellitus who met the eligibility criteria. This was deemed to be enough to test the relationships between RDW and metabolic-renal biomarkers. The sample size of 250 participants was considered adequate for detecting moderate correlations between RDW and renal biomarkers with a statistical power of 80% and

significance level of 0.05.

Eligibility Criteria

Inclusion Criteria: The following criteria were used to include participants in the study:

- Age between 30 and 75 years
- Diagnosed to have type 2 diabetes mellitus.
- Estimated glomerular filtration rate (eGFR) 60 mL/min/1.73 m 2 or above.
- Complete laboratory investigations such as complete blood count, serum creatinine, blood urea, fasting plasma glucose and HbA1c.

Exclusion Criteria: The participants were not included in case they had any of the following conditions:

- Chronic kidney disease diagnosed.
- eGFR <60 mL/min/1.73 m^2
- Acute infections or inflammatory disorder.
- Hematological disorders
- Severe anemia
- Chronic liver disease
- Active malignancy
- Recent blood transfusion in the last three months.

The following exclusion criteria were used to prevent the possible confounding factors which could affect hematological or renal parameters.

Data Collection

The data collection form was a standardized data collection form that was used to gather the demographic and clinical data. Each participant was recorded as follows:

- Age
- Sex
- Duration of diabetes
- Body mass index (BMI)
- Blood pressure
- Existing antidiabetic medication.

Calculated body mass index is as below:

BMI = weight(kg) / height(m)^2

The clinical histories were checked based on patient medical records to document it correctly.

Laboratory Investigations

Hematological Parameters: All the participants had their venous blood taken after overnight fasting (8-12 hours). Hematological parameters were measured using an automated hematology analyzer (e.g., Sysmex XN-1000). RDW was expressed as RDW-CV (%).

Serum creatinine and blood urea were measured using an automated chemistry analyzer with enzymatic methods.

Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI equation.

The hematological indices were the following:

Red cell distribution width (RDW)

- Red blood cell count
- Hemoglobin (Hb)
- Red blood cell count (RBC)
- Mean corpuscular volume (MCV)
- Platelet count

RDW was also measured in percentage (%) which was the difference between the red blood cell size.

Biochemical Parameters: An automated clinical chemistry analyzer was used to make biochemical analyses. The parameters measured were as follows:

- Serum creatinine (mg/dL)
- Blood urea (mg/dL)
- Fasting plasma glucose (mg/dL)
- Glycated hemoglobin (HbA1c, %)

The measurement of HbA1c was a measure of long-term glycemic control.

Renal Clinical Test

The assessment of renal functioning was performed by estimating the glomerular filtration rate (eGFR) through CKD-EPI equation that was based on serum creatinine levels.

Those whose eGFR was 60mL/min/ 1.73m2, were taken as having preserved renal filtration and were included in the study.

Early renal stress refers to a condition in which the organism is confronted with a significant environmental stressor that has not previously been faced (Sharma et al., 2016).

To assess the various covert renal abnormalities, the participants were divided into two groups according to the levels of renal biomarkers.

2.10.1 Normal Renal Status

Participants with:

- Normal serum creatinine
- Normal blood urea
- eGFR ≥60 mL/min/1.73 m^2

Early Renal Stress: Participants with:

- Serum creatinine and/or blood urea, borderline high.
- eGFR ≥60 mL/min/1.73 m^2

This categorization enabled detection of renal damage at an earlier stage even with a normal filtration capacity.

Statistical Analysis

The statistical tests were conducted on SPSS version 26.0 and GraphPad Prism software.

Descriptive Statistics: The use of mean and standard deviation was done to represent continuous variables whereas frequencies and percentages represented categorical variables.

Comparison Between Groups: The comparison of the normal renal status group and the early renal stress group was made with the help of:

and independent sample t-test of continuous variables.

- Chi-square categorical test.

These tests were employed in the comparison of RDW level and metabolic parameters of groups.

Correlation Analysis: To determine the association between RDW and the following metabolic-renal parameters, the analysis of correlation was done:

- Serum creatinine
- Blood urea
- eGFR
- Fasting plasma glucose
- HbA1c

Pearson correlation coefficients were determined based on the distribution of data.

The multivariate logistic regression assumes a model of the relationship between one or more independent variables and one dependent variable.

Multivariate Logistic Regression: The multivariate

logistic regression model assumes a relationship between a single or a combination of independent variables and a single dependent variable.

The analysis of multivariable logistic regression was conducted to establish the independent prediction of early renal stress by RDW. The dependent variable was the presence of early stress in relation to the kidney and independent variables were RDW, age, sex, years of diabetes, hemoglobin level and HbA1c.

Odds ratios that have been adjusted to 95% confidence intervals were determined.

Receiver Operating Characteristic (ROC) Analysis: The receiver operating characteristic (ROC) curves analysis was conducted to evaluate how RDW performed in diagnosing early renal stress. The area under the curve (AUC) was computed and the optimal value of RDW cutoff was determined in terms of sensitivity and specificity.

Ethical Considerations

The Institutional Ethics Committee of the institution in which the study took place approved the study protocol. All participants signed informed consent in written form before being enrolled. Patient confidentiality was ensured throughout the research and all data anonymized prior to statistical analysis.

RESULTS

Baseline Characteristics of the Study Population

A total of 250 participants with type 2 diabetes mellitus (T2DM) were included in the final analysis. All participants had preserved renal filtration function (eGFR ≥60 mL/min/1.73 m^2) and no clinical diagnosis of chronic kidney disease. Based on biochemical renal parameters, participants were categorized into two groups: normal renal status (n = 142) and early renal stress (n = 108).

The mean age of the study population was 54.6 ± 9.8 years, with 56% males and 44% females. The mean duration of diabetes was 8.3 ± 4.7 years. Individuals in the early renal stress group demonstrated slightly longer diabetes duration and higher fasting glucose levels compared with those with normal renal status.

Baseline demographic and clinical characteristics of the study participants are presented in Table 1. No statistically significant differences were observed between groups in terms of age or sex distribution. However, individuals with early renal stress exhibited significantly higher fasting glucose and HbA1c levels, suggesting poorer glycemic control.

Table 1
Baseline demographic and clinical characteristics of the study population.

Variable	Normal Renal Status (n=142)	Early Renal Stress (n=108)	p-value
Age (years)	53.9 ± 9.5	55.4 ± 10.2	0.28
Male (%)	55%	57%	0.72
Duration of diabetes (years)	7.6 ± 4.3	9.1 ± 5.0	0.03
BMI (kg/m^2)	27.1 ± 3.6	27.8 ± 3.9	0.19
Fasting glucose (mg/dL)	152 ± 38	168 ± 42	0.01
HbA1c (%)	7.8 ± 1.1	8.4 ± 1.3	0.002

These findings indicate that patients with early renal stress tend to have longer-standing diabetes and poorer glycemic control.

Laboratory Parameters According to Renal Status

Laboratory parameters including hematological indices and renal biomarkers were compared between the two study groups. As shown in Table 2, individuals classified as having early renal stress demonstrated significantly higher RDW levels, serum creatinine, and blood urea concentrations compared with participants with normal renal status.

Mean RDW was 13.8 ± 1.1% in the normal renal group compared with 15.1 ± 1.4% in the early renal stress group ($p < 0.001$). Similarly, serum creatinine and blood urea were modest but significantly elevated in the early renal stress group despite preserving eGFR.

Table 2
Laboratory Parameters According to Renal Status

Parameter	Normal Renal Status	Early Renal Stress	p-value
RDW (%)	13.8 ± 1.1	15.1 ± 1.4	<0.001
Hemoglobin (g/dL)	13.4 ± 1.3	13.2 ± 1.4	0.34
Creatinine (mg/dL)	0.88 ± 0.12	1.05 ± 0.15	<0.001
Urea (mg/dL)	28.4 ± 6.9	36.7 ± 8.2	<0.001
eGFR (mL/min/1.73 m^2)	92 ± 16	84 ± 14	0.004

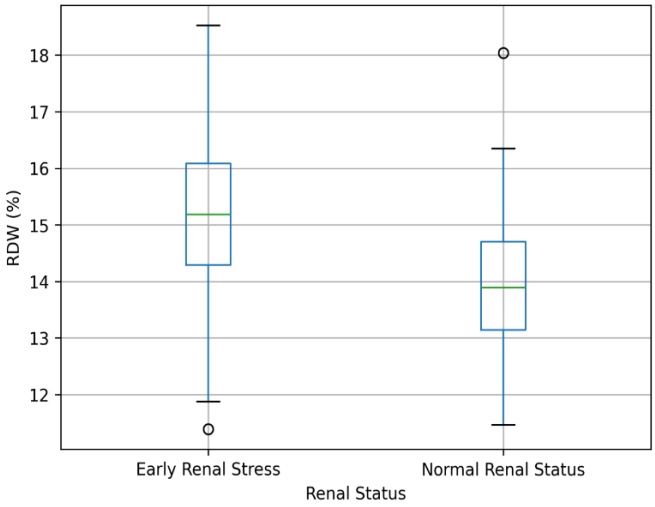
These findings suggest that elevated RDW is associated with subtle renal dysfunction even when eGFR remains within the normal range.

Distribution of RDW According to Renal Status

To further evaluate the relationship between RDW and renal status, RDW distribution was compared between the two groups using boxplot visualization.

As illustrated in Figure 1, participants with early renal stress exhibited a significantly higher median RDW compared with individuals with normal renal parameters. The distribution also showed greater variability in RDW among patients with early renal stress.

Figure 1
Distribution of Red Cell Distribution Width (RDW) According to Renal Status



The difference in RDW between the two groups remained statistically significant after adjusting for hemoglobin levels and diabetes duration.

Correlation Between RDW and Metabolic-Renal Parameters

Correlation analysis was performed to evaluate associations between RDW and key metabolic and renal biomarkers. The results demonstrated that RDW was positively correlated with serum creatinine, blood urea, fasting glucose, and HbA1c, while showing a negative correlation with eGFR.

The strength of correlations is summarized in Table 3.

Table 3

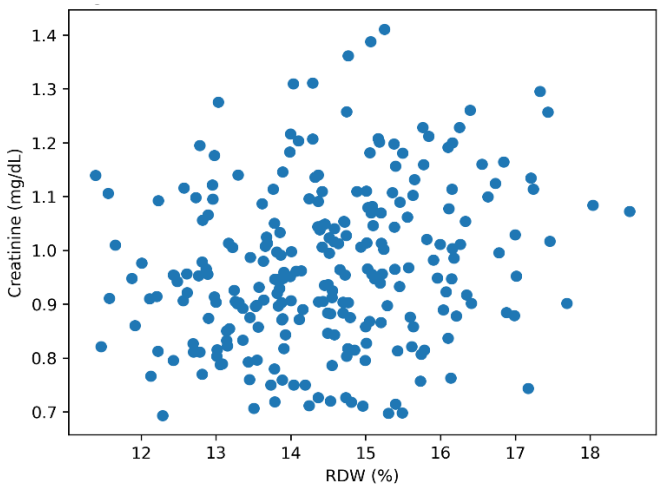
Correlation Analysis Between RDW and Metabolic-Renal Biomarkers.

Variable	Correlation Coefficient (r)	p-value
Creatinine	0.34	<0.001
Urea	0.29	<0.001
eGFR	-0.27	0.002
Fasting glucose	0.21	0.006
HbA1c	0.25	0.003

Scatterplot analysis further illustrated these relationships, showing clear trends between RDW and renal biomarkers.

Figure 2

Scatterplots Illustrate Correlations Between RDW and Creatinine



These findings suggest that RDW reflects both renal stress and metabolic dysregulation in individuals with T2DM.

Multivariable Logistic Regression Analysis

To determine whether RDW independently predicts early renal stress, a multivariable logistic regression model was constructed including RDW, age, sex, duration of diabetes, hemoglobin, and HbA1c.

The results are summarized in Table 4.

Table 4

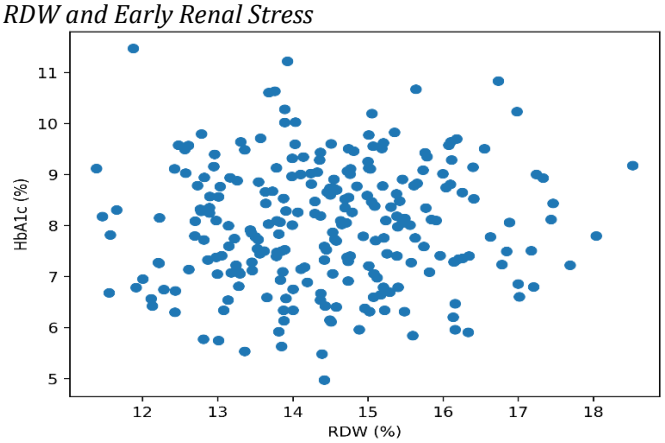
Multivariable Logistic Regression Analysis Predicting Early Renal Stress.

Variable	Odds Ratio (OR)	95% CI	p-value
RDW (%)	1.48	1.21–1.82	<0.001
Age	1.02	0.99–1.04	0.16
Diabetes duration	1.05	1.01–1.09	0.03
HbA1c	1.22	1.05–1.41	0.01
Hemoglobin	0.96	0.84–1.11	0.58

Elevated RDW remained an independent predictor of early renal stress, even after adjusting for potential confounders.

Figure 3

Logistic Regression Plot Illustrates the Association Between RDW and Early Renal Stress



A graphical representation of the logistic regression model is presented in Figure 3.

Diagnostic Performance of RDW for Detecting Early Renal Stress

Receiver operating characteristic (ROC) curve analysis was performed to assess the ability of RDW to discriminate individuals with early renal stress.

The ROC analysis demonstrated an area under the curve (AUC) of 0.72 (95% CI: 0.66–0.78), indicating moderate diagnostic accuracy.

The optimal RDW cutoff value for identifying early renal stress was 14.5%, which provided sensitivity of 68% and specificity of 70%.

Table 5

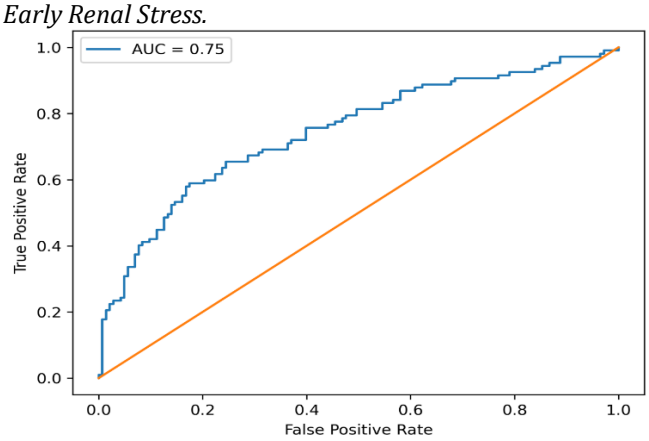
ROC Analysis for RDW Predicting Early Renal Stress

Parameter	Value
AUC	0.72
Sensitivity	68%
Specificity	70%
Optimal RDW cutoff	14.5%

The ROC curve is illustrated in Figure 4.

Figure 4

Receiver Operating Characteristic (ROC) Curve Demonstrating the Diagnostic Performance of RDW for Early Renal Stress.



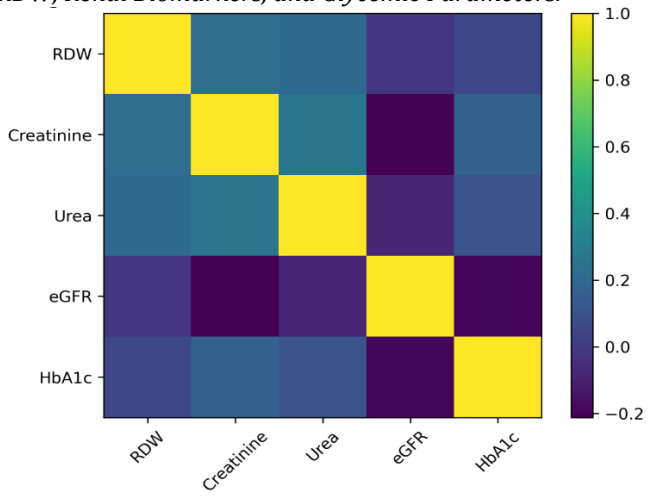
Integrated Metabolic-Renal Dysfunction Model

To conceptualize the relationship between RDW and metabolic-renal dysfunction, a correlation matrix and mechanistic pathway model were constructed.

The correlation heatmap (Figure 5) demonstrates clustering between RDW, renal biomarkers, and glycemic indicators, suggesting shared pathophysiological mechanisms such as inflammation, oxidative stress, and impaired erythropoiesis.

Figure 5

Correlation Matrix Illustrates the Relationships Among RDW, Renal Biomarkers, and Glycemic Parameters.



Collectively, the results indicate that RDW is significantly associated with early metabolic and renal abnormalities in patients with T2DM, even before the onset of overt chronic kidney disease.

DISCUSSION

The study shows that high Red Cell Distribution Width (RDW) is directly related to early metabolic-renal dysfunction in adults with Type 2 Diabetes Mellitus (T2DM) with preserved estimated glomerular filtration rate (eGFR ≥60 mL/min/1.73 m 2). Notably, RDW was significantly correlated with serum creatinine, urea, fasting glucose and HbA1c as well as was an independent predictor of early renal stress when adjusted by age, sex, duration of diabetes and hemoglobin concentration. These results can broaden the clinical applicability of RDW to an earlier stage of metabolic-renal imbalance than the known chronic kidney disease (CKD).

RDW and Renal Dysfunction: At an Earlier Disease Stage.

RDW has been linked to negative prognosis in CKD groups. Previous studies have revealed that high RDW is a predictor of increased rates of kidney failure, as well as increased mortality in non-dialysis and dialysis-dependent CKD groups [1-5]. Nonetheless, these studies were carried out mostly on patients of grossly low eGFR or with nephropathy. When eGFR gets less than 60 mL/min/1.73 m 2, a significant nephron loss has already taken place [6,7]. Early detection of risk prevents the possibility of prevention.

We limited the scope of our study to people who have preserved eGFR. Normal filtration rates nevertheless showed considerable relationships between RDW and creatinine and urea in high-normal ranges. This is an implication that RDW can detect some renal stress that is not indicated by the classical CKD thresholds. These findings are consistent with the emerging data that microvascular and inflammatory damage of diabetes is antecedent to that of GFR quantifiable deterioration [8-11].

Biological Plausibility

It is biologically plausible that there is an association between RDW and early metabolic-renal dysfunction. The presence of chronic hyperglycemia triggers oxidative stress, endothelial dysfunction, advanced glycation end products, and inflammatory pathway activation [12-14]. These processes are the main focus of diabetic kidney disease pathogenesis and also this determines erythropoiesis.

The inflammation not only impairs the iron metabolism including hepcidin-mediated pathways but also reduces the lifespan of erythrocytes leading to the anisocytosis and an increase in the RDW [15-17]. Oxidative stress causes damage to erythrocyte membranes and hinders maturation due to which size variability increases [18,19]. Therefore, RDW can serve as a combined indicator of systemic inflammatory-oxidative load, which is also manifested in both renal microvasculature and red cell morphology.

Past researches have demonstrated that RDW is correlated with inflammatory biomarkers including C-reactive protein and interleukin-6 [20,21]. RDW has been confounded, in CKD populations, with proteinuria and tubulointerstitial damage [2,4]. We have taken this pathophysiological model to earlier renal stress stages in diabetes.

RDW and Glycemic Control

RDW in the current study was significantly associated with fasting glucose and HbA1c. This confirms previous studies that have shown elevated RDW in diabtesic patients who are not under control [22-25]. Chronic hyperglycemia is associated with non-enzymatic glycation of the erythrocyte membrane proteins and a higher level of oxidative damage, which can change red cell deformability and survivability [12,26].

Additionally, the glycemic variation was linked to inflammatory activation regardless of the levels of mean glucose [27]. Thus, RDW might be an indirect evidence of cumulative metabolic instability instead of renal impairment. The twofold correlation of glycemic and renal parameters provides the idea of metabolic-renal dysfunction as a continuum of pathophysiologic mechanisms.

Univariate Predictive Value

RDW was positively linked to early renal stress after the hemoglobin concentration was adjusted. This is critical. The importance of RDW is frequently ignored as just a proxy of anemia, but most of the large cohort studies have shown that RDW is a predictor of cardiovascular and renal outcomes regardless of hemoglobin [3,28-30].

Our adjusted odds ratio indicates that patients with a high RDW (14.5 or higher) are about 2 times more likely to

experience early renal stress than the other patients with lower RDW. This is a moderate discriminative ability as shown by the ROC analysis (AUC 0.71) and can be compared with the others, which are inexpensive inflammatory markers employed in clinical risk stratification.

Clinical Implications

The practical value of RDW is in the fact that it is universal and cost neutral. It is produced automatically whenever a full count of blood is carried out, without any further test or cost. RDW can be used as an initial screening indicator in resource-constrained environments in which more sophisticated biomarkers (cystatin C, NGAL, or inflammatory panels, etc.) are too costly.

Patients who have high RDW despite preserved eGFR can be considered as those who need more rigorous Reno protective tactics, involving better glycemic regulation, better renin-angiotensin system blockade, and an earlier approach to SGLT2 inhibitors [31-33]. RF instead of substituting the current markers can add to the existing ones by detecting high-risk individuals at an earlier stage.

Comparison against Past Literature

Most of the previous research on the topic of RDW and diabetes involved well-known microvascular complications, such as apparent nephropathy and retinopathy [22,34-36]. Our study is different as it focuses on a population with pre-CKD. This is a clinically significant distinction. It is much easier to prevent progression rather than reverse the resultant loss of nephrons.

Also, past studies on CKD have stressed predicting mortality [3,5]. Although crucial, mortality is an outcome. We change our focus to prompt identification of renal stress which is more practical in everyday clinical practice.

Limitations

There are a few restrictions that should be considered. The cross-sectional design does not allow making conclusions regarding causality; longitudinal studies are needed to conclude whether high levels of RDW are a predictor of eGFR in the future. Second, the inflammatory biomarkers were not directly quantified, which restricted the possibility of mechanistic exploration. Thirdly, albuminuria was not taken as a primary outcome, yet most of the patients had had preserved filtration without clear proteinuria.

These limitations notwithstanding, the study has a strength in its limited population (preserved eGFR only) and multivariate adjustment of hematologic confounders.

Future Directions

Future cohort research ought to assess the hypothesis of the relationships between high RDW and the occurrence of CKD or the progression of eGFR in T2DM. The addition of albuminuria, cystatin C, and inflammatory cytokines may explain the mechanistic pathways. Also, the possibility of additive interaction between inadequate glycemic regulation and elevated RDW might be investigated, and its presence could be a sign of synergistic risk enhancement.

CONCLUSION

High RDW is independently linked to premature metabolic-renal dysfunction in T2DM patients with intact eGFR. The results can indicate that RDW is a potentially low-cost and easy-to-use early warning of renal stress before the usual CKD parameters. RDW may also be incorporated into the standard diabetic risk stratification procedure to inform preventive intervention earlier in the course, should it be proven to be valid longitudinally.

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