



RED CELL DISTRIBUTION WIDTH AS A BIOCHEMICAL MARKER OF METABOLIC RISK: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Red cell distribution width (RDW) is a routinely reported hematological parameter traditionally used in the evaluation of anemia. In recent years, it has gained attention as a potential biomarker of systemic inflammation, oxidative stress, and cardiometabolic dysregulation. Elevated RDW has been associated with adverse cardiovascular outcomes, metabolic disorders, and chronic inflammatory states, highlighting its emerging role as a simple, cost-effective prognostic and risk-stratification marker.

Objective: To investigate the association between RDW and metabolic risk parameters, including fasting blood glucose and lipid profile components, in an adult population using routine laboratory data.

Methods: A retrospective observational analysis was performed on 250 adult laboratory records. RDW values were analyzed in relation to fasting blood glucose, total cholesterol, triglycerides, and high-density lipoprotein cholesterol. Age- and gender-based differences were assessed using appropriate statistical methods.

Results: The mean RDW was $13.43 \pm 0.90\%$. RDW demonstrated a strong positive correlation with fasting blood glucose ($r = 0.524$) and moderate positive correlations with total cholesterol ($r = 0.380$) and triglycerides ($r = 0.274$), while showing a significant inverse correlation with high-density lipoprotein cholesterol ($r = -0.218$) (all $p < 0.001$). RDW values increased significantly with advancing age ($p < 0.001$). No statistically significant gender-related differences were observed.

Conclusion: RDW was significantly associated with adverse metabolic profiles and increases with age, supporting its potential utility as a low-cost adjunct marker for cardiometabolic risk assessment in routine clinical practice. Further prospective studies are warranted to establish its prognostic significance in cardiovascular disease.

Keywords: Red Cell Distribution Width, Cardiometabolic Risk, Dyslipidemia, Cardiovascular Biomarkers, Inflammation.

INTRODUCTION

Cardiovascular disease (CVD) continues to be the foremost cause of morbidity and mortality worldwide, with a substantial burden attributable to modifiable metabolic risk factors such as dysglycemia and dyslipidemia. These metabolic derangements contribute to endothelial dysfunction, accelerated atherosclerosis, and chronic low-grade inflammation, ultimately increasing cardiovascular

Risk. Early identification of individuals with underlying metabolic and inflammatory disturbances is therefore critical for timely intervention. In this context, there is growing interest in simple, inexpensive, and routinely available biomarkers that can reflect these complex pathophysiological processes in everyday clinical practice.^{1,2}

Red cell distribution width (RDW) is a quantitative measure of the heterogeneity in circulating erythrocyte size (anisocytosis) and is automatically reported as part of the complete blood count. Traditionally, RDW has been utilized in the evaluation and differential diagnosis of anemia. However, over the past decade, RDW has emerged as a novel prognostic marker in a wide range of



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clinical conditions, including cardiovascular disease, heart failure, diabetes mellitus, and metabolic syndrome. Its widespread availability and low cost make it an attractive candidate for risk assessment in large populations.^{3,4}

The biological mechanisms linking elevated RDW to cardiometabolic disorders are multifactorial. Chronic low-grade inflammation, oxidative stress, impaired iron metabolism, and dysfunctional erythropoiesis have all been implicated in increasing RDW values.⁵ These same mechanisms are integral to the development of insulin resistance, lipid abnormalities, and atherogenesis, suggesting a shared pathophysiological pathway.

Inflammatory cytokines and oxidative stress can interfere with erythrocyte maturation and survival, resulting in greater variability in red cell size, while simultaneously promoting metabolic dysregulation and vascular injury.⁵⁻⁸

Several epidemiological and population-based studies have demonstrated significant associations between higher RDW levels and insulin resistance, poor glycemic control, dyslipidemia, and adverse cardiovascular outcomes.

Elevated RDW has been shown to predict incident diabetes, progression of metabolic syndrome, and increased cardiovascular mortality, independent of traditional risk factors. These findings support the concept that RDW may serve as an integrated marker reflecting the cumulative burden of metabolic stress and inflammation.⁹⁻¹²

Despite the expanding body of international evidence, data evaluating the relationship between RDW and metabolic parameters in routine laboratory-based cohorts remain limited, particularly from the Indian subcontinent. Given the high and rising prevalence of diabetes and dyslipidemia in India, there is a need for region-specific data to better understand the clinical utility of RDW in this population.

The present study was therefore undertaken to assess the association between RDW and fasting blood glucose and lipid profile parameters across different age and gender groups using routinely available laboratory data, with the aim of exploring its potential role as a simple adjunctive marker of cardiometabolic risk.

MATERIALS AND METHODS

Study Design and Setting

A retrospective observational study was conducted in Sree Mookambika Institute of Medical Sciences in Clinical Biochemistry Laboratory using de-identified laboratory records obtained between January and June 2025.

Study Population

Laboratory data from 250 adults aged ≥ 18 years who had undergone complete blood count and fasting

lipid and glucose testing on the same visit were included.

Inclusion and Exclusion Criteria

Records were included if RDW, fasting blood glucose, and lipid profile were available. Subjects with hemoglobin < 11 g/dL, known hematological disorders, hemoglobinopathies, or acute inflammatory conditions were excluded to minimize confounding.

Study procedure

Laboratory Parameters

The following parameters were analyzed:

- RDW (%)
- Fasting blood glucose (mg/dL)
- Total cholesterol (mg/dL)
- Triglycerides (mg/dL)
- HDL cholesterol (mg/dL)

Participants were stratified into three age groups: 18–40, 41–60, and ≥ 61 years.

Statistical Analysis

Data were expressed as mean \pm standard deviation. Pearson's correlation coefficient assessed relationships between RDW and metabolic parameters. Independent t-test compared gender differences, and one-way ANOVA evaluated age-group differences, followed by post-hoc Tukey analysis. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS25.

Ethical Considerations

Ethical clearance for the study was obtained from the Institutional Ethics Committee of SMIMS

RESULTS

A total of 250 adult laboratory records were analyzed. The mean age of the study population was 49.6 ± 15.8 years, with 132 males (52.8%) and 118 females (47.2%). The overall mean red cell distribution width (RDW) was $13.43 \pm 0.90\%$, with values ranging from 11.8% to 15.9%.

RDW values demonstrated a progressive increase across age categories. Participants aged 18–40 years had a mean RDW of $12.98 \pm 0.77\%$, those aged 41–60 years had a mean RDW of $13.33 \pm 0.82\%$, and individuals aged ≥ 61 years showed the highest mean RDW of $14.06 \pm 0.90\%$.

One-way ANOVA revealed a statistically significant difference in RDW across age groups ($p < 0.001$). Post-hoc Tukey analysis confirmed significant differences between the ≥ 61 -year group and both younger age groups. (Table 1)

Table 1: Baseline Characteristics by Age Group and Gender

| Age Group | Gender | n | Age (years, mean) | RDW (% mean ± SD) | FBG (mg/dL, mean) | TC (mg/dL, mean) | TG (mg/dL, mean) | HDL (mg/dL, mean) |
|-----------|--------|-----|-------------------|-------------------|-------------------|------------------|------------------|-------------------|
| 18–40 | Female | 39 | 30.4 | 12.77±0.75 | 86.1 | 167.6 | 144.6 | 51.7 |
| | Male | 43 | 30.4 | 13.16±0.82 | 91.0 | 179.9 | 137.9 | 50.6 |
| 41–60 | Female | 42 | 50.3 | 13.26±0.88 | 94.0 | 184.6 | 144.7 | 48.6 |
| | Male | 51 | 49.4 | 13.39±0.91 | 95.5 | 184.0 | 151.2 | 51.6 |
| 61+ | Female | 30 | 68.1 | 14.08±0.92 | 99.8 | 185.9 | 157.0 | 48.0 |
| | Male | 45 | 70.0 | 14.04±0.88 | 102.9 | 193.7 | 162.4 | 49.2 |
| Total | | 250 | 48.2 | 13.43±0.90 | 94.8 | 184.3 | 149.4 | 50.1 |

Mean RDW values were marginally higher in males compared to females; however, this difference did not reach statistical significance. Independent samples t-test demonstrated no significant gender-based difference in RDW values ($p = 0.055$). (Table 1) Pearson correlation analysis demonstrated a strong positive correlation between RDW and

fasting blood glucose ($r = 0.524, p < 0.001$). Moderate positive correlations were observed between RDW and total cholesterol ($r = 0.380, p < 0.001$) as well as triglycerides ($r = 0.274, p < 0.001$). In contrast, RDW exhibited a significant inverse correlation with HDL cholesterol ($r = -0.218, p < 0.001$)

Table 2: Pearson Correlation Coefficients between RDW and Metabolic Parameters (n=250)

| Parameter | Correlation with RDW (r) | p-value |
|------------------------------------|--------------------------|---------|
| Fasting Blood Glucose (FBG, mg/dL) | 0.524 | <0.001 |
| Total Cholesterol (TC, mg/dL) | 0.380 | <0.001 |
| Triglycerides (TG, mg/dL) | 0.274 | <0.001 |
| HDL-Cholesterol (mg/dL) | -0.218 | <0.001 |

Based on predefined metabolic risk criteria, 191 individuals (76.4%) were classified as having low metabolic risk, while 59 individuals (23.6%) demonstrated no metabolic risk factors. None of the participants fulfilled criteria for moderate or high

metabolic risk. RDW values were higher among individuals with low metabolic risk compared to those without metabolic risk, although this difference did not reach statistical significance.

Distribution of Metabolic Risk Categories (n=250)

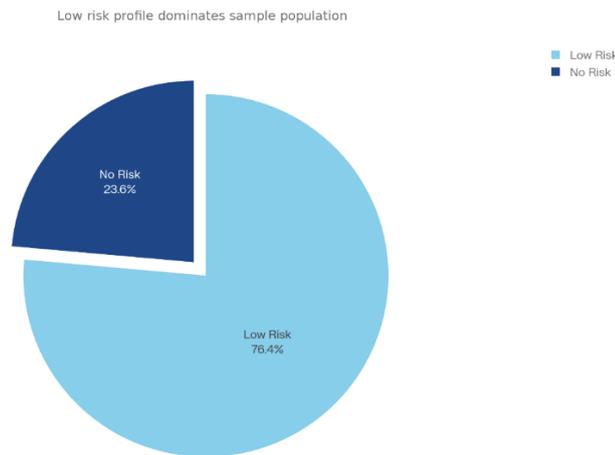


Fig 1: Distribution of Metabolic Risk Categories

DISCUSSION

The present study demonstrates a significant association between RDW and key metabolic risk parameters, supporting the growing evidence that RDW may serve as a surrogate marker of underlying cardiometabolic stress. In this study of 250 adults,

RDW showed a strong positive correlation with fasting blood glucose and moderate positive correlations with total cholesterol and triglycerides, along with an inverse association with high-density lipoprotein (HDL) cholesterol, indicating a close

relationship between erythrocyte size variability and metabolic dysregulation.

A significant positive correlation was observed between RDW and fasting blood glucose ($r = 0.524$, $p < 0.001$), suggesting an association between anisocytosis and impaired glyceemic control. Similar findings have been reported by Engström et al.¹³ who demonstrated that elevated RDW was independently associated with higher HbA1c levels and an increased risk of developing diabetes mellitus in a population-based cohort. Likewise, Liu et al.¹⁴ observed a positive relationship between RDW and indices of insulin resistance, implicating altered glucose metabolism in the elevation of RDW. These observations support the hypothesis that chronic hyperglycemia and insulin resistance induce oxidative stress and inflammatory cytokine release, thereby impairing erythropoiesis and reducing red blood cell survival.

In addition to glyceemic parameters, RDW was significantly associated with atherogenic lipid abnormalities in the present study. Positive correlations with total cholesterol and triglycerides, along with a negative correlation with HDL cholesterol, were observed. These findings are consistent with those of Ainiwaer et al.⁹ who reported significant associations between elevated RDW and components of dyslipidemia and metabolic syndrome. Similarly, Huang et al.⁶ demonstrated that higher RDW values were linked to unfavorable lipid profiles and increased cardiometabolic risk. The inverse relationship between RDW and HDL cholesterol aligns with the observations of Semba et al.¹⁵ who attributed elevated RDW to reduced antioxidant capacity and heightened inflammatory burden. Collectively, these findings suggest that lipid-induced oxidative stress and chronic inflammation may contribute to erythrocyte anisocytosis.

A progressive increase in RDW with advancing age was also evident, with significantly higher values observed in individuals aged ≥ 61 years. This is in agreement with findings by Hoffmann et al.¹⁶ who reported age-related shifts in RDW reference intervals independent of anemia. Furthermore, Salvagno et al.¹⁷ highlighted the role of aging-related oxidative stress, low-grade inflammation, and reduced bone marrow responsiveness in elevating RDW levels, underscoring the need to consider age when interpreting RDW values.

Clinically, RDW was an attractive biomarker due to its universal availability, reproducibility, and lack of additional cost. As demonstrated by Guo H et al.¹⁸ and Cao HX et al.¹⁹ RDW has prognostic significance in cardiovascular disease and heart failure. While RDW should not replace established metabolic or cardiovascular markers, the present findings support its utility as an adjunctive, easily accessible indicator for early identification of cardiometabolic risk in routine laboratory practice.

Study Limitations and Future Directions

The retrospective design and absence of inflammatory biomarkers such as C-reactive protein limit causal interpretation. Additionally, lack of data on dietary habits, physical activity, and medication use may have influenced metabolic parameters. Future prospective and longitudinal studies incorporating inflammatory and oxidative stress markers are warranted to elucidate the mechanistic pathways linking RDW to cardiometabolic risk.

CONCLUSION

RDW demonstrates significant associations with fasting glucose and lipid parameters and increases with age, supporting its potential role as an accessible adjunct marker in cardiometabolic risk assessment. Prospective longitudinal studies are warranted to establish its predictive utility for cardiovascular outcomes.

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