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Original Research Article

Correlation between Red Cell Distribution Width and Severity of Ischemic Cerebrovascular Stroke

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Abstract

Ischemic cerebrovascular stroke constitutes the majority of stroke burden worldwide and remains a leading cause of mortality and long-term disability. Despite advances in neuroimaging and reperfusion therapies, early identification of individuals at increased risk remains a major clinical challenge. Red cell distribution width (RDW), a routinely reported parameter in complete blood count, reflects variability in erythrocyte size and has emerged as a novel biomarker associated with adverse cardiovascular and cerebrovascular outcomes. Elevated RDW has been linked to systemic inflammation, oxidative stress, endothelial dysfunction, altered blood rheology, and prothrombotic states—key mechanisms implicated in ischemic stroke pathogenesis. This review examines the association between elevated RDW levels and ischemic stroke, synthesizing epidemiological evidence, exploring biological mechanisms, and evaluating clinical implications. Particular emphasis is placed on the relevance of RDW as a cost-effective biomarker in resource-limited settings such as South Gujarat. The potential role of RDW in stroke risk stratification and future research directions is discussed.

Keywords: Red Cell Distribution Width; Ischemic Stroke; Cerebrovascular Disease; Inflammation; Hematological Biomarkers; Risk Stratification.

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Introduction

Stroke represents a global public health emergency, ranking among the leading causes of death and long-term disability. Ischemic stroke accounts for approximately 80–85% of all cerebrovascular accidents, resulting from arterial thrombosis or embolism leading to cerebral infarction. In India, the burden of stroke has risen steadily over the past two decades due to population aging, increasing prevalence of hypertension, diabetes mellitus, dyslipidemia, and lifestyle-related risk factors. Early identification of individuals at increased risk for ischemic stroke is crucial for prevention and improved outcomes. While traditional risk factors explain a significant proportion of stroke risk, they fail to fully capture the complexity of cerebrovascular disease. Consequently, there is growing interest in novel, easily measurable biomarkers that reflect underlying pathophysiological processes and can complement existing risk prediction models. Red cell distribution width (RDW) is a routinely available hematological parameter derived from the complete blood count (CBC). Historically used in the evaluation of anemia, RDW has recently gained attention as a prognostic marker in cardiovascular diseases, heart failure, atrial fibrillation, and thromboembolic disorders. Increasing evidence suggests that elevated RDW is independently associated with the incidence, severity, and outcomes of ischemic stroke. Given its low cost and universal availability, RDW may be particularly valuable in low- and middle-income regions such as South Gujarat.

Red Cell Distribution Width: Definition and Clinical Context

RDW reflects the degree of anisocytosis in circulating erythrocytes and is expressed as the

coefficient of variation of mean corpuscular volume (MCV). Normal RDW values typically range from 11.5% to 14.5%, although laboratory-specific reference ranges may vary. Elevated RDW (>14.5%) indicates increased heterogeneity in red blood cell size.

RDW elevation may result from:

- Ineffective erythropoiesis
- Nutritional deficiencies (iron, vitamin B12, folate)
- Chronic kidney disease
- Chronic systemic inflammation
- Oxidative stress and bone marrow dysfunction

Importantly, RDW often increases independent of hemoglobin concentration, making it a sensitive indicator of systemic illness rather than anemia alone.

Literature Review: RDW and Cerebrovascular Disease

RDW and Stroke Incidence: Multiple epidemiological studies have demonstrated a strong association between elevated RDW and increased risk of first-ever ischemic stroke.

Prospective cohort studies have shown that individuals in the highest RDW quartiles have a significantly greater incidence of ischemic stroke, even after adjustment for age, sex, hypertension, diabetes, smoking, and lipid levels.

Population-based studies have suggested that RDW is an independent predictor of cerebrovascular events, supporting its role beyond being a surrogate marker for comorbid conditions.

RDW and Stroke Severity and Outcomes: Hospital-based studies have consistently demonstrated that elevated RDW at admission is associated with:

- Higher NIH Stroke Scale (NIHSS) scores
- Larger infarct volumes
- Increased risk of early neurological deterioration
- Poor functional outcomes (modified Rankin Scale)
- Higher short- and long-term mortality

These associations have been observed across different ischemic stroke subtypes, including large artery atherosclerosis, cardioembolic stroke, and small vessel disease.

Pathophysiological Mechanisms Linking RDW and Ischemic Stroke: The association between RDW and ischemic stroke is biologically plausible and likely multifactorial.

1. Chronic Inflammation: Chronic inflammation is central to atherosclerosis and plaque instability. Pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α impair erythrocyte maturation, shorten RBC lifespan, and increase anisocytosis. Elevated RDW thus reflects ongoing systemic inflammation, which contributes to endothelial activation and thrombogenesis.

2. Oxidative Stress: Oxidative stress damages erythrocyte membranes, reducing deformability and increasing variability in cell size. Reduced RBC deformability impairs microcirculatory flow, particularly in cerebral capillaries, exacerbating ischemia during arterial occlusion.

3. Increased Blood Viscosity and Impaired Rheology: Anisocytosis increases blood viscosity and disrupts laminar flow. This promotes platelet activation, endothelial shear stress, and microvascular dysfunction, facilitating cerebral ischemia.

4. Endothelial Dysfunction: Elevated RDW has been associated with impaired nitric oxide bioavailability and endothelial dysfunction, a key early event in atherogenesis and thrombosis.

5. Prothrombotic State: Higher RDW correlates with increased platelet reactivity, elevated fibrinogen levels, and activation of coagulation pathways, creating a prothrombotic milieu conducive to ischemic stroke.

6. Reflection of Underlying Comorbidities: RDW elevation often mirrors underlying conditions such as iron deficiency anemia, vitamin B12 deficiency, chronic kidney disease, and metabolic syndrome—all of which are independently associated with increased stroke risk.

Methods and Materials

Study Design: The current work is a narrative and evidence-based review of published literature evaluating the association between RDW and ischemic cerebrovascular stroke.

Data Sources: Relevant studies were identified through searches of PubMed, MEDLINE, and Google Scholar using keywords including red cell distribution width, ischemic stroke, cerebrovascular disease, and hematological biomarkers.

Inclusion Criteria

- Observational studies (cross-sectional, case-control, cohort)
- Studies evaluating RDW in ischemic stroke patients
- Studies reporting stroke incidence, severity, or outcomes in relation to RDW

Exclusion Criteria

- Hemorrhagic stroke–only studies
- Pediatric populations
- Non-English language publications without accessible translations

Observations: Across reviewed studies, several consistent observations emerged:

1. Mean RDW values were significantly higher in ischemic stroke patients compared to controls.
2. Elevated RDW correlated positively with stroke severity scores.
3. Patients with RDW >14.5% had higher in-hospital mortality and poorer functional outcomes.
4. RDW remained an independent predictor after adjustment for anemia and traditional vascular risk factors.

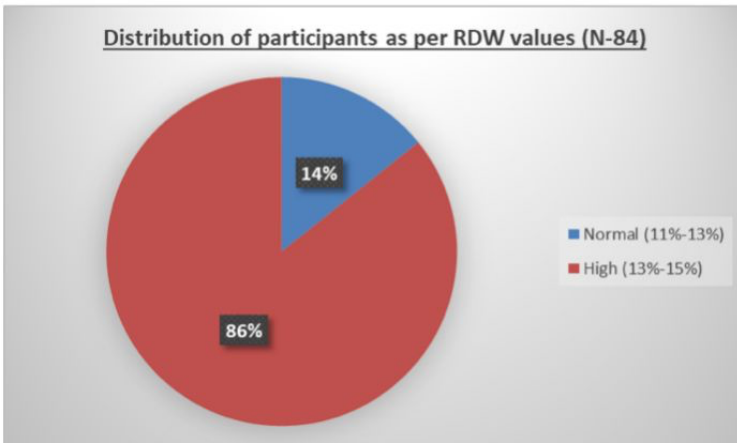

Figure 1: Distribution of participants as per RDW values (N-84)

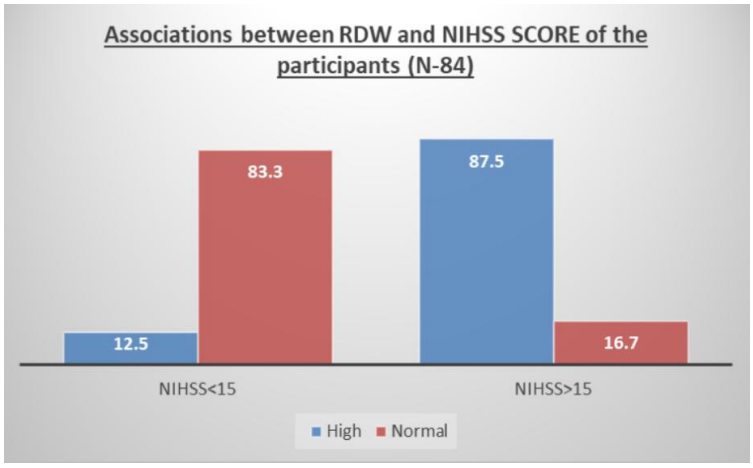

Figure 2: Associations between RDW and NIHSS SCORE of the participants (N-84)

In regional clinical practice in South Gujarat, similar trends have been observed, with ischemic stroke patients frequently presenting with elevated RDW levels, often in association with chronic kidney disease, nutritional deficiencies, and metabolic disorders.

Discussion

The accumulating evidence supports RDW as a robust, integrative biomarker reflecting inflammation, oxidative stress, endothelial dysfunction, and hematological alterations—all central to ischemic stroke pathophysiology.

Unlike novel biomarkers requiring specialized assays, RDW is universally available, inexpensive, and reproducible. In the context of South Gujarat, where resource constraints and high burden of metabolic and renal diseases coexist, RDW measurement may provide valuable additional information for stroke risk assessment and prognostication.

However, RDW is a non-specific marker influenced by multiple confounders. Its clinical interpretation must therefore consider nutritional status, renal function, and inflammatory conditions.

Clinical Implications

- Risk Stratification: RDW may enhance identification of high-risk individuals in primary and secondary prevention settings.
- Prognostication: Elevated RDW at admission can aid in predicting stroke severity and outcomes.
- Resource-Limited Settings: RDW offers a cost-effective tool where advanced biomarkers are unavailable.

- Integrated Assessment: RDW should complement, not replace, established clinical and radiological assessments.

Future Research Directions

1. Large prospective cohort studies to establish causality
2. Determination of optimal RDW cut-off values for stroke prediction
3. Integration of RDW into validated stroke risk models
4. Longitudinal assessment of RDW dynamics
5. Region-specific studies from India and South Gujarat

Conclusion

Elevated red cell distribution width is increasingly recognized as an independent biomarker associated with ischemic cerebrovascular stroke incidence, severity, and outcomes. Its strong pathophysiological basis, consistent epidemiological evidence, and universal availability make RDW a promising adjunct in stroke risk stratification. Further well-designed prospective studies are required to validate its role and integrate it into routine clinical practice, particularly in resource-limited regions such as South Gujarat.

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