ORIGINAL ARTICLE

NUREXUS

Journal of MedVerse Research & Practice

ISSN: 3107-4278

Association of Red Cell Distribution Width with Disease Activity in Systemic Lupus Erythematosus

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Submission Date: 02.09.2026	Accepted Date:11.10.2026	Published Date: 31.10.2026
DOI: 10.65188/nurexus.1106		

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disorder characterised by diverse clinical manifestations and fluctuating levels of disease activity. Red cell distribution width (RDW), a routinely measured haematological index, has emerged as a potential indicator of systemic inflammation and may provide additional insight into disease activity in patients with SLE.

Methods: This hospital-based observational study was conducted among 60 patients with SLE at Assam Medical College and Hospital, Dibrugarh. Disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). RDW, other haematological indices, inflammatory markers and complement levels were assessed. Statistical analysis was performed using Pearson's correlation coefficient and the independent-samples t-test.

Results: The mean age of the study population was 29.45 ± 8.57 years, with females comprising 95% of the participants. Based on SLEDAI-2K scores, 37 patients (61.7%) had scores below 10, while 23 (38.3%) had scores of 10 or higher. Mean RDW was significantly elevated in patients with high disease activity compared with those with low disease activity (17.38 ± 2.74% versus 14.57 ± 1.96%; $p < 0.001$). RDW showed a significant positive correlation with SLEDAI-2K scores ($r = 0.579$, $p < 0.001$), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), whereas negative correlations were observed with complement C3 and C4 levels.

Conclusion: RDW demonstrated a significant association with disease activity in patients with SLE, suggesting its potential role as an inexpensive and readily accessible adjunctive haematological marker. Further prospective studies involving larger populations are necessary to validate these findings and determine its clinical usefulness in routine disease monitoring.

Keywords: Systemic lupus erythematosus; Red cell distribution width; Disease activity; SLEDAI-2K; Erythrocyte sedimentation rate; C-reactive protein; Complement levels.

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disorder characterised by a relapsing and remitting clinical course, heterogeneous manifestations, and variable disease outcomes. It is associated with the production of diverse autoantibodies, of which antinuclear antibodies (ANA) exhibit high sensitivity, while anti-double-stranded DNA and anti-Smith antibodies possess greater diagnostic specificity. SLE predominantly affects women of reproductive age, although its prevalence varies considerably across ethnic and geographical populations. An epidemiological study conducted in India reported a prevalence of 3.2 cases per 100,000 population, emphasising the need for more extensive

epidemiological investigations in the Indian population [1,2].

The exact aetiopathogenesis of SLE remains unclear and is believed to involve a complex interplay of genetic predisposition, environmental factors, hormonal influences, and immune system abnormalities. The disease can involve several organ systems, including the renal, musculoskeletal, mucocutaneous, cardiovascular, respiratory, neurological, and haematological systems. Frequently reported clinical features include fatigue, photosensitivity, cutaneous eruptions, oral ulcers, inflammatory arthritis, and serositis. Among the major organ complications, lupus nephritis is particularly significant because of its association with increased morbidity and the potential progression to chronic renal impairment [1,3].

Haematological abnormalities constitute an important component of SLE and may affect erythrocytes, leukocytes, and platelets. Anaemia, leukopenia, and thrombocytopenia are commonly encountered and may occur either independently or simultaneously. Anaemia of chronic inflammation is frequently observed; however, nutritional deficiencies, impaired renal function, autoimmune haemolysis, and adverse effects of medications may also contribute to its development. These alterations reflect the underlying inflammatory, immunological, and haematopoietic disturbances associated with SLE [3].

Red cell distribution width (RDW) is a routinely reported parameter in the complete blood count that quantifies the degree of variation in circulating erythrocyte size, a phenomenon referred to as anisocytosis. Although traditionally employed in the differential evaluation of anaemia, RDW has increasingly attracted interest as a potential indicator of systemic inflammation and disease severity. Inflammatory mediators may interfere with erythropoiesis, erythrocyte maturation, and red blood cell survival, thereby increasing heterogeneity in cell size. Previous investigations have demonstrated associations between elevated RDW and inflammatory biomarkers, particularly erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [4,5].

In patients with SLE, emerging evidence suggests a relationship between RDW, inflammatory activity, and overall disease severity. Hu et al. reported a significant association between RDW and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), indicating its potential usefulness in evaluating disease activity [6]. Nevertheless, RDW is a nonspecific parameter and may also be influenced by several other conditions, including iron deficiency, vitamin B12 and folate deficiencies, haemoglobinopathies, haemolytic disorders, and renal dysfunction. Therefore, these potential confounding factors should be considered when interpreting RDW values in patients with SLE. The primary objective was to assess RDW levels among patients with SLE and determine their correlation with disease activity measured using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K).

Materials & Methods

Study Design and Setting

A hospital-based observational study was conducted in the Department of General Medicine, Dr. YSR University of Health Sciences, Vijayawada, Andhra Pradesh, India. The study was carried out over a period of one year, from 1 July 2021 to 30 June 2022. The primary objective was to evaluate red cell distribution width (RDW) as a potential marker of disease activity in patients with systemic lupus erythematosus (SLE).

Study Population and Sample Size

The study population comprised patients diagnosed with SLE who attended the outpatient departments or were admitted to the inpatient wards associated with the Department of General Medicine. A total of 60 patients were consecutively enrolled after fulfilling the predefined eligibility criteria. The sample size was calculated considering a 95% confidence interval, 90% statistical power, a standard deviation of 3.82% for RDW, and an allowable difference of 1% from the true population value.

Inclusion and Exclusion Criteria

Patients aged 13 years and above who fulfilled the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for SLE were included in the study. Patients younger than 13 years, those unwilling to provide informed consent, and individuals with haemoglobinopathies, other autoimmune disorders such as rheumatoid arthritis and inflammatory bowel disease, malignant diseases, chronic liver disease, or chronic kidney disease were excluded to minimise potential confounding factors that could influence RDW values.

Data Collection and Clinical Assessment

Following informed consent, a detailed clinical history was obtained, and a comprehensive physical examination was performed using a predesigned proforma. Demographic characteristics, presenting complaints, clinical manifestations, relevant medical history, and laboratory findings were systematically documented. Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), a validated scoring instrument incorporating clinical and laboratory parameters across multiple organ systems. Based on their SLEDAI-2K scores, patients were classified into two categories: low disease activity, with scores below 10, and high disease activity, with scores of 10 or above.

Laboratory Investigations and RDW Measurement

Routine laboratory investigations included complete blood count, haemoglobin concentration, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, total and differential leukocyte counts, platelet count, and erythrocyte sedimentation rate (ESR). Additional investigations, including renal function tests, urinalysis, 24-hour urinary protein estimation, C-reactive protein (CRP), antinuclear antibody testing, anti-double-stranded DNA antibody assessment, and serum complement C3 and C4 levels, were performed as clinically indicated.

RDW was measured using a six-part automated haematology analyser (Sysmex XN-550). Venous blood samples were collected in ethylenediaminetetraacetic acid (EDTA)-containing tubes for haematological analysis. RDW was expressed as the coefficient of variation (RDW-CV), calculated by dividing the standard deviation of red blood cell volume by the mean corpuscular volume and multiplying the result by 100. The association between RDW and SLE disease activity was subsequently evaluated in relation to other relevant clinical and laboratory parameters.

Statistical Analysis

The collected data were entered into Microsoft Excel and analysed using the Statistical Package for the Social Sciences (SPSS), version 20.0. Quantitative variables were expressed as mean and standard deviation, whereas categorical variables were summarised as frequencies and percentages. Differences in categorical variables were assessed using the chi-square test. Pearson's correlation coefficient was employed to determine the strength and direction of the relationship between RDW and SLEDAI-2K scores. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Approval was obtained from the Institutional Ethics Committee before the commencement of the study. Written informed consent was obtained from all participants or their legally authorised representatives, wherever applicable. Confidentiality and privacy of participant information were maintained throughout the study, and the research was conducted in accordance with established ethical principles for biomedical research involving human participants.

Result

Table 1. Sociodemographic characteristics of patients with SLE (n = 60)

Characteristic	Category	Number (%)
Age (years)	≤19	9 (15.0)
	20–29	24 (40.0)
	30–39	22 (36.7)
	40–49	4 (6.7)

	≥50	1 (1.7)
Gender	Male	3 (5.0)
	Female	57 (95.0)
Marital status	Married	39 (65.0)
	Unmarried	21 (35.0)

Mean age: 29.45 ± 8.57 years.

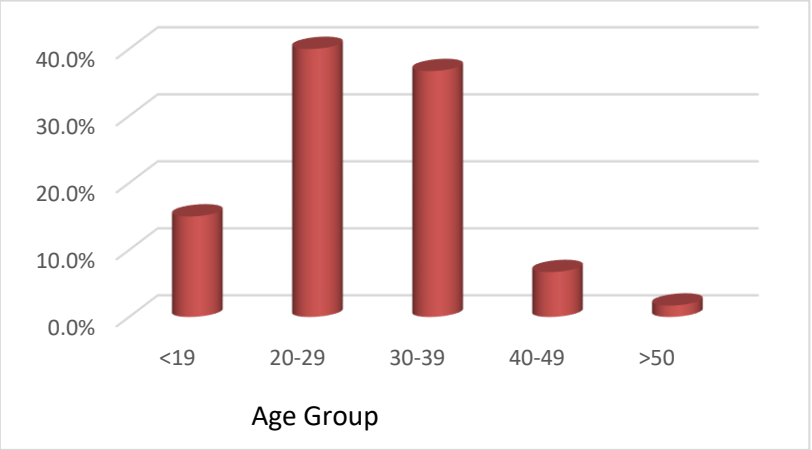


Figure 1: Age Distribution

Among the 60 patients with systemic lupus erythematosus, the majority belonged to the 20–29 years age group (40%), followed by those aged 30–39 years (36.7%). Females constituted 95% of the study population, with a female-to-male ratio of 19:1. Regarding marital status, 39 (65%) patients were married, while 21 (35%) were unmarried. (Table 1 & Figure 1)

Table 2: Biochemical, haematological and inflammatory parameters in SLE patients with SLEDAI 2K Score

Parameter	SLEDAI 2K <10		SLEDAI 2K ≥10		P value
	Mean	Std.Deviation	Mean	Std.Deviation	
Hemoglobin(g/dl)	11.14	2.06	9.16	1.11	<0.001
MCV (fl)	82.36	6.53	85.64	7.17	0.074
RDW (%)	14.57	1.96	17.38	2.74	<0.001
Serum Creatinine(mg/dl)	0.79	0.37	1.62	1.12	<0.001
Platelet count ($x10^3$ cells/mm^3)	1.89	0.83	1.48	0.59	0.043
24HourUrinary Protein(g)	0.77	0.71	2.40	1.16	<0.001
ESR (mm AEFH)	47.70	35.36	69.95	43.38	0.034
CRP (mg/dl)	0.60	0.49	1.36	1.10	0.001
C3 (mg/dl)	42.14	22.25	31.78	21.46	0.081
C4 (mg/dl)	10.09	5.91	7.69	6.18	0.140

Patients with high disease activity (SLEDAI-2K ≥10) had significantly higher RDW, serum creatinine, 24-hour urinary protein, ESR, and CRP levels, along with lower haemoglobin and platelet counts, compared with patients with SLEDAI-2K scores below 10 ($p < 0.05$). RDW was notably higher in the high-activity group (17.38 ± 2.74%) than in the low-activity group (14.57 ± 1.96%; $p < 0.001$). Differences in MCV, complement C3, and C4 levels were not statistically significant ($p > 0.05$).

Table 3: SLEDAI 2K score in SLE patients

SLEDAI 2K Score	Number of patients	Percentage	Mean±s.d
<10	37	61.7	5.89±1.66
≥10	23	38.3	16±4.63
Total	60	100.0	
Min-Max	2- 29		

Among the 60 patients, 37 (61.7%) had a SLEDAI-2K score below 10, with a mean score of 5.89 ± 1.66. The remaining 23 (38.3%) had a score of 10 or above, with a mean of 16.00 ± 4.63. The overall SLEDAI-2K scores ranged from 2 to 29, indicating varying levels of disease activity among the study participants.

Table 4. Correlation of SLEDAI-2K Score with RDW, Haemoglobin, Inflammatory Markers, and Platelet Count in Patients with SLE

Variable	SLEDAI 2K Score	
	r value	p value
RDW (%)	0.579	<0.001
Hemoglobin (g/dl)	-0.442	<0.001
CRP (mg/dl)	0.668	<0.001
ESR (mm AEFH)	0.449	<0.001
Platelet count (x10^5 cells/mm^3)	-0.313	0.015

The correlation analysis demonstrated a statistically significant positive correlation between SLEDAI-2K score and RDW levels ($r = 0.579$, $p < 0.001$), indicating that RDW increased with increasing disease activity. CRP ($r = 0.668$, $p < 0.001$) and ESR ($r = 0.449$, $p < 0.001$) also showed significant positive correlations with disease activity. In contrast, haemoglobin ($r = -0.442$, $p < 0.001$) and platelet count ($r = -0.313$, $p = 0.015$) showed significant negative correlations.

Table 5: Correlation between SLEDAI 2K score and RDW values in anemic SLE and non-anemic SLE patients

Variable		SLEDAI 2K SCORE	
		Anemia patient (39)	Non-anemic patient (21)
RDW (%)	0.595	0.595	0.530
	<0.001	<0.001	0.013
	15.9±2.70	15.9±2.70	15.17±2.56

A significant positive correlation was observed between RDW and SLEDAI-2K scores in both anaemic patients ($r = 0.595$, $p < 0.001$) and non-anaemic patients ($r = 0.530$, $p = 0.013$). The correlation was numerically stronger among anaemic patients, suggesting that RDW was associated with disease activity irrespective of anaemia status.

Table 6: Correlation between RDW with C3 and C4 levels in SLE patients

Variable	RDW (%)	
	r value	p value

C3 (mg/dl)	-0.25	0.04
C4 (mg/dl)	-0.38	0.003

A significant negative correlation was observed between RDW and complement C3 ($r = -0.25$, $p = 0.04$) and C4 levels ($r = -0.38$, $p = 0.003$). The findings indicate that higher RDW levels were associated with lower complement levels, with a stronger negative correlation observed for C4.

Discussion

The present study investigated the potential role of red cell distribution width (RDW) as an indicator of disease activity in patients with systemic lupus erythematosus (SLE). The major finding was a significant positive correlation between RDW and the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score ($r = 0.579$, $p < 0.001$). Furthermore, patients with high disease activity (SLEDAI-2K ≥10) exhibited significantly higher mean RDW values than those with lower disease activity (17.38 ± 2.74% versus 14.57 ± 1.96%, $p < 0.001$). These observations indicate that increased RDW is associated with greater disease activity and may provide additional information alongside established clinical and laboratory parameters during the assessment of SLE.

The demographic profile revealed that most participants belonged to the young adult age group, with a mean age of 29.45 ± 8.57 years. Females accounted for 95% of the study population, resulting in a female-to-male ratio of 19:1. This distribution reflects the well-established female predominance of SLE, particularly among individuals of reproductive age. Previous literature has emphasised the heterogeneous nature of SLE and the importance of integrating clinical and laboratory findings for comprehensive disease assessment, given its variable manifestations and clinical course [15].

The positive association between RDW and disease activity observed in the present study is consistent with findings from earlier investigations. Previous research has demonstrated a significant correlation between RDW and SLEDAI-2K scores, along with associations with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [7]. Similarly, a positive relationship between RDW and disease activity has been reported in both anaemic and non-anaemic patients with SLE, suggesting that this association is not exclusively attributable to reduced haemoglobin levels [8].

More recent studies have provided further evidence supporting the relationship between RDW and SLE activity. Significantly elevated RDW levels have been observed in patients with active SLE compared with those with inactive disease, with a positive correlation between RDW and SLEDAI scores [9]. Associations between RDW and various indicators of clinical and serological disease activity, including SLEDAI-2K scores and inflammatory cytokines, have also been reported [10]. In a study involving 284 patients with SLE and 181 healthy controls, RDW remained associated with disease activity and accumulated organ damage even after adjustment for potential confounding variables [13]. Additional evidence from 2025 has further highlighted the potential relevance of RDW in monitoring SLE activity. Higher RDW values have been reported during lupus flares compared with periods of remission, along with a positive correlation between RDW and SLEDAI-2K scores. However, the diagnostic performance of RDW differed depending on the comparison group, suggesting that it may be more appropriately considered an adjunctive parameter rather than an independent diagnostic marker [14].

An important observation in the present study was the persistence of a positive correlation between RDW and SLEDAI-2K scores across both anaemic and non-anaemic subgroups. Among patients with anaemia, the correlation coefficient was $r = 0.595$ ($p < 0.001$), whereas among non-anaemic patients, it was $r = 0.530$

($p = 0.013$). Although the correlation was numerically stronger in the anaemic subgroup, this difference cannot be considered statistically significant without a formal comparison between the correlation coefficients. These findings suggest that the association between RDW and disease activity may extend beyond the influence of anaemia alone. Similar observations have been reported, demonstrating a positive association between RDW and SLEDAI-2K irrespective of anaemia status [8]. Additional evidence has identified relationships between RDW, disease activity, and serological abnormalities, further supporting its potential relevance in SLE assessment [10].

The present study also demonstrated significant relationships between conventional inflammatory markers and disease activity. CRP exhibited the strongest positive correlation with SLEDAI-2K scores ($r = 0.668$, $p < 0.001$), followed by ESR ($r = 0.449$, $p < 0.001$). In addition, RDW showed significant positive correlations with ESR ($r = 0.524$, $p < 0.001$) and CRP ($r = 0.496$, $p < 0.001$). These findings suggest that increased RDW may occur alongside heightened systemic inflammatory activity in patients with SLE. Comparable associations between RDW, disease activity, and inflammatory parameters have been documented in previous studies [9,10]. The association may reflect the influence of inflammatory processes on erythropoiesis, red blood cell maturation, and erythrocyte survival. Nevertheless, the observed correlations do not establish a direct causal relationship between inflammation and increased RDW.

An inverse association was identified between RDW and serum complement levels. RDW demonstrated a significant negative correlation with complement C3 ($r = -0.250$, $p = 0.040$) and C4 ($r = -0.380$, $p = 0.003$). These findings suggest that higher RDW values may be associated with lower complement levels in patients with SLE. Previous research has similarly reported associations between haematological parameters and hypocomplementemia in SLE [10]. Complement consumption is an important feature of immune complex-mediated disease activity and may accompany active lupus manifestations. However, despite the significant correlations, differences in mean C3 and C4 levels between the low- and high-disease-activity groups in the present study were not statistically significant. This distinction highlights the need to interpret correlation findings and between-group comparisons separately and cautiously. Several haematological parameters were also associated with disease activity. Haemoglobin concentration demonstrated a significant negative correlation with SLEDAI-2K scores ($r = -0.442$, $p < 0.001$), with lower mean haemoglobin levels observed among patients with high disease activity. Similarly, platelet count showed a significant inverse correlation with SLEDAI-2K scores ($r = -0.313$, $p = 0.015$).

Strengths and Limitations: An important strength of the present study was the systematic assessment of RDW in relation to disease activity using the validated SLEDAI-2K scoring system. The evaluation of its relationship with inflammatory markers, complement levels, and anaemia status provided a broader understanding of the potential association between RDW and disease activity in SLE. However, certain limitations should be acknowledged. The relatively small sample size and single-centre design may restrict the generalisability of the findings to the wider SLE population. The observational nature of the study does not permit the establishment of a causal relationship between RDW and disease activity.

Conclusion

The study demonstrated a significant positive association between RDW and SLE disease activity, with higher RDW values observed among patients with elevated SLEDAI-2K scores. RDW also showed significant relationships with inflammatory markers and serum complement levels, suggesting its potential relevance in reflecting disease activity. These findings support the use of RDW as a simple, cost-effective and readily accessible adjunctive parameter for disease activity assessment in patients with SLE. However, further large-scale prospective studies are necessary to validate these observations and establish its clinical applicability in routine practice.

Declaration

Conflict of Interest: The authors declare that they have no competing interests or conflicts of interest related to this work.

Funding: Nil

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