Original Research Article

Clinical Significance of Haematologic Indices as Indicators for Systemic Lupus Erythematosus Activity

ABSTRACT

Background: Lupus erythematosus is a diverse autoimmune disorder that is capable of afflicting a variety of organs and has a clinical history that is inconsistent. Despite substantial improvements in systemic lupus erythematosus (SLE) patient survival, the pathophysiology of the disease remains unexplained, despite the fact that genes play a key role in its propensity.

Objective: To evaluate the several haematological indicators (neutrophil- to- lymphocyte ratio (NLR), platelet -to- lymphocyte ratio (PLR), platelet distribution width (PDW), red cell distribution width (RDW), mean platelet volume (MPV) in SLE patients and their correlation with disease manifestations.

Patients and Methods: In our study, a cross-sectional comparative study that enrolled 100 SLE patients (30 male and 70 female patients) aged from 18-55y who are recruited from the Internal Medicine Department, Rheumatology Unit (inpatient wards and outpatient clinics) the patients were categorized into three groups according to the (SLE disease activity index 2000. (SLEDAI-2K): Group (I): Inactive (SLEDAI-2K, <6) Include thirty-one patients. Group (II): Moderately active (SLEDAI-2K, 6-10) Include twenty-nine patients. Group (III): Highly active (SLEDAI-2k, ≥11) Include forty patients.

Results: Our study showed clinical parameters such as vasculitis, nephritis, serositis, CNS involvement are significant and indicate severe activity. Also, our study showed laboratory data as ESR, ANA, anti-dsDNA, and consumption of complement showed a significant correlation with systemic lupus activity. The highly active group had higher PLR, NLR, PDW, and MPV than other groups. However, the highly active group showed a decrease in lymphocyte median. CNS symptoms indicated a negative correlation that is statistically significant with lymphocytes. While it demonstrated a statistically significant positive correlation, with NLR, however, CNS showed a significant positive correlation with PDW. Nephritis had a significant positive correlation with NLR and PLR. Vasculitis had a positive highly significant correlation with lymphocytes and a positive significant correlation with PLR.

Conclusion: Patients with SLE in both high and moderate activity of disease exhibited significant renal manifestations, vasculitis, serositis, CNS symptoms, consumed C3 and C4 while ESR and Anti-dsDNA were elevated in all groups. The highly active group had higher NLR, PLR, PDW, and MPV than other groups. However, it showed a decrease in lymphocyte median. Further, CNS symptoms revealed a negative correlation that is statistically significant with lymphocytes, while it showed a positive statistically significant correlation with PDW and NLR. Nephritis had a positive significant correlation with NLR, and PLR and vasculitis had a positive highly significant correlation with lymphocytes and PLR.

Keywords: Systemic lupus erythematosus, rheumatoid arthritis

Introduction

Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder having a high degree of heterogeneity in terms of clinical symptoms and progression of disorder, distinguished by the of immune complexes deposition, production of pathogenic autoantibodies, and end-organ

damage [1]. It is a chronic inflammatory disorder with remission phases that is defined by the production of autoantibodies against cytoplasmic and antigens nucleic. [2]

SLE is one of the most prevalent autoimmune diseases in females which usually occurs in the childbearing period [3].

SLE patients continue to have disease manifestations 10 years after diagnosis even with appropriate management and the disease has Three patterns of disease activity that have emerged: inactive, moderately active, and highly active [4].

Numerous laboratory markers can be utilized evaluate activity of disease like levels of anti-double-stranded deoxyribonucleic acid (anti-dsDNA) antibody and serum complement concentrations that are good markers of disease manifestations [5].

The challenge is to evaluate disease activity with high sensitivity simple, available, and low-cost laboratory markers.

A complete blood count (CBC) is a non-invasive laboratory test that is performed on a routine basis utilized to diagnose and monitor rheumatic disorders. White blood cells and their subgroups, such as lymphocytes and neutrophils, have been recognized indicators of inflammation in a variety of diseases [6]. Occasionally, indices of hematology such as platelet-to-lymphocyte ratio (PLR), the neutrophil-to-lymphocyte ratio (NLR), platelet distribution width (PDW), mean platelet volume (MPV), and red cell distribution width (RDW) have been suggested as predictive indicators to ascertain the reaction to inflammation at the systemic level and they have been utilized in conjunction with other markers of inflammation to assess inflammation in a variety of conditions, includes autoimmune disorders [7-9]. Indices hematology are derived from the CBC and may be regarded as affordable and simply accessible indicators of inflammation [9].

Numerous research published in the last few years have demonstrated that PLR and NLR can be effective for assessing the activity of autoimmune disorders such as SLE and rheumatoid arthritis (RA) [10-13].

MPV is a biomarker for turnover of platelets, while activation of platelets is an indication of inflammation. [5] MPV has been associated with the process of inflammation and disease manifestations in ankylosing spondylitis and RA in previous research, although the link between MPV and SLE continues debatable [5].

AIM OF THE WORK

Our study was aimed to evaluate the different hematological indices (PLR, NLR, MPV, RDW, PDW) in SLE patients and their correlation to disease activity.

PATIENTS AND METHODS

Our study was done on:

100 SLE patients (30 male and 70 female patients) aged from 18-55y who are recruited from the Internal Medicine Department, Rheumatology Unit (inpatient wards and outpatient clinics); the Patients were classified according to their (disease activity index 2000. (SLEDAI-2K) into three groups: **Group (I)** Inactive (SLEDAI-2K, <6). Including 31 patients. **Group (II)** Moderately active (SLEDAI-2K, 6-10). 29 patients. **Group (III)** Highly active (SLEDAI-2k, ≥11). 40 patients.

Study design: Cross-Sectional Comparative Study between all Groups.

Inclusion criteria: We included patients aged 18-55 y with proven SLE (newly diagnosed and relapsed) The diagnosis was made using the Classification Criteria for Systemic Lupus International Collaborating Clinics (SLICC).

Exclusion criteria: We excluded in our study cases with severe comorbidities like renal failure, heart failure and hepatic failure. Parathyroid disorders, thyroid disorders, Concurrent infections, Malignancies, Blood transfusion last 4 months, and Acute coronary syndrome.

All cases underwent: taking of history including name, age, sex, onset, duration of symptoms, complaint, history of renal failure, thyroid disorders, parathyroid disorders, concurrent infections, malignancies, blood transfusion last 4 months, and family history of SLE or other immunological diseases. Clinical examination including general examination for the presence of; malar rash, discoid rash, photosensitivity, oral ulcers, hair loss, peripheral edema, arthritis, serositis, fever, CNS affection (fit, psychosis), hypertension, purpuric eruption, vasculitis, lymph node, examination of the thyroid gland, signs of renal failure as (generalized edema, uraemic breath), and signs of hepatic failure as (tense ascites, jaundice). Laboratory investigations including Investigations used for diagnosis of SLE and its activity as (ANA, anti-dsDNA), Serum complement 3 & 4 (C3&C4), Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and serum urea and creatinine. CBC including hemoglobin, platelets, and Blood indices: as NLR, PLR, PDW, RDW and MPV.

SLEDAI 2000. [14]

Classified into three groups: **Group (I)** Inactive (SLEDAI-2K, <6). **Group (II)** Moderately active (SLEDAI-2K, 6-10). **Group (III)** Highly active (SLEDAI-2k, ≥11).

Table (1): The SLEDAI 2000:[14]

SLEDAI-2K score	Descriptor	Definition
8	**Seizure**	Recent onset, exclude metabolic, infectious or drug causes.
8	**Psychosis**	Altered ability to function in normal activity due to severe disturbance in the perception of reality.
8	**Organic brain syndrome**	Altered mental function with impaired orientation, memory or other intellectual function.
8	**Visual disturbance**	Retinal changes.
8	**Cranial nerve disorder**	New onset of sensory or motor neuropathy involving cranial nerves.
8	**Lupus headache**	Severe, persistent headache which may be migrainous, but must be nonresponsive to narcotic analgesia.
8	**Cerebrovascular accident**	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	**Vasculitis**	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter haemorrhages, or biopsy or angiogram proof of vasculitis.
4	**Arthritis**	≥2 joints with pain and signs of inflammation (i.e. tenderness, swelling or effusion).
4	**Myositis**	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or biopsy showing myositis.
4	**Urinary casts**	Heme granular or red blood cell casts.
4	**Haematuria**	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	**Proteinuria**	>0.5 gram/24 hours.
4	**Pyuria**	>5 white blood cells/high power field. Exclude infection.
2	**Rash**	Inflammatory type rash.
2	**Alopecia**	Abnormal, patchy or diffuse loss of hair.
2	**Mucosal ulcers**	Oral or nasal ulcerations.
2	**Pleurisy**	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	**Pericarditis**	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	**Low complement**	Decrease in CH50, C3 or C4.
2	**Increased DNA binding**	Increased DNA binding by Farr assay.
1	**Fever**	>38°C. Exclude infectious cause.
1	**Thrombocytopenia**	<100 000 platelets / $x10^9$/L, exclude drug causes.
1	**Leukopenia**	<3000 white blood cells / $x10^9$/L, exclude drug causes.

Consent: Each participant signed an informed consent form after a full explanation of the benefits and the risks. There was a code number for each patient's file that include all investigations, so all data of the patients was strictly confidential.

Method:

ANA: Was conducted on a substrate containing human nuclei, like HEp-2 cells.

Anti-ds DNA: Was done by ELISA supplied by Calbiotech, catalog NO. DD037G. Reference value: Positive: > 60 U/ ml. Negative: < 40 U/ ml. Equivocal: 40-60 U/ ml. Serum complements levels (C3& C4): C3 was done by turbidimetry, supplied by BioSystems; catalog No COD 31084. Reference value: 90-180mg/dL. C4 was done by turbidimetry, supplied by BioSystems; catalog No COD 31085 (190). Reference value: 10-40 mg/dL.

Full Blood Count with manual platelet count: Was performed using BCC-3000 Auto Hematology Analyzer. The NLR was determined by dividing the absolute neutrophil count by the absolute lymphocyte count in a pre-treatment CBC. PLR was established by dividing the platelet count by the absolute lymphocyte count in a pre-treatment CBC. RDW, PDW, and MPV were obtained from CBC taken before treatment. Normal values of: HB male (14 to 18 gm/dL) / female (12 to 16 gm/dL). Platelets (150, 000 to 450, 000 platelets /microliter of blood). TLC: (4.00-11.0 x 10^9/L). Absolute Neutrophils: (2.5–7.5 x 10^9/L). Absolute Lymphocytes: (1.5–3.5 x 10^9/L). NLR:

(is roughly 1-3) %. PLR: (43.36-172.68) %. MPV: (around 7-12 Fl). PDW: (range 25-65) %. RDW: (12.2 to 16.1 %in females and 11.8 to 14.5 % males).

Statistical Methods

SPSS version 21 was utilised in assessment. Non-parametric Quantitative data were presented by a median, Interquartile range, and evaluated by Kruskal Wallis. Categorical data were presented by number and percent and assessed by the chi-square test and when it was inappropriate it was replaced by Monte Carlo Exact test. Spearman correlation was done for the linear relation between non-parametric variables. Significant P-values were defined as those less than 0.05, while those greater than 0.001 were regarded highly significant.

RESULTS

Table (2): Demographic data of the patients:

Variables	SLE patients			P-value
	Inactive SLE (n = 31)	**Moderate active SLE (n=29)**	**Highly active SLE (n=40)**	
Age				P=0.099
Median	35 (25 – 39)	26 (22 – 36)	31 (27 – 35)	P1= 0.05 P2= 0.105 P3= 0.387
Gender				P= 0.665
Male	8 (25.8%)	8 (27.6%)	14 (35 %)	P1= 0.876
Female	23 (74.2%)	21 (72.4%)	26 (65%)	P2= 0.514 P3= 0.406

Table (3): Clinical characteristics of the patients:

Variables	SLE patients			P-value
	Inactive SLE (n = 31)	Moderate active SLE (n=29)	Highly active SLE (n=40)	
nephritis				P <0.001* P1= 0.049* P2= 0.011* P3 <0.001*
-ve	31 (100%)	25 (86.2%)	23 (57.5%)	
+ve	(0%)	4 (13.8%)	17 (42.5%)	
Vaculitis				P= 0.005* P1= 1 P2= 0.0165* P3= 0.012*
-ve	30 (96.8%)	28 (96.6%)	30 (75%)	
+ve	1 (3.2%)	1 (3.4%)	10 (25%)	
Hemolytic anemia				P= 0.231 P1= 1 P2= 0.235 P3= 0.222
-ve	30 (96.8%	28 (96.6%	35 (87.5%)	
+ve	1 (3.2%	1 (3.4%	5 (12.5%)	
Thrombocytopenia				P= 0.231 P1= 1 P2= 0.235 P3= 0.222
-ve	30 (96.8%	28 (96.6%	35 (87.5%)	
+ve	1 (3.2%)	1 (3.4%)	5 (12.5%)	
IDA				P= 0.284 P1= 0.170 P2= 0.897 P3= 0.174
-ve	16 (51.6%)	20 (69%)	27 (67.5%)	
+ve	15 (48.4%)	9 (31%)	13 (32.5%)	
Skin symptoms				P= 0.201 P1= 0.459 P2= 0.332 P3= 0.078
-ve	24 (77.4%)	20 (69%)	23 (57.5%)	
+ve	7 (22.6%)	9 (31%)	17 (42.5%)	
Arthritis				P= 0.403 P1= 0.185 P2= 0.391 P3= 0.572
-ve	25 (80.6%)	19 (65.5%)	30 (75.0%)	
+ve	6 (19.4%)	10 (34.5%)	10 (25.0%)	
Serositis				P< 0.001* P1= 0.173 P2= 0.03* P3 <0.001*
-ve	26 (83.9%)	20 (69%)	17 (42.5%)	
+ve	5 (16.1%)	9 (31 %)	23 (57.5%)	
CNS symptoms				P= 0.005* P1= 0.049* P2= 0.286 P3< 0.001*
-ve	31 (100%)	25 (86.2%)	27 (67.5%)	
FITS	(0%)	4 (13.8%)	10 (25 %)	
Psychosis	(0%)	(0 %)	1 (2.5%)	
FITS, psychosis	(0%)	(0%)	2 (5%)	

Table (4): Comparison between studied groups regarding serology:

Variables	SLE patients			P-value
	Inactive SLE (n = 31)	Moderate active SLE (n=29)	Highly active SLE (n=40)	
ESR mm/h				P <0.001* P1= 0.002* P2<0.001* P3<0.001*
Normal	25 (80.6%)	12 (41.4%	3 (7.5%)	
Elevated	6 (19.4%)	17 (58.6%)	37 (92.5%)	
Urea mg/dl				P= 0.11 P1= 0.229 P2= 0.690 P3= 0.064
Normal	31 (100 %)	27 (93.1%)	35 (87.5%)	
Abnormal	(0%)	2 (6.9%)	5 (12.5%)	
Creatinine mg/dl				P= 0.11 P1= 0.229 P2= 0.690 P3= 0.064
Normal	31 (100 %)	27 (93.1%)	35 (87.5%)	
Abnormal	(0%)	2 (6.9%)	5 (12.5%)	
ANA				P= 0.604 P1= 0.379 P2= 0.888 P3= 0.413
Normal	7 (22.6%)	4 (13.8%)	6 (15%)	
Positive	24 (77.4%)	25 (86.2%)	34 (85%)	
Anti-dsDNA				P<0.001* P1< 0.001* P2= 0.592 P3= 0.002*
Normal	18 (58.1%)	5 (17.2%)	9 (22.5%)	
Positive	13 (41.9%)	24 (82.8%)	31 (77.5%)	
C3 mg/dl				P <0.001* P1= 0.029* P2= 0.053 P3 <0.001*
Normal	16 (51.6%)	7 (24.1%)	3 (7.5%)	
Decreased	15 (48.4%)	22 (75.9%)	37 (92.5%)	
C4 mg /dl				P= 0.005* P1= 0.128 P2= 0.108 P3< 0.001*
Normal	12 (38.7%)	6 (20.7%)	3 (7.5%)	
Decreased	19 (61.3%)	23 (79.3%)	37 (92.5%	

Table (5): Comparison between studied groups regarding hematological indices:

	SLE patients			P-value
	Inactive SLE (n = 31)	**Moderate active SLE(n=29)**	**Highly active SLE (n=40)**	
Hemoglobin (gm/dl)				P= 0.633 P1= 0.859 P2= 0.539 P3= 0.344 P4= 0.485
Median	8.7 (7.6-10.2)	8.9 (7.5 – 10.2)	8.7 (7.13 – 10)	
Platelets $\times 10^3$/ mm^3				P= 0.298 P1= 0.224 P2= 0.139 P3= 0.894 P4= 0.599
Median	150 (125 – 160) × 10^3	125 (105 – 165.5) × 10^3	147.5 (116.25 – 189) ×10^3	
TLC cell/mm^3				P= 0.633 P1= 0.335 P2= 0.661 P3= 0.577 P4= 0.399
Median	4000 (2800 – 4300)	3600 (2950 – 4100)	3800 (2800 – 4375)	
Absolute Neutrophils cell/mm^3				P= 0.411 P1= 477 P2= 0.601 P3= 0.18 P4= 0.222
Median	2600 (2000 – 3100)	2700 (2250 – 3150)	3000 (2100 – 3475)	
Absolute Lymphocytes cell/mm^3				P<0.001* P1 <0.001* P2= 0.044* P3 <0.001* P4 <0.001*
Median	900 (800 – 1100)	450 (350 – 650)	400 (300 – 500)	
NLR %				P <0.001* P1 <0.001* P2= 0.004* P3 <0.001* P4 <0.001*
Median	2.9 (2.08 – 3.6)	5.6 (5.1 – 6.85)	6.9 (5.6 – 10.45)	
PLR %				P<0.001* P1 <0.001* P2= 0.002* P3 <0.001* P4 <0.001*
Median	166 (134 – 185)	350 (255 – 428)	480 (355 – 622.5)	
MPV FL				P <0.001* P1 <0.001* P2 <0.001* P3 <0.001* P4 <0.001*
Median	8.1 (7.6 – 9)	10.8 (9.95 – 11)	13 (12.4 – 13.35)	
PDW %				P <0.001* P1 <0.001* P2 <0.001* P3 <0.001* P4 <0.001*
Median	9.3 (8.9 – 9.8)	11 (10.8 – 11.5)	13.9 (13 – 14.15)	
RDW %				P= 0.196 P1= 0.082 P2= 0.555 P3= 0.195 P4= 0.088
Median	13.5 (12.3 – 14)	14 (13.55 – 15)	13.7 (13.2 – 16.35)	

Table (6): Correlation between Specific Organ Involvement and Hematological Indices in inactive SLE Patients:

		NLR	PLR	MPV	PDW	RDW	Lymphocytes
Vasculitis	r_s	0.153	0.307	- 0.093	0.174	0.289	0.282
	p	0.410	0.093	0.619	0.348	0.115	0.125

Table (7): Correlation between Specific Organ Involvement and Hematological Indices in moderately active SLE Patients:

		NLR	PLR	MPV	PDW	RDW	Lymphocytes
Nephritis	r_s	0.246	0.102	- 0.042	- 0.228	- 0.048	0.230
	p	0.199	0.600	0.829	0.234	0.665	0.230
Vaculitis	r_s	- 0.294	- 0.316	- 0.114	0.272	- 0.045	0.137
	p	0.121	0.094	0.558	0.153	0.815	0.478
CNS symptoms	r_s	0.515	0.287	-0.024	0.270	0.258	- 0.587
	p	0.004*	0.131	0.902	0.156	0.177	0.001*

Table (8): Correlation between Specific Organ Involvement and Hematological Indices in highly active SLE Patients:

		NLR	PLR	MPV	PDW	RDW	Lymphocytes
Nephritis	r_s	0.327	0.432	- 0.101	0.077	0.095	- 0.288
	p	0.040*	0.005*	0.533	0.635	0.562	0.071
Vacuities	r_s	0.018	0.268	- 0.136	- 0.068	0.003	0.398
	p	0.915	0.095	0.403	0.676	0.988	0.011*
CNS symptoms	r_s	0.314	0.131	0.031	0.405	0.239	- 0.567
	p	0.048*	0.525	0.848	0.009*	0.137	<0.001*

Table (9): Correlation between Specific Organ Involvement and Hematological Indices in (active SLE Patients) (moderately and highly active groups):

		NLR	PLR	MPV	PDW	RDW	Lymphocytes
Nephritis	r_s	0.349	0.409	0.224	0.266	0.017	- 0.174
	p	0.003*	<0.001*	0.064	0.027*	0.892	0.153
Vacuities	r_s	0.058	0.275	0.185	0.248	- 0.017	0.234
	p	0.638	0.022*	0.128	0.040*	0.890	0.053
CNS symptoms	r_s	0.419	0.231	0.205	0.385	0.235	- 0.594
	p	<0.001*	0.056	0.091	0.001*	0.052	<0.001*

DISCUSSION

SLE is a clinically heterogeneous autoimmune disorder marked by the development of autoantibodies targeted in opposition to nuclear antigens. [15] It is a multisystem disease which manifests itself in a variety of ways. [16] The prevalence varies but is generally expected to be nearly 1 per 1000, with a male to female ratio of 9: 1. [17] The most frequent manifestations include arthritis, rash, and fatigue and affect multisystem organs such as the kidney, CNS. ANA are present in almost 95% of patients with SLE. [18]

Most of the pathology in SLE is caused by immune complex deposits in numerous organs, which activates complement and other inflammatory mediators. [19] Symptoms vary according to individual and with periods of exacerbation and remission and activity may be mild, moderate, or severe [19].

Numerous biological markers accurately define multiple facets of SLE and may be utilised to predict prognosis, assessing disease activity and guiding therapy like anti-dsDNA antibody levels and complement serum **levels** which **are** good markers of disease activity [20].

The purpose of our study was to determine the association between haematological markers and SLE activity [21].

Our study's objective was to determine the different hematological indices (PDW, MPV, NLR, PLR, RDW) in SLE patients and their correlation with disease manifestations.

Our research was cross-sectional in nature was done between the end of June 2020 to June 2021.

It was a comparative study that included 100 SLE patients (30 male and 70 female patients) aged from 18-to 55 y, and the patients were categorized in accordance with (SLEDAI-2K) into three groups:

- **Group (I) Inactive:** including thirty-one patients (8 males and 23 females) their ages ranging from (25-39) y with a median age group of (35) y.
- **Group (II) moderate active:** including twenty-nine patients (8 males and 21 females) their age ranging from (22-36) y with a median age group (26) y.
- **Group (III) highly active:** including forty patients (14 males and 26 females) their age ranging from (27-35) y with a median age group (31) y.

All patients underwent taking of full history and clinical examination including general examination for the presence of; malar rash, discoid rash, photosensitivity, oral ulcers, hair loss, signs of renal failure (generalized edema, uremic breath), and signs of hepatic failure as (tense ascites, jaundice).

In our study, it was found with nephritis was 42.5% of patients (highly active), 13.8% of patients (Moderate active), and (inactive) patients had no renal manifestations so Nephritis showed a significant difference and is commonly presented in highly active patients and associated with activity and flaring and lupus nephritis patients had statistically significantly higher SLEDAI.

Inconsistent with our results**, Reppe Moe et al., (2019)** [22] carried out cohort research which comprised all SLE cases. The findings indicated that 98/325 SLE patients (30%) had lupus nephritis (LN), with 92 % developing it within the first five years of disease beginning.

In agreement with our results, **Hanly et al., (2016)** [23] assessed patients in the SLICC classification criteria cohort of origin (15 months after diagnosis of SLE)) for estimated proteinuria, glomerular filtration rate, and end-stage renal disease. The Short Form (36-question) health survey questionnaire (SF-36) subscales, additionally to the mental and physical component summary scores, were used to assess health-related quality of life. The results indicated that there were 1827 cases, 89 % of whom were female, with a mean (SD) age of 35.1 (13.3) years. 700 (38.3%) patients had LN: 134/700 (19.1%) during follow-up and 566/700 (80.9%) at enrolment.

Also, **Feldman et al., (2015)** [24] covered the years 2000–2006 through the Medicaid analytic extract database where they detected patients with SLE aged 18–64 years, as well as a subpopulation with lupus nephritis. They identified patients of significant hospitalization activity, Moreover, they established mortality rates during the first 30 days. They analyzed the data using multivariable Cox proportional hazards models and Poisson regression and calculated activity incidence rates, adjusted for sociodemographic factors, a risk-adjustment score specific to SLE, and medication use. The study's findings indicated that 7,113 people with SLE had LN amongst 33,565.

In our results, vasculitis was recorded in 25% of highly active patients, 3.4 % in moderate active patients, and 3.2% in inactive patients.

In line with our results, **Kallas et al., (2020)** [25] executed prospective cohort research on cases diagnosed with SLE using the SLICC classification criteria. The results showed that amongst 2580 patients; in 449 patients, cutaneous small-vessel vasculitis was detected (17.3 %). After SLE diagnosis, the mean time to develop cutaneous vasculitis was 4.78 years (95 % CI 3.96 to 5.60). At least 159 (35%) cases reported Vasculitis lesions recur.

In agreement with our results, **Gheita et al., (2017)** [26] the purpose of their study was to ascertain the clinical characteristics of cutaneous vasculitis in cases with SLE. Around fifty female adults with SLE completed a thorough clinical examination, history taking, and laboratory testing.

The SLEDAI was used to determine the level of disease activity, while the Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI) was used to assess cumulative damage. The findings indicated that 30% of individuals had cutaneous vasculitis. All individuals with cutaneous vasculitis had musculoskeletal symptoms and hypocomplementemia.

In our results, it was found that serositis was found in 25 (57.5%) patients (highly active), 9 (31 %) patients (moderately active), and 5 (16.1%) (Inactive) patients Serositis had a significant positive relation with SLE activity.

In line with our results, **Jung et al., (2019)** [27] conducted a case-control study within a cohort to examine the relationship between various clinical factors, such as the usage of glucocorticoids, and significant manifestations. Clinical signs were more prevalent in SLE patients than in controls.; serositis (30.0% vs. 15.4%, $p = 0.001$).

In our results, it was found that 13 (32.5%) from highly active patients presented with CNS symptoms in the form of (fits, psychosis, and both fits and psychosis 10 (25%), 1 (2.5%), and 2 (5%) respectively. In moderately active patients, 4 (13, 8%) had CNS symptoms in the form of fits, while the inactive group had no CNS symptoms.

In agreement with our results, **Nikolopoulos et al., (2020)** [28] constituted a mixed group of SLE was diagnosed in 555 Caucasian patients, both prevalent and incident. The findings indicated that 11.5 % had neuropsychiatric involvement as presenting signs. During the first six months following disease diagnosis, 17.8 % developed irreversible impairment, which was attributable primarily to thrombotic and disorder of the neuropsychiatric system. During the most recent examination, 202 (36.4 %) cases had developed serious illness, with more than half receiving pulse cyclophosphamide treatment.

In line with our results, **Imam et., (2019)** [29] conducted case-control research comparing laboratory findings, clinical and SLE-related characteristics, and the SLAM index in patients with SLE who had polyneuropathy " PN " with those who did not. A total of 30 were diagnosed with SLE. The results indicated that the most frequently encountered pathology was axonal deterioration, that appeared in 19 (63.3%) patients; the most frequently encountered PN subtype was sensorimotor PN, which transpired in 18 (60%) patients; and the most frequently encountered associated entrapment of nerve was carpal tunnel syndrome, which occurred in 10 (33.3%) cases.

In our study, **ESR** increased significantly in cases in the active group than in the inactive it was found that ESR was determined in 37(92.5%) highly active patients, 17(58.6%) moderate active patients, and about 6 (19.4%) inactive patients.

Inconsistent with our results, **Stojan et al., (2013)** [30] analyzed thousands in a prospective SLE cohort to determine the relationship between ESR and disease activity. They examined whether variations in ESR were related with alterations in the clinical symptoms of disease, whether ESR was associated with disease activity cross-sectionally, and whether changes in ESR predicted future changes in disease activity. The results showed that ESR recorded marked (>75 mm/h), moderate (51–75 mm/h) and mild (25–50 mm/h) Rises in levels of ESR during a single visit were associated with an increase in the SLEDAI. Significant correlations existed between raised ESR and disease activity.

Also, from 2006 to 2015, a retrospective examination of 371 consecutive incidences of SLE inpatients was conducted by **Schäfer et al., (2018)** [31. The results showed that ESR levels were associated with disease activity.

Anti-dsDNA antibodies were revealed to be effective indicators for estimating SLE activity in our investigation. Anti-dsDNA titer has been found to have a direct correlation with illness

severity and progression and in our study; we found that Anti-dsDNA antibodies associated positively to disease activity was determined in 31(77.5%) highly active patients, 24 (82.8%) moderate active patients, and 13 (41.9%) inactive patients.

Parallel with our results, **Fabrizio et al., (2015)** [32] conducted a prospective cohort study among 393 SLE patients where they classified patients into three groups: anti-dsDNA + (persistent positivity), anti-dsDNA ± (initial positivity and subsequent negativity during disease progression), and anti-dsDNA − (persistent negativity). The findings indicated that anti dsDNA was higher significantly in active SLE patients (anti-dsDNA +: 62.3%; anti-dsDNA ±: 13.3%; anti-dsDNA −: 24.4%).

In our study, it was found that C3 and C4 were significantly decreased in active SLE cases.

In line with our results, **Tang et al, (2019)** [33] the purpose of their study was to determine the link between cytokines and complements and their clinical importance in relation to SLE activity. Serum samples were taken from 140 SLE patients and 36 age- and gender-matched healthy controls. All samples were tested for serum interleukin-6, IL-17, high-sensitivity C-reactive proteins, and complements (C3, C4). These patients were divided into three subgroups based on their (SLEDAI-2K) scores: high activity, moderate activity, and mild activity. C3 and C4 levels in active SLE patients were significantly lower than those in the healthy control group (0.80 – 0.28 and 0.21 – 0.08 g/L) vs. (1.49 – 0.08 and 0.36 – 0.02 g/L) respectively.

Also, **Hou et al., (2018)** [34] carried out a retrospective analysis, and data were gathered on 173 case histories of 142 hospitalised patients. They discovered a 50.7 % incidence rate in patients with SLE. The results showed that C_3 (0.67 ± 0.36 0.75 ± 0.29 0.05) and C_4 (0.18 ± 0.16 0.18 ± 0.10 0.04) were relatively low in active SLE patients.

However, **Qu et al., (2019)** [35] carried out a retrospective study including 194 patients with SLE and 106 patients with the non-SLE rheumatic disease were selected as a disease control group and 120 healthy subjects as a group of healthy controls. The results showed that both C3 and C4 were higher in both groups where C3 was (87.11 %) and C4 was (82.74%) in the patient group. This difference between both studies can be justified by ethnic differences and a larger sample size.

The current study showed that, the absolute lymphocytes recorded lower lymphocytes levels in the highly active patients.

In agreement with our results, **Sobhy et al., (2020)** [36] conducted cross-sectional research on 124 patients who met the SLICC criteria. criteria. Two groups of patients were formed. 57 patients with lymphopenia (1500 cells/mm3) were included in group I, while 67 patients without lymphopenia (1500 cells/mm3) were included in group II. The clinical presentation, immunological profile, laboratory findings, disease activity, and damage index, as well as the drugs administered, were compared between the two groups. The findings indicated that 57 (47 %) of the patients investigated had lymphopenia.

In line with our results, **Hum et al., (2020)** [37] obtained data from a cohort of 141 patients with SLE and compared it with healthy controls (n=79). As a result, lymphocyte counts were decreased (median 1.3 vs 1.7×109 /L; p<0.0001).

In our study, it was found that the highly active group had higher NLR than the moderately active group, and the inactive group and NLR showed a positive correlation with activity.

In agreement with our results, **Wang et al., (2020)** [38] conducted a meta-analysis study where they included 14 papers with 1,781 SLE patients and 1,330 healthy controls. The results showed NLR was higher significantly in SLE patients than in healthy controls (SMD=1.43; 95% CI, 0.98–1.88). Five studies including 697 people compared NLR in patients with active versus inactive SLE. Due to the significant heterogeneity among the five research, the analysis of the five

studies was also conducted using a random-effects model (I^2=97.0%, p <0.001). Increased NLR was found to be strongly associated with active SLE (SMD=2.05; 95% CI, 0.87–3.23). Additionally, it was highlighted that NLR was considerably higher in patients with SLE compared to those without LN (SMD=0.77; 95% CI, 0.57–0.97).

Also, Soliman et al., (2020) [39] conducted a cross-sectional study that included 60 patients with SLE who had LN, 60 patients with SLE who did not have renal involvement, and 30 healthy controls. The results indicated that SLE patients had a significantly higher NLR than controls. Both ratios demonstrated statistically significant increases in SLE patients with active illness. The results NLR of SLE patients was much higher and correlated with activity than those of the controls. Both ratios demonstrated statistically significant increases in SLE patients with active illness (2.21 (1.84–4.08) vs 3.88 (2.84–5.55).

In our study, it was found that the highly active group had higher PLR than the moderately active group and inactive group.

In line with our results**, El -said et al., (2022)** [40] carried out a comparative cross-sectional study of 52 adult SLE patients identified using the SLICC categorization criteria. The findings indicated that the PLR was significantly higher in SLE patients and correlated with activity (189.9 ± 136.4; 23.9–782.9) than in control (95 ± 29.9; p < 0.0001).

In our study, it was found that the highly active group had higher MPV than the moderately active group and inactive group Our study showed that **MPV** positively related to SLEDAI which is in agreement with, and this result agrees with **(Xie et al., 2018)** [5].

However, **Hartmann et al., (2018)** [41] conducted a cross-sectional study in which 81 cases with SLE in accordance with the ACR diagnostic classification criteria and 58 healthy controls were included. The results indicated that patients with active SLE had a lower MPV than those with inactive illness. (10.0±0.7fL *vs*. 10.7±1.0fL, p=0.005, respectively) as well as in comparison to the control group (10.9±1.0fL, p<0.001). They discovered a weak negative correlation between the SLEDAI and the MPV in their investigation. (r=-0.29, p=0.009). This contradiction between both studies can be justified by ethnic differences, different categorizations, and large size.

Also, **Khan et al., (2017)** **[42]** conducted a cross-sectional study fifty patients were recruited using a non-probability sequential sampling strategy. The patients were divided into two equal groups: 25 with active SLE and another 25 with stable, quiescent lupus. The results showed that the MPV of patients with active SLE was numerically statistically significantly lower than those in the inactive-SLE group (n=25, mean [M]=7.12, SD=1.01) vs. (n=25, M= 10.12, SD=0.97), (p<0.001). This contradiction between both studies can be justified by a larger included sample size in their study compared with ours can explain this variability in results in addition to different categorizations.

In our study, it was found that PDW in the highly active group had higher PDW than the moderately active group and inactive group.

Inconsistent with our results**, Chen et al., (2018)** [9] conducted a cross-sectional study in which 204 study participants were recruited, comprising 91 SLE patients and 113 age- and gender-matched healthy controls. They were divided into three groups: those with no SLE (n = 113), those with active SLE (n = 54), and those with inactive SLE (n = 37). The results showed that PDW was statistically higher in SLE patients than that in the control group (13.54 ± 2.67 vs. 12.65 ± 2.34, p = 0.012), and inactive group, PDW was significantly increased compared to the inactive group (14.31 ± 2.90 vs. 12.25 ± 1.55, p < 0.001).

In our study, it was found that nephritis had a positive highly significant correlation with PLR {(r_s =0.409), (p<0.001)}.

In agreement with our results, **Abdulrahman et al., (2020)** [43] conducted a cross-section study that includes 110 SLE patients, Patients were separated into two groups: those with active nephritis (n = 80) and those who did not have active nephritis (n = 30). Patients with LN were classified into two subgroups: Naive (1st presentation) (n = 60) and Relapsing (Flare) (n = 20). Additionally, fifty age-matched healthy individuals (hospital and laboratory workers) were included as controls. The results showed that the correlation of NLR and PLR with different disease characteristics in LN patients revealed a significant correlation with the ESR, proteinuria, SLEDAI, IL-6.

Inconsistent with our results, **El-Said et al., (2022) (**[40] highlighted that PLR and PLR were significantly correlated with nephritis and could predict it. In SLE, the PLR was substantially higher in patients exhibiting hematological disorders and nephritis in the course of SLE.

Parallel to our results**, Soliman et al, (2018)** [39] highlighted that NLR and PLR had a positive correlation with SLEDAI, ESR, and CRP, but a negative correlation with C4.

In the present study, it was found that nephritis had a positive significant correlation with PDW.

However, **Yu et al., (2020)** [44] performed a retrospective analysis on 212 SLE patients and 201 healthy controls. Their medical records were analyzed for clinical features and laboratory data. The results indicated that PDW levels were considerably lower in patients with SLE, and were negatively correlated with SLEDAI score, disease duration, and 24-hour urine protein. Additionally, there were more patients with LN in the low-PDW group than in the normal-PDW or high-PDW groups. Reduced PDW in conjunction with a high 24-hour urine protein level demonstrated an excellent diagnostic value for LN. Notably, in the low PDW group, 16.67% of LN patients with negative 24-hour urine protein can be found. This contradiction between both studies can be justified by a larger sample size in both groups and applied laboratory analysis.

CONCLUSION

Patients with SLE in both high and moderate activity of disease exhibited significant renal manifestations, vasculitis, serositis, CNS symptoms, consumed C3 and C4 while ESR and Anti-dsDNA were elevated in all groups. The highly active group had higher NLR, PLR, PDW, and MPV than other groups. However, it showed a decrease in lymphocyte median. Further, CNS symptoms showed a negative statistically significant correlation with lymphocytes, while it showed a positive statistically significant correlation with NLR and PDW. Nephritis had a positive significant correlation with NLR, and PLR and vasculitis had a positive highly significant correlation with lymphocytes and PLR.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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