

Platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios as noninvasive predictors for renal involvement in systemic lupus erythematosus in health clinics

Mona M. Soliman^a, Yasmine S. Makarem^b, Ahmed A. El Wafaa^c,
Marwa K.A. Khairallah^a

Departments of ^aInternal Medicine,
^bRheumatology and Rehabilitation, Faculty of
Medicine, Assiut University Hospital, Assiut,
^cDepartment of Internal Medicine, Luxor
General Hospital, Luxor, Egypt

Correspondence to Marwa Kamal Abdo
Khairallah, MD Nephrology and Renal
Transplantation, Lecturer of Nephrology and
Renal Transplantation, Internal Medicine
Department, Assiut University Hospital, Faculty
of Medicine, Assiut University, 71511, Egypt.
Mob: 002/01097878113; fax: +20 71515;
e-mail: marwa.kamal82@hotmail.com

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Objective

Renal injury is a prevalent complication related to lupus erythematosus and its occurrence is linked with bad alarms. Yet, a noninvasive procedure to predict renal impairment in health clinics has not been settled. Consequently, the authors postulated that platelet-to-lymphocyte (PLR) ratio and neutrophil-to-lymphocyte ratio (NLR) might be used as valid noninvasive indicators for kidney impairment.

Participants and methods

In this cross-sectional research, 270 participants were enrolled into the research after exclusion of 70 patients; the included patients were classified into four groups: 80 patients with lupus nephritis (LN) diagnosed by renal biopsy, 12 active lupus patients without renal involvement, 28 lupus patients on remission, and 80 healthy participants as controls. The authors evaluated levels of PLR and NLR in addition to other renal and lupus markers.

Results

The results have shown that PLR and NLR had significantly higher levels in active lupus patients as in biopsy-proven LN in comparison to inactive systemic lupus erythematosus and control groups. NLR was positively correlated with serum creatinine in patients with LN; however, they did not show significant association with other predictors of renal diseases. The study demonstrated that PLR and NLR had significant association to advanced classes of LN. Furthermore, the receiver-operating characteristic curve showed a higher sensitivity of PLR in early detection of kidney function impairment in LN patients (88.9%) while NLR showed more specificity (87.5%).

Conclusion

PLR and NLR could act as noninvasive markers for detection of renal involvement in lupus patients in health clinics as for the prediction of renal pathological class.

Keywords:

lupus nephritis, neutrophil to lymphocyte, platelet to lymphocyte

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Introduction

Lupus erythematosus is an inveterate immune disorder with autoantibodies to cytoplasmic and nuclear antigens, associated with multisystem inflammation, variable clinical manifestations, and a remitting and a relapsing course [1]. The clinical manifestation has a diversity of aspects and targets the renal system, the lung, the skin, and the musculoskeletal system. Lupus nephritis (LN) attacks more than 50% of systemic lupus erythematosus (SLE) patients, which usually ends in chronic renal affection ending in dialysis or renal transplantation and thus increasing the risk of mortality [2,3]. Invasive renal biopsy is still the standard stone in the diagnosis of LN and its flare [4]. However, simple laboratory markers guiding the management of LN are still not settled in health clinics. In this issue, traditional investigations for rapid evaluation for renal impairment are scanty and invasive as a kidney biopsy; however, they do affect

the decision about the optimal therapy. Even though classical markers like complement deficiency and anti-ds-DNA antibodies are vastly used as tools to estimate lupus flare, their ability to specify the activity is generally weak, and they seem to be more useful in confirming the diagnosis after the presence of clinical suspicion [5]. In the settings of generalized inflammation the prevalent white blood cells show particular changes mainly in the form of decrease in the lymphocyte count and increase in the neutrophil count [6]. Clinicians use the changes in peripheral blood cell components as in autoimmune and nonautoimmune disorders [7,8] as a predictor of immunological activity. The most significant

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components of the complete blood count (CBC) is the platelet-to-lymphocyte (PLR) and neutrophil-to-lymphocyte (NLR) ratios. NLR could be utilized as a provocative biomarker in multiple immunological related disorders, for example, inflammatory bowel disorders [9], psoriasis [10], and Sjögren's syndrome [11]. PLR has been used as a biomarker for differentiating between two or more disorders or as a predictor of multiple pathological conditions as inflammatory diseases and cancer [12]. Researchers found NLR to be associated with activity in SLE disease [8]. Subsequently, we pursued to assess the use of hematological ratios as noninvasive early indicators for both lupus flares and kidney involvement in those patients with estimation to their relations with renal pathological classes in health clinics.

Participants and methods

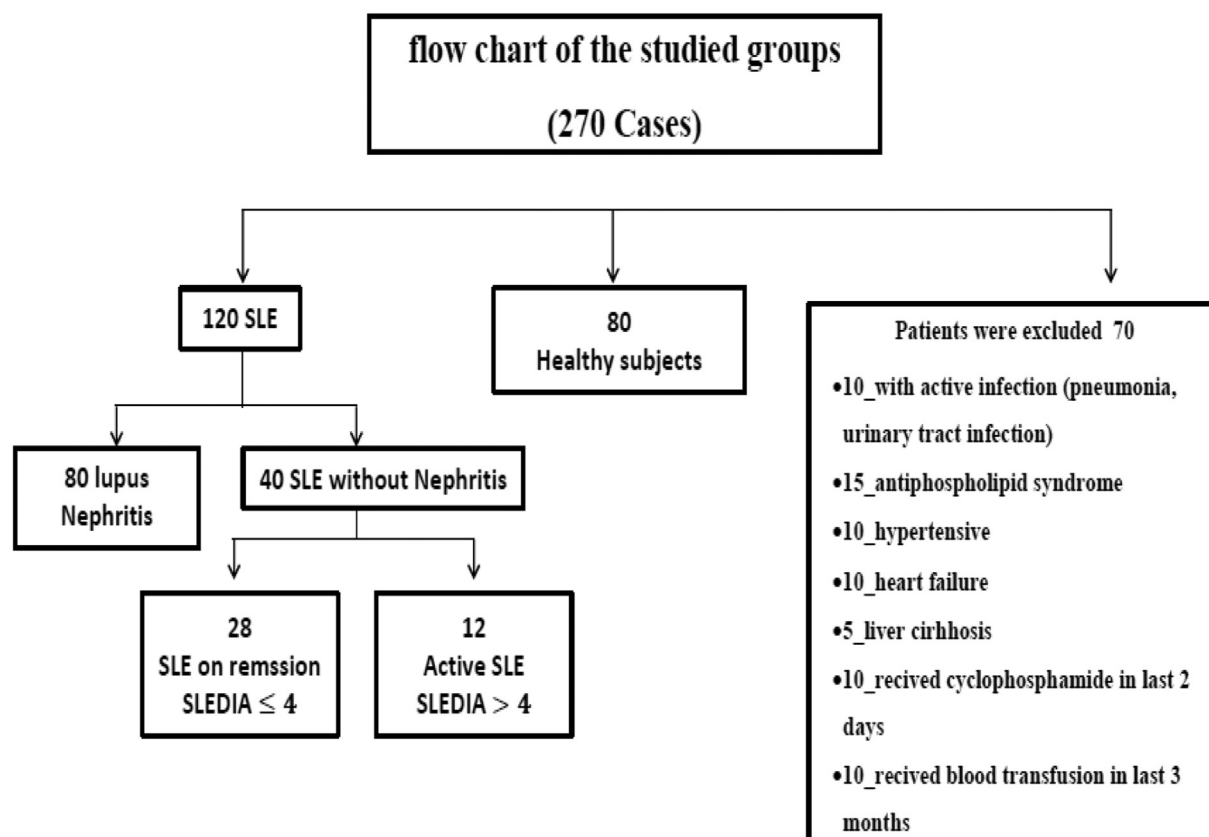
In this cross-sectional research, 270 participants were enrolled into the study from which 190 adult patients diagnosed to have lupus erythematosus were enrolled after admission to Assiut University Hospital, division of Internal Medicine, Rheumatologic Diseases and Nephrology Units from December 2017 till April 2019. The present study was approved by the local ethics and research committee of Assiut University

hospital no:17/0/055. All patients gave informed consent before participation. Seventy patients had been excluded as shown in Fig. 1. The reminder 120 lupus participants were divided into three groups depending on two parameters: 80 out of 120 patients were diagnosed as LN based on renal pathological examination associated with laboratory and clinical findings. The rest of the lupus participants were further classified into two groups, depending on the SLEDAI score assessing lupus activity [24]. Inactivity was considered when SLEDAI index less than or equal to 4 (24 participants). Activity was considered when SLEDAI index greater than 4 (12 participants). LN participants were further categorized into five classes depending on WHO classification [25], majority were of class III and IV (19 and 51 LN participants, respectively). We enrolled 80 healthy, matched participants as the control group.

Laboratory investigations

PLR and NLR were determined from the routine CBC test. Other investigations include serum urea, serum creatinine, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and protein collected from a sample of 24h urine, using criterion experimenter procedures. Furthermore, complement

Figure 1



Flow diagram showing the studied population.

activity (C3, C4) and anti-ds-DNA were evaluated using usual procedures.

Statistics

SPSS (Statistical Package for the Social Sciences, version 20; IBM, Armonk, New York, USA) was used for datum collection and statistical analysis. Continuous datum was shown in the form of mean±SD or median (range), while nominal variable was shown in the form of frequency (percentage). χ^2 -Test was utilized to confront the nominal variable of various groups in the research, while Student's *t*-test was utilized to confront the mean of various two groups and analysis of variance test for more than two groups. The receiver-operating characteristic curve (ROC) curve was utilized to evaluate the diagnostic accuracy of NLR and PLR in diagnosing SLE and renal involvement in lupus patients. The level of confidence was kept at 95% and the *P* value was significant if less than 0.05.

Results

Studied population characteristics

Table 1 shows the entire baseline and laboratory features of the studied participants. Variations regarding age and

sex between the studied groups have no significant differences. As a result of the categorization in our research regarding the renal involvement, LN patients had statistically significant increase in both proteinuria and serum creatinine in comparison to patients with lupus erythematosus and healthy controls. Moreover, patients with renal involvement had statistically significant hypo-complement levels (C3 and C4) and significant elevated CRP in comparison to healthy participants, still the CRP in the LN group remained at lower levels than in the active SLE group (Table 1). PLR showed statistically significant increased values in SLE patient groups as compared with the control group (*P*=0.01). Even in comparison with one another in the SLE groups, there was statistically significant increase in the PLR where the highest ratio was in the active SLE group followed by the LN group and the lowest PLR was in the SLE with the remission group. While NLR showed a nonsignificantly increased value (*P*=0.2) in the SLE on the remission group in comparison to the control group, a significant increase in NLR was noticed in the active SLE group, followed by the LN group in comparison to the SLE on remission and the control groups.

Table 1 Baseline and laboratory characteristics in the studied population

	SLE on remission [n (%)]	Active SLE [n (%)]	Lupus nephritis [n (%)]	Control [n (%)]	<i>P</i> ₁	<i>P</i> ₂	<i>P</i> ₃	<i>P</i> ₄	<i>P</i> ₅	<i>P</i> ₆
Number	28	12	80	40						
Age (years)	29.07±7.32	27.56±5.67	29.99±8.73	29.16±7.33	0.34	0.11	0.09	0.98	0.55	0.76
Sex										
Male	2 (7.1)	3 (25)	14 (17.5)	15 (18.7)	0.06	0.10	0.21	0.87	0.11	0.87
Female	26 (92.9)	8 (75)	66 (82.5)	55 (81.3)						
ESR (mm/h)	30.11±8.11	44.56±11.56	41.76±10.76	19.09±5.89	0.03	0.01	0.01	0.01	0.01	0.01
CRP (mg/l)	6.18±0.56	13.33±5.13	11.56±3.45	2.11±0.96	0.01	0.01	0.34	0.05	0.01	0.03
ANA (%) (number of +patients)	(83.3)	(89.3)	(86.3)	0	0.11	0.46	0.01	0.49	0.01	0.01
Anti-ds DNA (%)	(50)	(91.7)	(66.3)	0	0.02	0.56	0.01	0.49	0.02	0.01
C3	102 (80.9–120)	85.50 (45–114.25)	77.6 (42.2–107)	112 (96.9–130)	0.01	0.46	0.01	0.04	0.9	0.01
C4	22.50 (15.00–35.00)	18.9 (13.6–23.2)	18.1 (8.6–24.5)	23.2 (20.0–28.4)	0.01	0.5	0.02	0.05	0.10	0.01
Hemoglobin (g/dl)	11.97±4.65	11.67±2.76	11.98±4.44	12.76±1.87	0.45	0.14	0.39	0.40	0.10	0.09
Platelets (×10 ⁶ /ml)	274.11±34.08	243.76±56.7	250.40±34.98	275.98±44.44	0.52	0.12	0.21	0.34	0.43	0.24
TLC (×10 ⁶ /ml)	6.11±2.66	7.45±2.22	7.11±3.11	7.19±2.02	0.45	0.11	0.65	0.40	0.53	0.06
Neutrophil (×10 ⁶ /ml)	3.31±1.85	6.36±3.85	5.91±3.30	4.53±1.51	0.01	0.01	0.13	0.94	0.10	0.04
Lymphocytes (×10 ⁶ /ml)	1.78±0.83	0.65±0.37	1.17±0.73	2.23±0.69	0.02	0.01	0.02	0.89	0.01	0.03
Creatinine (mg/dl)	0.71±0.18	0.71±0.20	3.41±1.31	0.82±0.15	1.00	0.01	0.98	0.01	0.99	0.01
Proteinuria (g/day)	0.17±0.06	0.15±0.06	1.77±1.20	0.16±0.07	1.00	0.01	1.00	0.01	1.00	0.01
PLR	178.92±19.85	411.57±69.41	281.98±20.18	134.22±51.67	0.01	0.01	0.05	0.01	0.01	0.01
NLR	2.02±0.93	10.54±1.81	6.88±2.90	2.14±1.77	0.01	0.01	0.2	0.05	0.01	0.01

Data were estimated in the form of mean (SD) and frequency (percentage). *P* value was significant if less than 0.05. ANA, antinuclear antibody; anti-ds DNA, anti-double-stranded DNA; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LN, lupus nephritis; *P*₁, compared between active SLE group and SLE on remission; *P*₂, compared between active SLE group and lupus nephritis; *P*₃, compared between active SLE group and control group; *P*₄, compared between SLE on remission with lupus nephritis group; *P*₅, compared between SLE on remission and control group; *P*₆, compared between lupus nephritis group and control group; SLE, systemic lupus erythematosus.

Table 2 Correlations between platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio with markers of systemic lupus erythematosus activity and of renal impairment in lupus nephritis

	NLR		PLR	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Serum creatinine	0.32	<0.001	0.14	0.19
Urea	0.44	0.004	0.11	0.08
ESR	0.10	0.34	0.09	0.14
CRP	0.29	0.05	0.15	0.05
24-h urinary proteins	0.18	0.10	-0.04	0.69
C3	-0.20	0.24	-0.30	0.60
C4	-0.37	0.17	-0.48	0.02
SLEDAI	0.53	0.001	0.50	0.01

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Table 4 Regression analysis for the prediction of advanced pathological classes (class III, IV, and V) of lupus nephritis

	Odd's ratio	95% confidence interval	<i>P</i> value
CRP	0.44	0.11–1.98	0.33
24-h urinary protein	1.87	1.33–3.45	0.01
Ant-ds DNA	0.98	0.33–2.80	0.44
NLP	1.11	1.09–2.01	0.01
PLR	1.03	1.01–1.59	0.04
Creatinine	1.09	0.67–1.88	0.50
ESR	0.98	0.55–1.11	0.13

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio.

Correlations between platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio with markers of renal impairment in lupus nephritis patients

To detect the relevance between PLR and NLR levels and diagnostic markers in LN, correlation coefficients (Spearman's ρ) were calculated. Table 2 showed significant evidence for positive correlation between NLR with serum creatinine, urea, and CRP with no correlation between NLR and 24 h urinary proteins; furthermore, the PLR demonstrated significant positive correlation with CRP only.

Platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio relation with different pathological classes of lupus nephritis

Table 3 demonstrate the relation between NLR and PLR and different pathological classes in renal biopsy. The regression analysis in Table 4 shows that PLR, NLR, and 24 h urinary proteins had statistically significant association with the advanced classes of renal pathology in SLE patients.

Receiver-operating characteristic analyses

NLR cutoff value of more than 3.8 with 98% sensitivity and 58% specificity was typical for speculating the lupus activity, while the typical PLR cutoff value was 190.5 with 90% sensitivity and 58% specificity (Fig. 2).

Table 3 Platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio levels in different pathological classes of lupus nephritis

Stages	PLN	NLR
II	202.96±48.17	4.01±1.44
III	222.32±68.38	5.55±2.10
IV	267.94±35.34	6.27±2.30
V	300.13±27.60	8.24±2.38
<i>P</i> ₁	0.04	0.02
<i>P</i> ₂	0.01	0.01
<i>P</i> ₃	0.03	0.04
<i>P</i> ₄	0.01	0.04
<i>P</i> ₅	0.01	0.03
<i>P</i> ₆	0.03	0.01

Data were estimated in the form of mean (SD). NLR, neutrophil lymphocyte ratio; *P*₁, compared between stages II and III; *P*₂, compared between stages II and IV; *P*₃, compared between stages II and V; *P*₄, compared between stages III and IV; *P*₅, compared between stages III and V; *P*₆, compared between stages IV and V; PLR, platelet lymphocyte ratio. *P* value was significant if less than 0.05.

For speculating renal involvement in SLE patients, the ROC/AUC analysis showed a sensitivity of 88.9% for PLR, and a specificity of 87.5% for NLR when a cutoff value of more than 2.83 was used for NLR. However, the sensitivity of PLR was 88.9% and specificity 50% when the cutoff value is 0.72 (Fig. 3).

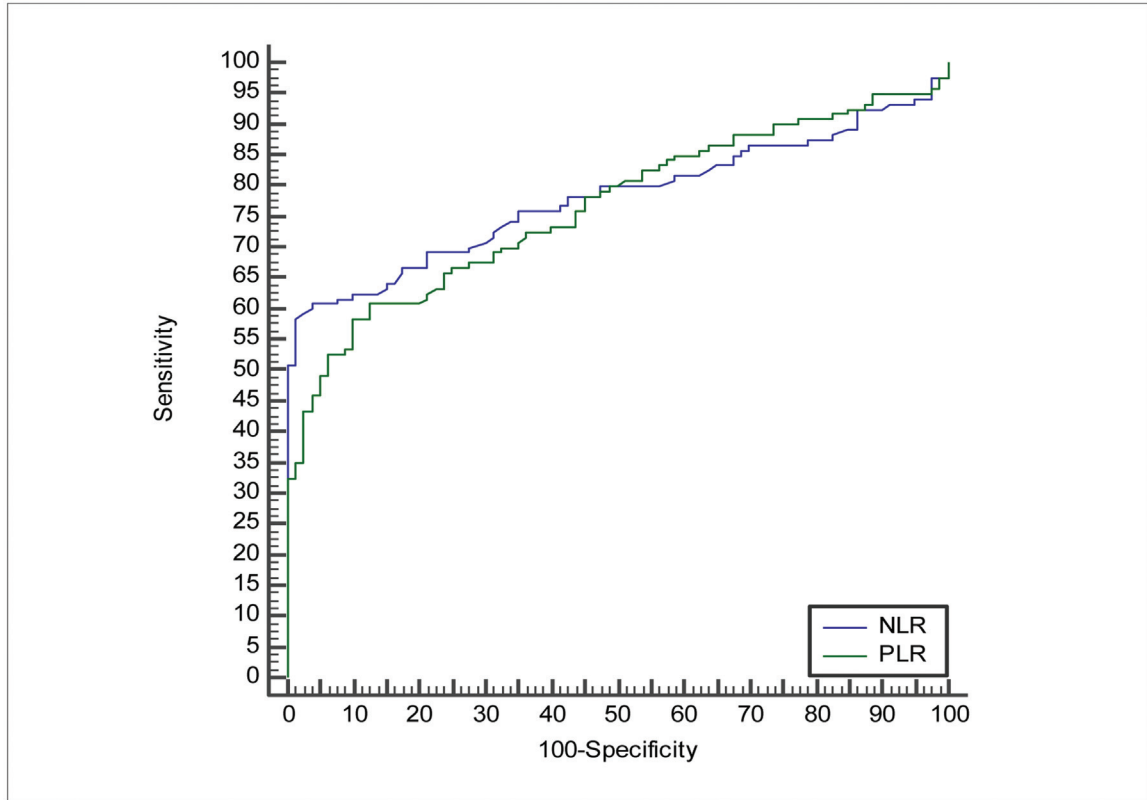
Analyses of the datum estimated on the ROC for NLR and PLR to predict SLE activity. The ideal NLR cutoff value of more than 3.8 had 98% sensitivity and 58% specificity [95% confidence interval (CI): 0.542–0.875, *P*=0.024], while the optimal PLR cutoff value of more than 190.5 had 90% sensitivity and 58% specificity (CI: 0.614–0.911, *P*=0.005).

ROC analysis of both hematological indices (PLR and NLR) in the prediction of renal involvement in lupus patients. The ROC/AUC analysis showed a sensitivity of 83.3%, and a specificity of 87.5% when a cut off value of more than 2.83 was used for NLR (95% CI: 0.594–0.901, *P*=0.007). However, the sensitivity of PLR was 88.9% and specificity was 50% when the cutoff value is more than 111.3.

Discussion

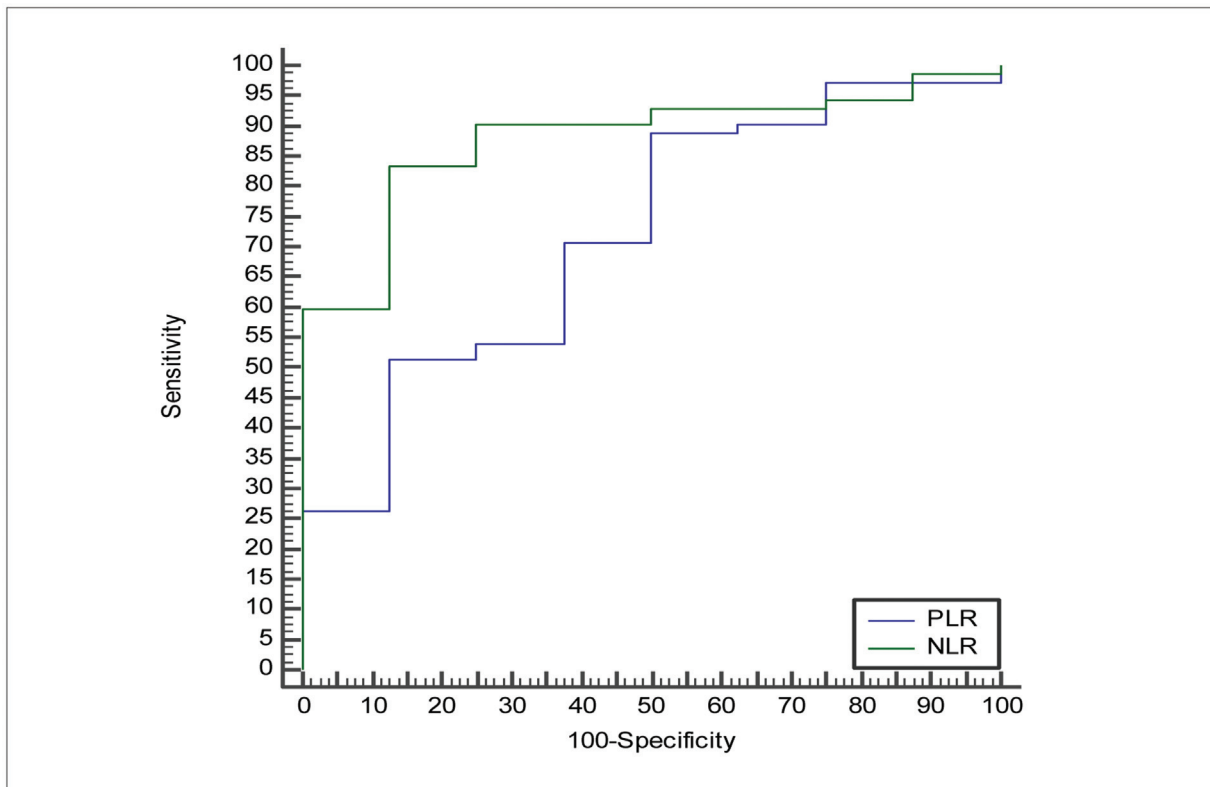
Our current study showed that PLR and NLR were high in patients with SLE with renal involvement in comparison to both healthy controls, and surprisingly, in comparison to SLE patients on remission without renal involvement. It was also worthy to note that both ratios increased significantly in active lupus patients as compared with those with remission. Besides, we found that NLR correlated with kidney functions (serum creatinine and urea) and with CRP (acute-phase

Figure 2



Diagnostic accuracy of platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios in diagnosing activity in patients with systemic lupus erythematosus.

Figure 3



Diagnostic accuracy of platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios in diagnosing renal impairment in patients with systemic lupus erythematosus.

reactant). Another interesting finding was the negative correlation found between PLR and C4. Interestingly, our study showed a statistically significant association between both ratios and the renal WHO pathological classes of LN, which is known to be the cornerstone in the diagnosis of LN and seems to be important for evaluating the level of kidney injury in LN. It is worth noting that the study showed that both ratios were elevated significantly in advanced pathological classes. From the ROC analyses and the calculation of correlations between PLR, NLR, and renal markers we conclude that PLR and NLR are the most promising candidates to act as noninvasive biomarkers in health clinics for renal involvement in SLE where the cutoff to predict activity in SLE was more than 3.8 for NLR and more than 190.5 for PLR. Also, we recorded the highest accuracy with an NLR level of 2.83 for predicting LN, with a sensitivity of 83.3% and a specificity of 87.5%.

It is well known that CBC is a routine, simple, and frugally used requisite laboratory test, which include the count of blood cells mainly platelet count, red blood cell, and white blood cell. The most considerable white blood cells in healthy populations are neutrophils, which have important roles during the inflammation process and during development of immune disorders [13]. It is familiar that the blood assembly undergoes relative changes in situations of systemic inflammation, mainly in the form of neutrophilia, lymphopenia, and anemia [14]. In modern years, neutrophil, lymphocyte, and platelet levels have been known as markers of inflammation in several disorders. NLR has been used in incorporation with other inflammatory markers to predict systemic inflammation in both autoimmune and nonautoimmune diseases [8]). PLR had been estimated in patients with multiple medical conditions including chronic inflammatory disorders, cardiovascular disorders, myeloproliferative disorders, malignancies, and infectious conditions [15,16]. Lupus is an inveterate immunological disorder that is characterized by remitting-relapsing paths. Resulting comorbidities might be reduced when health clinics realize relapse. Considering that renal embroilment is one of the main determinants of bad alarms of SLE prompt and rapid prediction and management of LN are highly desirable for SLE patients [17]. So, the aim of the current study was the evaluation of potential relevance of both hematological ratios (NLR and PLR) to SLE activity and renal participation in health clinics and we found that PLR and NLR can do as dependable and readily measurable markers of renal involvement in SLE. Our results are in harmony with Qin *et al.* [8], who detected high levels of PLR and NLR in SLE

patients in contrast to healthy controls. In his research, NLR was positively correlated with CRP, ESR, and SLEDAI score. PLR was positively correlated with SLEDAI score. In addition, the NLR level of 2.06 was determined as a predictive cutoff value for the diagnosis of SLE, and the NLR level of 2.66 as a predictor of LN. However, no cutoff value to predict LN could be determined for PLR as the AUCs were less than 0.7 that is different from our results which showed that PLR could be used in the prediction of LN as the cutoff value in our results was more than 111.3 with a sensitivity of 88.9% and specificity of 50%. This finding could be explained by the increased serum creatinine level in the advanced classes of LN, which is known to be associated with increased PLR and NLR [18]. The results of Wu *et al.* [19] showed that PLR and NLR levels were increased in SLE patients in comparison to healthy control. Both ratios were connected significantly with lupus activity index 2000 (SLEDAI-2K); moreover, NLR alone was significantly increased in LN and the best NLR cutoff value to predict SLE patients with severe disease was 2.26 with 75% sensitivity and 50% specificity, where the preferable PLR cutoff value for the intense disease was 203.85 with 42.3% sensitivity and 83.9% specificity. Other studies as those of Ayna *et al.* [20] found NLR to be significantly increased in the LN group of patients as parallel to SLE patients without renal involvement. All these previously mentioned results were in concordance with ours. In addition, our results documented also a positive association between CRP and NLR in the LN group. Another important finding by Ayna *et al.* [20] who found that a cutoff of 1.93 for NLR had 83% sensitivity and 54% specificity in classifying lupus patients with nephritis from those without. Other studies as that of Oehadian *et al.* [21] stated that a cutoff value greater than or equal to 1.93 for NLR had a sensitivity of 0.70 and a specificity of 0.67 in identifying lupus patients from healthy control. Hematological aberrations are usually found in lupus patients. A decrease in red blood cells, white blood cells, and platelets may happen as a result of the associated bone marrow immunological suppression or exaggerated peripheral cell devastation. A decrease in the white blood cell in lupus might be as a result of decrease in the lymphocyte count and/or the neutrophils. Neutropenia is a widespread merit in lupus disorder that is mediated by antineutrophil antibodies. Different potential reasons for hematological aberrations in lupus patients are infections and drugs [22]. Interestingly, NLR was found to be increased progressively with progression of renal diseases [23]. The major utility we benefit from

our results is that both hematological ratios (PLR and NLR) could be simply estimated from regular CBC checked in health clinics and are cheaper and simple than other inflammatory biomarkers. In addition, these ratios are comparatively stable as each leukocyte count might be changed by dehydration, rehydration, and diluted blood samples and so they can be used for the prediction of renal involvement and renal pathological classes in LN. Unfortunately, few limitations to the study is present. First, the comparatively small specimen size that might obstacle the popularization of our findings in this field. Finally, the effect of drug therapy on PLR and NLR was not studied. In conclusion, we document a statistical proof that we can use PLR and NLR as inflammatory biomarkers to estimate lupus flare as there is a correlation between both PLR and NLR and SLEDAI. And the most important finding is the ability, simplicity, and feasibility of using hematological ratios in early prediction of renal involvement in lupus patients in health clinics as it is correlated to renal markers in SLE and is linked with the different classes of its histological staging.

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Conflicts of interest

There are no conflicts of interest.

References

- 1 Putterman C, Caricchio R, Davidson A, Perlman H. Systemic lupus erythematosus. *Clin Dev Immunol* 2012; 12:437282.
- 2 Gaballah NM, El-Najjar AR. Clinical characteristics and health related quality of life (HRQoL) in Egyptian patients with systemic lupus erythematosus. *Egypt Rheumatol* 2019; 41:117–21.
- 3 Bertsias GK, Tektonidou M, Amoura Z, Aringer M, Bajema I, Berden JH, *et al.* Joint European League Against Rheumatism and European Renal Association European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and pediatric lupus nephritis. *Egypt Rheumatol* 2019; 41:117–21.
- 4 Giannico G, Fogo AB. Lupus nephritis: is the kidney biopsy currently necessary in the management of lupus nephritis?. *Clin J Am Soc Nephrol* 2013; 8:138–45.
- 5 Donnelly S, Roake W, Brown S, Young P, Naik H, Wordsworth P, *et al.* Impaired recognition of apoptotic neutrophils by the C1q/calreticulin and CD91 pathway in systemic lupus erythematosus. *Arthritis Rheum* 2006; 54:1543–56.
- 6 Soliman W, Sherif N, Ghanima IM, El-Badawy MA. Neutrophil to lymphocyte and platelet to lymphocyte ratios in systemic lupus erythematosus: relation with disease activity and lupus nephritis. *Rheumatol Clin* 2018; 27: S1699.
- 7 Mercan R, Bitik B, Tufan A, Bozbulut UB, Atas N, Ozturk MA, *et al.* The association between neutrophil / lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis. *J Clin Lab Anal* 2016; 30:597–601. 13
- 8 Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, *et al.* Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. *Mod Rheumatol* 2016; 26:372–6.
- 9 Celikbilek M, Dogan S, Ozbakir O, Zararsiz G, Kucuk H, Gursoy S, *et al.* Neutrophil-lymphocyte ratio as a predictor of disease severity in ulcerative colitis. *J Clin Lab Anal* 2013; 27:72–6.
- 10 Sen BB, Rifaioglu EN, Ekiz O, Inan MU, Sen T, Sen N. Neutrophil to lymphocyte ratio as a measure of systemic inflammation in psoriasis. *Cutan Ocul Toxicol* 2014; 33:223–7.
- 11 Hu ZD, Sun Y, Guo J, Huang YL, Qin BD, Gao Q, *et al.* Red blood cell distribution width and neutrophil/lymphocyte ratio are positively correlated with disease activity in primary Sjögren's syndrome. *Clin Biochem* 2014; 47:287–90.
- 12 Feng JF, Huang Y, Chen QX. Preoperative platelet lymphocyte ratio (PLR) is superior to neutrophil lymphocyte ratio (NLR) as a predictive factor in patients with esophageal squamous cell carcinoma. *World J Surg Oncol* 2014; 12:1.
- 13 Bonaventura A, Montecucco F, Dallegri F, Carbone F, Lüscher TF, Camici GG, *et al.* Novel findings in neutrophil biology and their impact on cardiovascular disease. *Cardiovasc Res* 2019; 115:1266–1285.
- 14 Yu H, Jiang L, Yao L, Gan C, Han X, Liu R, Su N. Predictive value of the neutrophil to lymphocyte ratio and hemoglobin in systemic lupus erythematosus. *Experiment Ther Med*. 2018; 16:1547–1553.
- 15 Alan S, Tuna S, Türkoğlu EB. The relation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume with the presence and severity of Behçet's syndrome. *Kaohsiung J Med Sci* 2015; 31:626–31.
- 16 Kim DS, Shin D, Lee MS, Kim HJ, Kim DY, Kim SM, *et al.* Assessments of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in Korean patients with psoriasis vulgaris and psoriatic arthritis. *J Dermatol*. 2016; 43:305–10.
- 17 Grande JP. Experimental models of lupus nephritis. *Exp Models Renal Dis* 2011; 169:183–97.
- 18 Toraman A, Aras F, Hekimsoy Z, Kursat S. Is There a relationship between parathyroid hormone and neutrophil lymphocyte ratio or platelet lymphocyte ratio? *Acta Endocrinologica (Buc)* 2019; 5:96–101. doi: 10.4183/aeb.2019.96.
- 19 Wu Y, Chen Y, Yang X, Chen L, Yang Y. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were associated with disease activity in patients with systemic lupus erythematosus. *Int Immunopharmacol* 2016; 36:94–9.
- 20 Ayna AB, Ermurat S, Coskun BN, Harman H, Pehlivan Y. Neutrophil to lymphocyte ratio and mean platelet volume as inflammatory indicators in systemic lupus erythematosus nephritis. *Arch Rheumatol* 2017; 32:021–5.
- 21 Oehadian A, Suryadinata H, Dewi S, Pramudyo R, Alisjahbana B. The role of neutrophil lymphocyte count ratio as an inflammatory marker in systemic lupus erythematosus. *Acta Med Indones* 2013; 45: 170–4.
- 22 Hepburn AL, Narat S, Mason JC. The management of peripheral blood cytopenia in systemic lupus erythematosus. *Rheumatology* 2010; 49:2243–54.
- 23 Kocuyigit I, Eroglu E, Unal A, Sipahioglu MH, Tokgoz B, Oymak O, Utas C. Role of neutrophil/lymphocyte ratio in prediction of disease progression in patients with stage-4 chronic kidney disease. *J Nephrol* 2013; 26:358–365.
- 24 Xuejing Z, Jiazhen T, Jun L, Xiangqing X, Shuguang Y, Fuyou L. Urinary TWEAK level as a marker of lupus nephritis activity in 46 cases. *J Biomed Biotechnol* 2012; 2012:359647.
- 25 Markowitz GS, D'Agati VD. The ISN/RPS 2003 classification of lupus nephritis: An assessment at 3 years. 2007; 71:491–495.