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Original article

Validation of the neutrophil/albumin ratio in discriminating infection from disease activity among systemic lupus erythematosus patients

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ABSTRACT

Background: The neutrophil/albumin ratio (NAR) has emerged as a novel biomarker in inflammatory conditions. This work aimed to assess the role of the neutrophil/albumin ratio in the differentiation between systemic lupus erythematosus (SLE) activity and infection in lupus patients. **Methods:** A cross-sectional study was conducted on SLE patients classified into two groups according to the evidence of infection: 36 non-infected lupus patients and 53 infected lupus patients at the Rheumatology and Rehabilitation Department. The Neutrophil/albumin ratio (NAR), erythrocyte sedimentation rate/C-reactive protein ratio (ESR/CRP), neutrophil/lymphocyte ratio (NLR), Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K), and evidence of bacterial infection were detected in both groups. **Results:** NAR had significant positive correlations with other parameters of infections, including procalcitonin levels (r = +0.73, P≤0.001) and NLR (r = +0.582, P≤0.001). Additionally, there was a significant negative correlation between NAR and ESR/CRP ratio (r = -0.450, P≤0.001); however, the correlation between NAR and SLEDAI was very weak (r = +0.080, P=0.455). NAR at a cut-off of 110.85 and 95% CI was 96.2% sensitive, 80.6% specific, and 89.9% accurate for the detection of infection among SLE patients; however, at the same cut-off, it was 70.9% sensitive, 44.1% specific, and 60.7% accurate for prediction of flare among SLE patients. **Conclusion:** NAR is a rapid, feasible, affordable, and valid test for detecting infection in SLE patients. It has 96.2% sensitivity, 80.6% specificity, and 89.9% accuracy, which would be valuable in distinguishing infection from flare-up in SLE.

Introduction

Infections are common complications in patients with systemic lupus erythematosus (SLE) and affect 25–50% of them [1]. Lupus patients are more susceptible to infections due to a combination of factors, including immune dysregulation, high disease activity, immunosuppressive treatments, renal and vascular involvement, and organ failure with irreversible damage [2]. Infection is one of the main causes of morbidity, mortality, and hospital admissions in lupus patients [3].

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In clinical practice, it might be difficult to distinguish between activity and infection in SLE because of their similarities in clinical spectra. Infections and disease activity need different treatment regimens [4]. Fever is a typical symptom not only of infection but also of SLE flare-up. When SLE patients present with fevers, physicians should determine the cause of the fever [2]. Appropriate treatment of lupus flare with immunosuppressive drugs is often delayed until an infectious process is ruled out, so an accurate diagnosis is essential [5].

Numerous biomarkers have been identified to distinguish between an infection and a flare in SLE, but they have certain drawbacks. Inflammatory biomarkers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), low serum albumin, and white blood cell count (WBC) are of limited utility since they cannot particularly discriminate bacterial infections from SLE flare-ups [6-9]. Furthermore, confirming or ruling out infection likely requires more than one biomarker. This suggests that new scores, including different biomarkers, could better differentiate these two clinical spectrums [10].

As previously reported in active-SLE patients, neutrophils are the first inflammatory cells present at the inflammatory site, leading to neutrophilia [11]. Although high neutrophil count is a significant indicator of systemic infection, neutrophil counts alone are of limited value in differentiating infection from flare in SLE [12,13]. This is attributed to the multiple causes of neutrophilia in lupus patients, such as flare-ups, infection, corticosteroid bursts, or pregnancy [14].

Hypoalbuminemia is common in SLE and occurs in 30% to 50% of patients. Low serum albumin levels in SLE may be due to increased fractional catabolism of albumin in active disease, nephrotic range proteinuria, poor protein and calorie intake, chronic lupus peritonitis with ascites, protein-losing enteropathy, and liver disease [15]. Additionally, albumin is a negative acute-phase reactant and decreases in acute infection [16]. The clinical importance of these results is that hypoalbuminemia alone will not be a reliable marker for determining disease activity in SLE [17].

Neutrophil/albumin ratio (NAR) is a novel peripheral inflammatory biomarker that indicates systemic inflammation and mortality [18]. Recently, NAR has been evaluated in patients with COVID-19 infection, cancer, cardiogenic shock, and schizophrenia because higher NAR denotes an enhanced inflammatory condition [18, 19]. To our knowledge, no studies have been done to clarify the utility of the neutrophil/albumin ratio in the differentiation between SLE activity and infection in SLE. Therefore, the current research aimed to evaluate the role of the neutrophil/albumin ratio for this purpose.

Methods

Design and Setting

A cross-sectional study was conducted in the inpatient and outpatient clinics at the Rheumatology & Rehabilitation Department, Zagazig University hospitals, Egypt, between February 2023 and May 2024.

Study participants

All patients enrolled in the study were > 16 years old and diagnosed to have SLE if they fulfilled the Systemic Lupus International Collaborating Clinics (SLICC) criteria revision of the American College of Rheumatology (ACR) classification criteria for SLE [20]. On the other hand, patients with other auto-immune diseases, malignancies, chronic infection (e.g., osteomyelitis, endocarditis, HIV), and ischemic heart disease were excluded from this study. Moreover, any patient with a history of antimicrobial use during the 7 days before the assessment day was also excluded.

Sample size and patient selection

The sample size was calculated using Epi software version 6 at a confidence interval of 95%, the percentage of infection among SLE patients according to the Dorgham et al. study was 69,6% [3]. So, the sample was 89 SLE patients selected by a simple random sample.

The SLE patients were classified into two groups according to the evidence of infection as follows: 36 SLE patients without infections and 53 patients with infections. Evidence of bacterial infections, such as positive microbial culture or polymerase chain reaction, was done for viral infection. The fungal infection was detected by an expert dermatologist who took a scraping from infected skin or nails for analysis by molecular tests, while protozoal infections were diagnosed by microscopic analysis or biochemical tests such as stool analysis.

Data was collected from patient records and clinical consultations, including history taking, general, musculoskeletal, and systemic examinations. Additionally, patients were assessed

for disease activity by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score [21]. SLE activity was categorized according to Yee et al. as follows: Active SLE: SLEDAI > 4, Inactive SLE: SLEDAI ≤4 [22].

All laboratory tests were done in Zagazig University Hospital laboratories, such as complete blood cell count (CBC), including differential cell count, was done by an automated cell counter symex KX21, erythrocyte sedimentation rate (ESR) by using the Westergren method recorded in mm/hr, C-reactive protein (CRP) by Nephelometer System BN ProSpec, Siemens, serum albumin using Dimension RxL max auto-analyzer, and serum procalcitonin levels by immunoassay techniques (Electrochemoluminescence on cobas 6000).

All routine laboratory tests, including full blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and serum albumin, were done. The erythrocyte sedimentation rate/ C-reactive protein (ESR/CRP) ratio was calculated by dividing the ESR value by the CRP value [9]. The neutrophil/lymphocyte ratio (NLR) was calculated by dividing the absolute value of neutrophils by the absolute value of lymphocytes [4]. The neutrophil/albumin ratio (NAR) was calculated by dividing the absolute neutrophil counts by the albumin levels [18]. Serum procalcitonin levels were also obtained.

Administrative & Ethical Design:

Official approval had been received from the Institutional Review Board (IRB) (ZU-IRB#8072) at the Faculty of Medicine, Zagazig University Hospitals, as well as the Rheumatology& Rehabilitation Department at this University. Written informed consent was gained from every participant. This research was conducted in compliance with The Code of Ethics of the World Medical Association for research including humans, which is the 1964 Helsinki Declaration.

Statistical analysis:

The collected data were coded, entered, presented, and analyzed by computer using a database software program, Statistical Package for Social Science software (SPSS) (Version 20.0, Armonk, NY: IBM Corp). Quantitative variables were expressed as the mean ± standard deviation (SD) (and median with range for not normally distributed data), while the qualitative variables were expressed as a number and percentage. For quantitative variables, independent samples t-test (t) was used as appropriate for normally distributed data, while nonparametric data was evaluated with the Mann-Whitney U Test. Chi-square test ($\chi 2$) or Fisher's exact test was used to assess and detect the relation between different qualitative variables. Sensitivity, specificity, predictive value for positive (PVP), predictive value for negative (PVN), and accuracy were calculated at a 95% confidence interval (CI) to measure the validity. Spearman correlation (r) was used to correlate NAR with procalcitonin, ESR/CRP, and SLEDAI. The results were considered statistically significant and highy statistically significant when the significance probability (P value) was ≤ 0.05* and ≤0.001**, respectively.

Results

A total of 89 SLE patients were included in this study. They were classified according to the evidence of infection into two groups: 36 SLE patients without infections and 53 patients with infections, with a percentage of 40.4% and 59.6%, respectively **(Figure 1)**. The most common type of infection in our patients was urinary tract infection (UTI), 34 %, and the most frequent pathogen was bacterial infections, 66% , as shown in **Table 1**.

As shown in **Table 2**, the mean age of our patients was 33.3±8.5 years old and the higher proportion of them were females (87.6%) with a disease duration median of 7 years. Assessment of SLE disease activity by SLEDAI revealed that 61.8% of our patients had active SLE (SLEDAI >4); however, 38.2% of them had inactive disease (SLEDAI ≤4). SLEDAI grades are illustrated in **Figure 2.**

By assessing the relation between the clinical parameters of SLE patients and the presence of infection, there was a significant relation between the disease activity measured by SLEDAI-2K and the presence of infection (P= 0.044). Additionally, in our patients' infections were significantly associated with the presence of comorbidities (P=0.003), especially diabetes mellitus and dyslipidemias. Also, there was a significant relation between infections and the use of azathiopurine, corticosteroids, cyclophosphamide, and mycophenolate mofetil. Relations among the infection and the laboratory findings in SLE patients are shown in **Table 3**. There were highly significant associations (P ≤0.001) among the presence of

infection and the number of leucocytes, especially neutrophils, serum albumin, CRP, procalcitonin levels, NLR, and the lower median of the ESR/CRP ratio. Moreover, the levels of NAR were significantly higher in SLE patients with infections than those without infections, with a median of 191.3 and 76.4, respectively (**Figure 1).**

Correlations of NAR with the other parameters of infections in **Figure 3** showed a statistically significant positive correlation between NAR and procalcitonin levels (r = +0.73, P≤0.001) and also with the NLR (r = +0.582, P≤0.001). Additionally, there was a highly statistically significant negative correlation between NAR and ESR/CRP ratio (r = -0.450, P≤0.001); however, the correlation between NAR & SLEDAI was very weak (r = +0.080, P=0.455). Moreover, the correlation of SLEDAI with procalcitonin, ESR/CRP, NLR among SLE patients demonstrated that there was statistically significant positive correlation between SLEDAI & ESR/CRP (r = +0.309, P=0.003*) but there was weak positive correlation between SLEDAI & procalcitonin (r = +0.201, P=0.059) as well as with NLR (r = +0.162, P=0.129) **(Figure 4)**.

The ROC curve analysis was done to determine the cut-off value of the NAR to detect the presence of infections in SLE patients, and it was found to be 110.85 with an area under the curve 0.969.

In terms of validity, NAR at cut-off 110.85 and 95% CI was 96.2% sensitive, 80.6% specific, and 89.9% accurate for prediction of infection among SLE patients; however, at the same cutoff it was 70.9% sensitive, 44.1% specific, and 60.7% accurate for prediction of flare among SLE patients (**Table 4, Figure 5**).

Table 1. Characteristics of infections among SLE patients (n=53).

Characters	**Infected SLE(n=53)** **No (%)**
Site of infection	
UTI	18 (34%)
Chest	11 (20.8%)
Skin	6 (11.3%)
Oropharangeal	6 (11.3%)
Sinusitis	4 (7.5%)
GIT	6 (11.3%)
Vaginal	2 (3.8%)
Type of pathogen	
Bacterial	35 (66 %)
Viral	10 (18.9%)
Fungal	4 (7.5%)
Protozoal	4 (7.5%)

Table 2. Relations between clinical features of SLE patients and the presence of infection (n=89).

Features	**All SLE (n=89) No (%)**	**SLE without infection (n=36) No (%)**	**SLE with infection (n=53) No (%)**	**P value**
Age in years (mean ± SD)	33.3±8.5	34.1±8.1	32.7±8.8	[a]0.424
Gender				
Male	11 (12.4%)	3.0 (27.3%)	8.0 (72.7%)	[b]0.342
Female	78 (87.6%)	33 (42.3%)	45 (57.7%)	
Disease duration (years)				
Median (range)	7(1-25)	5.5(1.5-17)	7 (1-25)	[c]0.344
SLEDAI				
Median (range)	6 (0.0-23)	4 (0.0-20)	6 (0.0-23)	[c]**0.044***
≤4 Inactive SLE	34 (38.2%)	20 (58.8%)	14 (41.2%)	
>4 Active SLE	55 (61.8%)	16 (29.1%)	39 (70.9%)	
SLEDAI Grades				
No activity	23 (25.8%)	13 (56.5%)	10 (43.5%)	[d]0.074
Mild activity	17 (19.1%)	9.0 (52.9%)	8.0 (47.1%)	
Moderate activity	24 (27.0%)	6.0 (25.0%)	18 (75.0%)	
High activity	17 (19.1%)	7.0 (41.2%)	10 (58.8%)	
Very high activity	8.0 (9.0%)	1.0 (12.5%)	7.0 (87.5%)	
1. Co-morbidities	28 (31.5%)	5.0 (17.9%)	23 (82.1%)	[d]**0.003***
Hypertension	16 (18.0%)	5.0 (31.2%)	11 (68.8%)	[d]0.408
Diabetes mellitus	8.0 (9.0%)	0.0 (0.0%)	8.0 (100%)	[b]**0.015***
Dyslipidemia	8.0 (9.0%)	0.0 (0.0%)	8.0 (100%)	[b]**0.015***
Hypothyroidism	1.0 (1.1%)	0.0 (0.0%)	1.0 (100%)	[b]0.407
Osteoporosis	2.0 (2.2%)	0.0 (0.0%)	2.0 (100%)	[b]0.238
Medications				
Azathioprine	31 (34.8%)	17 (54.8%)	14 (45.2%)	[d]**0.043***
Hydroxychloroquine	80 (89.9%)	33 (41.2%)	47 (58.8%)	[d]0.646
Corticosteriods	63 (70.8%)	18 (28.6%)	45 (71.4%)	[d]**≤0.001****
Mycophenolatemofetil	28 (31.5%)	5.0 (17.9%)	23 (82.9%)	[d]**0.003***
Vitamin	49 (55.1%)	16 (32.7%)	33 (67.3%)	[d]0.097
Cyclophosphamide	24 (27.0%)	4.0 (16.7%)	20 (83.3%)	[d]**0.005***
Analgesic	26 (29.2%)	12 (46.2%)	14 (53.8%)	[d]0.481
Methotrexate	10 (11.2%)	6.0 (60.0%)	4.0 (40.0%)	[b]0.181
Rituximab	2.0 (2.2%)	2.0 (100%)	0.0 (0.0%)	[b]0.083

SD: Standard deviation, [a] Independent samples t-test, [b] Fisher's exact test, [c] Mann-Whitney U Test, [d] Chi square test, Statistically significant (P≤0.05*), Highly statistically significant (P≤0.001**)

Table 3. Relations between laboratory findings and infection in SLE patients (n=89).

Findings Median (range)	**All SLE (n=89) No (%)**	**SLE without infections (n=36) No (%)**	**SLE with infections (n=53) No (%)**	**P value**
Complete blood picture (CBC):				
Leucocytes (×103/mm3)	7.3(1.9-17.9)	5.8 (1.9-9.9)	9.1(2.1-17.9)	**[a]0.001****
Lymphocyte (×103/mm3)	1.8(0.30-4.3)	1.75(0.30-4.3)	1.8(0.4-3.9)	[a]0.598
Neutrophil(×103/mm3)	5.2(0.60-13.1)	3.1(0.60-5.9)	6.7(3.5-13.1)	**[a]≤0.001****
HGB (g/dl)	11.6(7.8-14)	11.6 (8.1-13.8)	11.6 (7.8-14)	[a] 0.828
Platelet(×103/mm3)	265(117-607)	243.5(176-451)	282(117-607)	**[a] 0.003***
Inflammatory markers				
Serum albumin(g/dl)	3.8(2.7-41)	4.26(3.2-41)	3.7(2.7-41)	**[a]≤0.001**[a]**
ESR(mm/h)	34(9-109)	34(12-109)	39(9-109)	[a]0.245
CRP(mg/dl)	5.7(0.60-62.6)	4(0.66-13)	9.1(0.6-62.6)	**[a]≤0.001****
Procalcitonin	0.08(0.0-1.9)	0.0045(0.0-0.23)	0.57(0.05-1.9)	**[a]≤0.001****
ESR/CRP	6.3 (1.03-55)	9.5 (3.07-48.7)	3.9(1.03-55)	**[a]≤0.001****
NLR	2.9(0.68-32)	2.17(0.68-32)	3.8(2.1-22.7)	**a≤0.001****
NAR	128.5(16-335.7)	76.4(16-143.9)	191.3 (109- 335.7)	**[a]≤0.001****

SD: Standard deviation, [a] Mann-Whitney U Test, [b] Fisher's exact test, [c] Chi square test, [d] Independent samples t-test, statistically significant (P≤0.05*), Highly statistically significant (P≤0.001**)

Table 4. Validity of Neutrophil/Albumin Ratio for prediction of infection and flare among SLE patients (n=89).

Neutrophil/Albumin Ratio		**Evidence of infection**						
CI (95%)	**Cutoff**	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**	**P value**
	110.85	0.969	96.2%	80.6%	87.9%	93.5%	89.9%	≤0.001**
Neutrophil/Albumin Ratio		**SLEDAI**						
CI (95%)	**Cutoff**	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**	**P value**
	110.85	0.566	70.9%	44.1%	67.2%	48.4%	60.7%	0.299

CI= Confidence Interval, PVP=Predictive value for positive, PVN= Predictive value for Negative

Figure 1. Box plot showing the difference in Neutrophil/Albumin Ratio (NAR) between SLE without infections and SLE with infections (n=89).

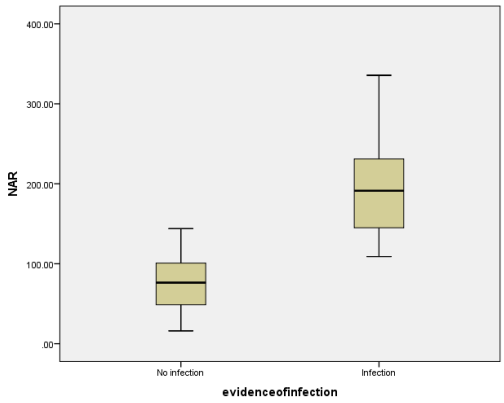


Figure 2. Pie diagram for distribution of SLEDAI Grades among the SLE patients (n=89).

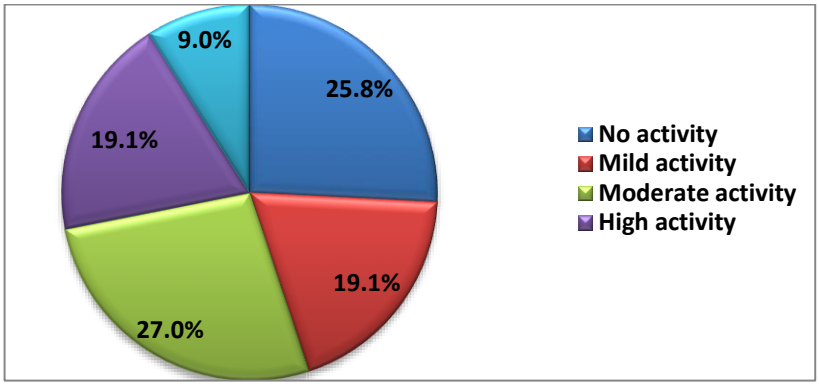
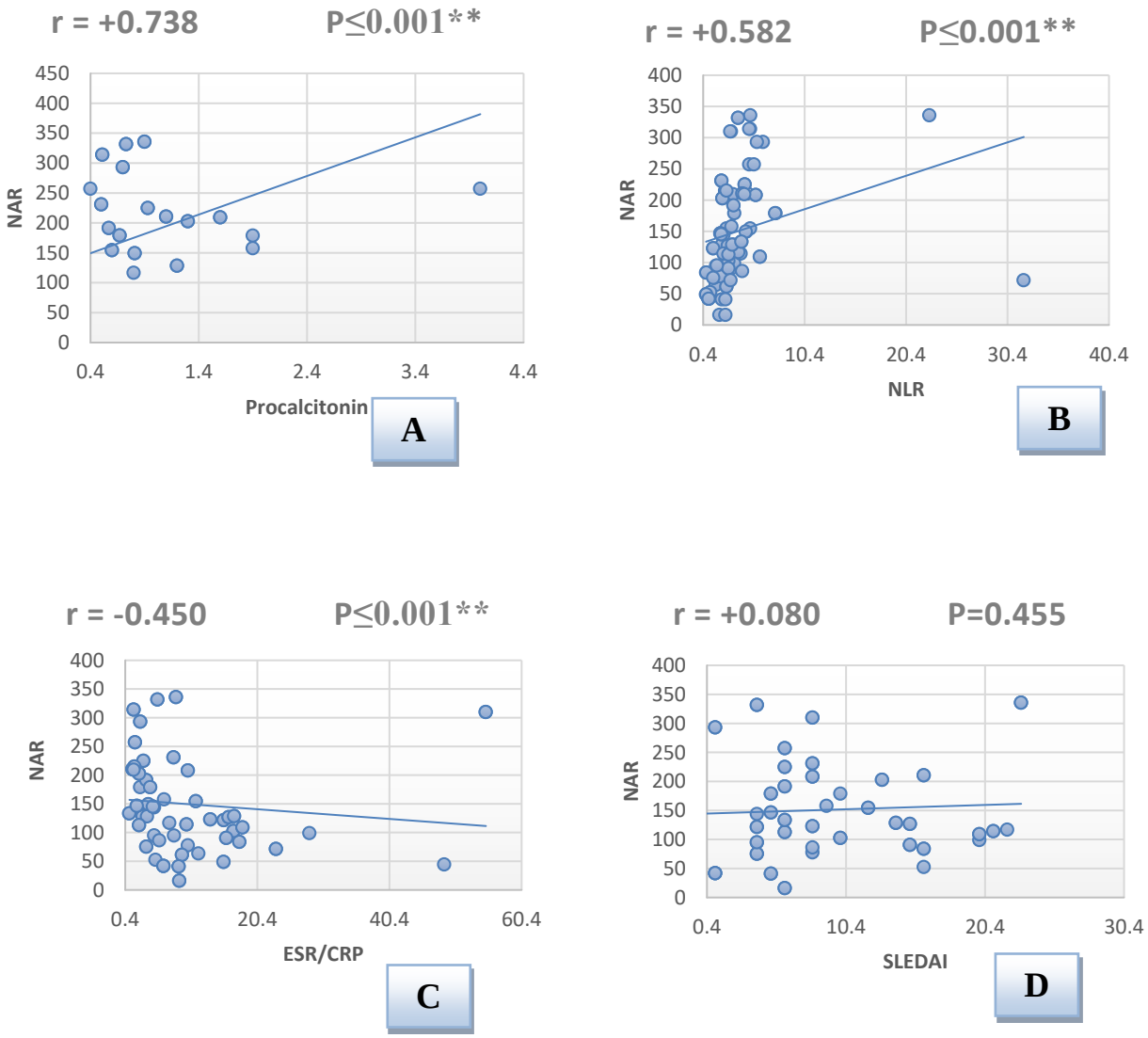
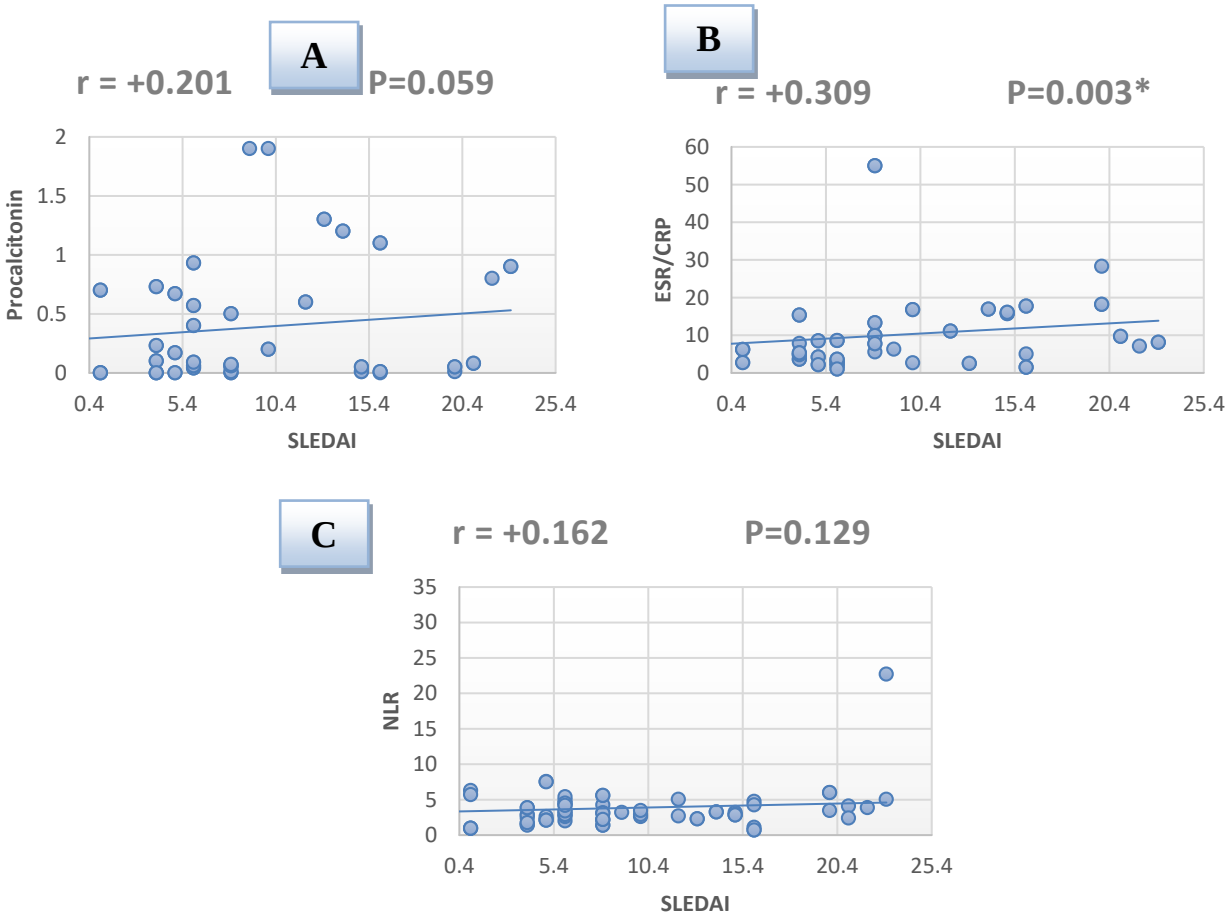


Figure 3. Correlation of Neutrophil/Albumin Ratio (NAR) with procalcitonin (A), NLR (B), ESR/CRP (C), SLEDAI (D) among SLE patients (n=89).



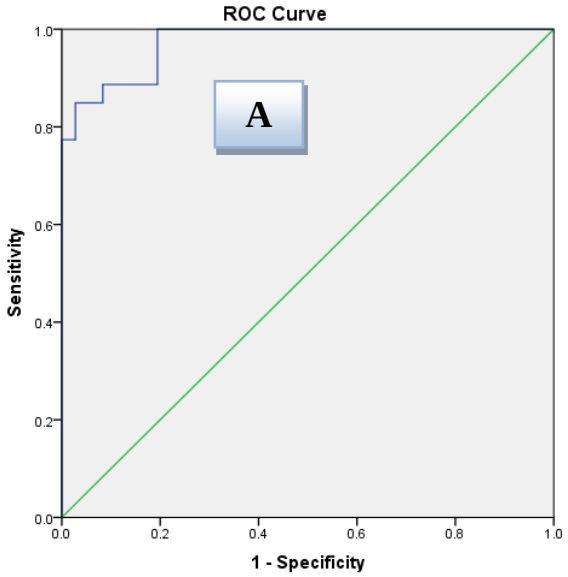
Statistically significant (P≤0.05*), highly statistical significant (P≤0.001**)

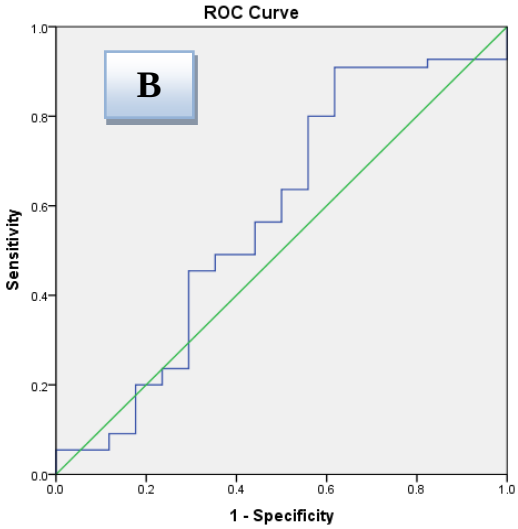
Figure 4. Correlation of SLEDAI with procalcitonin (A), ESR/CRP (B), and NLR (C) among SLE patients (n=89).



Statistically significant (P≤0.05*), Highly statistical significant (P≤0.001**)

Figure 5. ROC curve for validity of Neutrophil/Albumin Ratio for prediction of infection (A) and flare (B) among SLE patients (n=89).





Discussion

Infection is one of the most serious complications in lupus patients that could be life-threatening and require urgent appropriate treatment [1]. Differentiating infections from SLE flare is crucial for the optimal management of lupus patients; hence, in the current study, we evaluated the role of NAR in distinguishing infection from SLE disease activity and compared it with the other parameters of infections in lupus patients [9]. In our work, the most prevalent types of infections were urinary tract infections, 34 %, and chest infections, 20.8%, followed by skin, gastrointestinal tract (GIT), and oropharyngeal infections, 6%. Similarly, Skare et al reported that UTI was the most common infection among their patients [23]. In other studies, chest and cutaneous infections were the most frequent [3, 24].

In this study, the presence of infection was highly associated with SLE disease activity, assessed by SLEDAI-2K, and the presence of comorbidities such as diabetes mellitus and dyslipidemia. These findings were in agreement with other studies [3, 25, 26]. While the grades of activity by SLEDAI-2K showed a non-significant association with infection occurrence in SLE. Additionally, infections were significantly associated with the usage of immunosuppressive medications, including azathioprine, corticosteroids, cyclophosphamide, and Mycophenolate mofetil. Similar results have also been reported with others [23, 27]. On the other hand, *Dorgham et al.* reported a significant association between infections and only the use of cyclophosphamide in lupus patients [3].

On evaluating the laboratory markers of infections, patients with infections had leukocytosis with neutrophil predominance, low serum albumin, and significantly higher levels of CRP, procalcitonin (PCT), and NLR than those without infections. These results were in line with *Luo et al.*, who found that CRP levels, PCT levels, percentage of lymphocytes, and NLR were independent factors for anticipating the presence of infection in lupus patients [10]. Additionally, they stated that CRP has more sensitivity and specificity than PCT in detecting bacterial infection in lupus [10, 28]. On the contrary, some studies reported that PCT is more specific than CRP in the diagnosis of infection; however, it could be more costly and less available than CRP [29-31].

In another study by *Broca-Garcia et al.*, they found significant associations between the presence of infection and neutrophil count, CRP level, and NLR. They also evaluated the role of NLR in lupus patients and concluded that NLR could be a promising new biomarker for infection in SLE, especially when combined with CRP [4].

A recent study by Abdel-Magied et al [2] comes in agreement with our results. They found a statistically significant differences between SLE patients with infection and without infection in the mean value of neutrophils ($p = 0.008$), neutrophils to lymphocyte ratio (NLR) ($p = 0.023$), ESR 1st hour ($p = 0.002$), CRP value ($p = 0.005$), the mean value of the ESR/CRP ratio ($p = 0.029$) and the value of PCT ($p = 0.002$).

On the other hand, *Littlejohn et al* have introduced the ESR/CRP ratio as a useful method for differentiating infections from flares in lupus patients with fever. They also stated that the

increased value of the ESR/CRP ratio is more suggestive of flare than infections [9]. Similarly, in our study, we found a highly significant association between infections and the lower median value of the ESR/CRP ratio; however, there was no significant association between infections and ESR alone.

Recently, many studies have drawn great attention to the role of NAR as a biomarker for the inflammatory process in several conditions such as COVID-19 infections, cardiogenic shock, schizophrenia, and Behcet's disease [18,19, 32,33].

To the best of our knowledge, this is the first study to evaluate the role of NAR as a marker of infection in SLE. We found a highly significant association between the presence of infection and the NAR, with higher values in lupus patients with infections. Furthermore, the NAR showed highly significant correlations with the studied parameters of infections, including procalcitonin levels, NLR, and ESR/CRP ratio. On the other hand, the correlation between NAR and SLEDAI was a very weak positive correlation. Accordingly, NAR showed high convergent validity with the other methods of detecting infections in SLE patients and could be a reliable test for diagnosing infection in lupus patients.

In our study, the best cut-off value of NAR to detect infection was 110.85 with 96.2% sensitivity, 80.6% specificity, and 89.9% accuracy. On assessment of the validity of the same cut-off value of NAR to detect SLE disease activity, it was found to be 70.9% sensitive, 44.1% specific, and 60.7% accurate. Therefore, NAR at a cut-off value of 110.85 was considered a valid test for the detection of infection among SLE patients, but not a valid test for the detection of flare among SLE patients.

Although the majority of our patients had active disease and a large proportion of them showed moderate activity, NAR showed a weak correlation with the SLEDAI, and this added to the value of NAR in differentiating SLE flare from infection. In addition, we studied many parameters of infections in SLE and compared them with the performance of NAR, which showed a strong convergent validity with them and added more strength to our work. Moreover, NAR is a simple, rapid, and applicable tool that can be easily used in the day-to-day practice and follow-ups of lupus patients. As a result, we strongly recommend the use of NAR, in combination with the other clinical and laboratory parameters of infections, to help in solving the dilemma of distinguishing infections from SLE disease activity. This study has been conducted in one center with the same ethnic groups; a wider cohort and multicenter research are strongly recommended.

Conclusion:

NAR is a rapid, feasible, affordable, and valid test for detecting infection in SLE patients with 96.2% sensitivity, 80.6% specificity, and 89.9% accuracy, which would be valuable in distinguishing infection from flare in SLE.

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Authors' contributions:

D.E & N.A: designed the work and shared in the drafting of the article, D.E & S.A: acquisition of data, analysis and interpretation of data, and shared in the drafting of the article, R.H & S.A: shared in the drafting of the article and substantively revised it. All authors have read and approved the final manuscript.

Ethical standards:

An official permission was obtained from Institutional Review Board NO. (ZU-IRB#8072). At the Faculty of Medicine, Zagazig University Hospitals and from the Rheumatology& Rehabilitation. The study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki 1964) for studies involving humans. A written informed consent was obtained from the participants.

Consent for publication:

Not applicable.

Competing interests:

The authors declare that they have no competing interests.

Availability of data and materials:

We approve the availability of our data upon request.

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References

1- Beltrán-Ostos A, Moreno S, Vega-Hoyos D, Daza Lesmes A, Marriaga Calderón OJ, Daza Uribe S, et al. Infection detection in patients with systemic lupus erythematosus using a hospital administrative database. Rev Colomb Reumatol 2022; 29(3):171-6.

2- Abdel-Magied RA, Mokhtar NW, Abdullah NM, Abdel-Naiem AM. Infection versus disease activity in systemic lupus erythematosus patients with fever. BMC Rheumatol 2024;8(1):34. doi: 10.1186/s41927-024-00395-6.

3- Dorgham DA, Anwar S. Infection in systemic lupus erythematosus patients. Egyptian Rheumatologist 2021;43(2):115-8.

4- Broca-Garcia B, Saavedra M, Martínez-Bencomo M, Montes-Cortes D, Jara L, Medina G, et al. Utility of neutrophil-to-lymphocyte ratio plus C-reactive protein for infection in systemic lupus erythematosus. Lupus 2019;28(2):217-22.

5- Rao M, Mikdashi J. A Framework to Overcome Challenges in the Management of Infections in Patients with Systemic Lupus Erythematosus. Open Access Rheumatol: Res Revi 2023:125-37.

6- Mehta P, Singh K, Anand S, Parikh A, Patnaik A, Chatterjee R, et al. Differentiating flare and infection in febrile lupus patients: derivation and validation of a calculator for resource constrained settings. Lupus 2022;31(10):1254-62.

7- Karlsson J, Wetterö J, Weiner M, Rönnelid J, Fernandez-Botran R, Sjöwall C. Associations of C-reactive protein isoforms with systemic lupus erythematosus phenotypes and disease activity. Arthritis Res Ther 2022;24(1):139.

8- Schäfer VS, Weiß K, Krause A, Schmidt WA. Does erythrocyte sedimentation rate reflect and discriminate flare from infection in systemic lupus erythematosus? Correlation with clinical and laboratory parameters of disease activity. Clin Rheumatol 2018;37:1835-44.

9- Littlejohn E, Marder W, Lewis E, Francis S, Jackish J, McCune WJ, et al. The ratio of erythrocyte sedimentation rate to C-reactive protein is useful in distinguishing infection from flare in systemic lupus erythematosus patients presenting with fever. Lupus 2018;27(7):1123-9.

10- Luo K-L, Yang Y-H, Lin Y-T, Hu Y-C, Yu H-H, Wang L-C, et al. Differential parameters between activity flare and acute infection in pediatric patients with systemic lupus erythematosus. Sci Rep 2020;10(1):19913.

11- Wang L, Wang C, Jia X, Yang M, Yu J. Relationship between neutrophil-to-lymphocyte ratio and systemic lupus erythematosus: a meta-analysis. Clinics 2020;75:e1450.

12- Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HH, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infec 2020;81(1):e6-e12.

13- Kim H-A, Jung J-Y, Suh C-H. Usefulness of neutrophil-to-lymphocyte ratio as a biomarker for diagnosing infections in patients with systemic lupus erythematosus. Clin rheumatol 2017;36:2479-85.

14- Lewis EE, McCune WJ, Knight JS, editors. Neutrophilia in systemic lupus erythematosus as a potential indicator of

disease activity. ARTHRITIS RHEUMATOl;: WILEY 111 RIVER ST, HOBOKEN 2016 07030-5774, NJ USA.

15- Chen Z, Li M-T, Xu D, Yang H, Li J, Zhao J-L, et al. Protein-losing enteropathy in systemic lupus erythematosus: 12 years experience from a Chinese academic center. PloS one 2014;9(12):e114684.

16- Akirov A, Masri-Iraqi H, Atamna A, Shimon I. 'Low Albumin Levels Are Associated with Mortality Risk in Hospitalized Patients' Am J Med 2017: 130 (12): 1465-e11.

17- Yip J, Aghdassi E, Su J, Lou W, Reich H, Bargman J, et al. Serum albumin as a marker for disease activity in patients with systemic lupus erythematosus. J rheumatol 2010;37(8):1667-72.

18- Varim C, Yaylaci S, Demirci T, Kaya T, Nalbant A, Dheir H, et al. Neutrophil count to albumin ratio as a new predictor of mortality in patients with COVID-19 ınfection. Rev Assoc Méd Bras 2020;66:77-81.

19- Balcioglu YH, Kirlioglu SS. C-reactive protein/albumin and neutrophil/albumin ratios as novel inflammatory markers in patients with schizophrenia. Psychiatry inves 2020;17(9):902.

20- Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012;64(8):2677-86.

21- Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol 2002;29(2):288-91.

22- Yee C-S, Farewell VT, Isenberg DA, Griffiths B, Teh L-S, Bruce IN, et al. The use of Systemic Lupus Erythematosus Disease Activity Index-2000 to define active disease and minimal clinically meaningful change based on data from a large cohort of systemic lupus erythematosus patients. Rheumatol 2011;50(5):982-8.

23- Skare TL, Dagostini JS, Zanardi PI, Nisihara RM. Infections and systemic lupus erythematosus. Einstein (São Paulo) 2016;14:47-51.

24- Al-Rayes H, Al-Swailem R, Arfin M, Sobki S, Rizvi S, Tariq M. Lupus Around the World: Systemic lupus erythematosus and infections: a retrospective study in Saudis. Lupus 2007;16(9):755-63.

25- Ruiz-Irastorza G, Olivares N, Ruiz-Arruza I, Martinez-Berriotxoa A, Egurbide M-V, Aguirre C. Predictors of major infections in systemic lupus erythematosus. Arthritis res ther 2009;11:1-8.

26- Gladman D, Hussain F, Iban D, Urowitz M. The nature and outcome of infection in systemic lupus erythematosus. Lupus 2002;11(4):234-9.

27- Navarro-Zarza J, Alvarez-Hernández E, Casasola-Vargas J, Estrada-Castro E, Burgos-Vargas R. Prevalence of community-acquired and nosocomial infections in hospitalized patients with systemic lupus erythematosus. Lupus 2010;19(1):43-8.

28- Kim H-A, Jeon J-Y, An J-M, Koh B-R, Suh C-H. C-reactive protein is a more sensitive and specific marker for diagnosing bacterial infections in systemic lupus erythematosus compared to S100A8/A9 and procalcitonin. J Rheumatol 2012;39(4):728-34.

29- Song GG, Bae SC, Lee YH. Diagnostic accuracies of procalcitonin and C-reactive

protein for bacterial infection in patients with systemic rheumatic diseases: a meta-analysis. Clin Exp Rheumatol 2015;33(2):166-73.

30- Serio I, Arnaud L, Mathian A, Hausfater P, Amoura Z. Can procalcitonin be used to distinguish between disease flare and infection in patients with systemic lupus erythematosus: a systematic literature review. Clin rheumatol 2014;33:1209-15.

31- Yu J, Xu B, Huang Y, Zhao J, Wang S, Wang H, et al. Serum procalcitonin and C-reactive protein for differentiating bacterial infection from disease activity in patients with systemic lupus erythematosus. Mod Rheumatol 2014;24(3):457-63.

32- Peng Y, Xue Y, Wang J, Xiang H, Ji K, Wang J, et al. Association between neutrophil-to-albumin ratio and mortality in patients with cardiogenic shock: a retrospective cohort study. BMJ open 2020;10(10):e039860.

33- Kamal DE, Zaghlol RS, Hussien MH, Makarm WK. Utility of neutrophil/albumin ratio and C-reactive protein/albumin ratio as novel inflammatory markers in Behcet's disease. Reumatol Clín (English Edition) 2023;19(4):188-96.

Kamal DE, Hassan RA, Abdelsalam SA, Abdelsalam NA. Validation of neutrophil/albumin ratio in discriminating infection from disease activity among systemic lupus erythematosus patients. Microbes Infect Dis 2025; 6(4): 6764-6776.