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A Clinical Utility of Neutrophil Lymphocyte Ratio as A Prognostic Indicator of Systemic Lupus Erythematosus Disease Activity

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with significant morbidity and mortality. Neutrophil lymphocyte ratio (NLR) is associated with different inflammatory diseases.

Objective: To assess NLR as a prognostic indicator of SLE disease activity.

Patients and Methods: this cross sectional study included 100 patients with SLE. Baseline characteristics (age, sex, history of smoking, BMI, smoking status. Disease duration, disease activity index measured by SLEDAI, medications taken, and) were recorded. NLR was measured.

Results: The mean age of patients was 32.01±10.14 years. Females were 91(91%). The mean values of NLR in active SLE was significantly higher than its value in the inactive SLE patients (2.859 ± 0.2151 N=85 VS 1.743 ± 0.2317 N=15, p=0.035). The NLR was a fair valid test to differentiate between active and inactive SLE (area under the curve (AIC)=0.70, p=0.007). At the optimum cutoff value o≥ 2.19, the accuracy was 65% with sensitivity 63.5%, specificity 73.3%, and PPV at pretest 50% was 70.4% and PPV at pretest 90% was 95.5%. and the NPV at 10% was 94.8%. There was no statistical significant correlation between baseline characteristics of the patients (age, sex, BMI, positive smoking history, duration of the disease, prednisolone, hydroxychloroquine, mycophenylate mofetil, and cyclophosphamide intake) with the NLR

Conclusions: NLR was significantly higher in active SLE compared to inactive SLE. It was a valid fair test to differenrentiate between active and inactive SLE with good accuracy and high PPV.

Keywords: Neutrophil lymphocyte ratio (NLR), systemic lupus erythematosus (SLE), inflammatory marker., SLE disease activity index.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic multisystemic autoimmune disease of unknown etiology with different clinical and laboratory characteristics [1[. Neutrophils and lymphocytes play major roles in inflammatory processes. Under inflammatory conditions, neutrophil and lymphocyte counts undergo temporary changes. Neutrophil to lymphocyte ratio (NLR) is calculated as the absolute count of neutrophils divided by the absolute count of lymphocytes. As an index of systemic inflammation, NLR has been identified to be a useful index for the differential diagnosis or prognostic prediction of diseases [2,3]. Many studies have shown that NLR is positively associated with inflammatory diseases, different malignancies, ischemic injury, cardiovascular disease and diabetic nephropathy [4-8] NLR is also a readily available marker that can convey important information about the patient inflammatory activity. NLR can be calculated easily and less costly as compared with detection of other inflammatory cytokines that could be used as biomarkers for inflammatory response or disease activity in SLE patient [9]. The aim of this study was to evaluate the role of NLR in SLE and whether NLR is an independent predictor of SLE activity.

PATIENTS AND METHODS

Study design

This cross sectional study was conducted at the Rheumatology Unit, Department of Medicine in Baghdad Teaching Hospital from November 2012 to 2013. Ethical approval was received from Medical Department of College of Medicine and A signed informed consent was taken from each participants in the study.

Participants

Patients eligible for inclusion in the study had age >20 years and SLE diagnosed by a rheumatologist according to the criteria developed by the American College of Rheumatology [10]. Patients were excluded if they had overlapping other inflammatory arthritis or connective tissue diseases or other chronic diseases that may affect NLR.

Data entry and evaluation

Data using questioners form included: age, sex, history of smoking, weight in kilograms, hight in meter square. disease activity index measured by SLEDAI [11], medication history of steroid and immunosuppressant's. Body mass index was calculated according to following formula [12]: BMI =Body weight (kg)/[Body height(m)]². Complete blood count (CBC), erythrocyte sedimentation rate (ESR), Anti-ds-DNA, Complements (C3, C4, CH50) were recorded. NLR was measured. Urinalysis for measurement of protein, white blood cells, red blood cells and cellular casts was done.

Statistical analysis

Statistical analysis was done using statistical package for social sciences (SPSS) software for windows version 18. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables with normal distribution and as frequencies and proportions (%) for categorical variables. Student's t test was used to compare means of continuous variables between active and inactive SLE.. Receiver operating curve used to see the validity of NLR to differentiate between active and inactive SLE. if AUC ≥ 0.9 mean excellent test, 0.8 – 0.89 means good test, 0.7 – 0.79 fair test otherwise unacceptable. Trapezoidal method used for calculate the curve. Multiple linear regression analysis was done to assess effect of baseline characteristics on NLR.. P<0.05 was considered significant.

RESULTS

A total of 100 patients with SLE were involved in the study. Of them females were 91(91%). The mean age of patients was 32.01±10.14 years. Other demographic and clinical characteristics are shown in Table 1

BMI, body mass index, SLEDAI, systemic lupus erythematosus disease activity index; MMF, mycophenolate mofetil; CYC, cyclophosphamide; AZT. Azathioprine; SD, standard deviation, PMHX, past medical history; n, number.

The mean values of NLR in active SLE was significantly higher than its value in the inactive SLE patients (2.859 ± 0.2151 N=85 VS 1.743 ± 0.2317 N=15, p=0.035) as shown in Figure 1.

Table 1. Demographic and clinical characteristics of SLE patients and controls

Variable	SLE (N=100)
Age (means ± SD) yrs	32.01±10.14
Female n.(%)	91 (91.0)
BMI (mean s± SD) kg/m^2 Smoking Hx positive	27.41±6.04 14(14%)
Duration of SLE (mean s± SD) yrs	5.22 ± 4.64
SLEDAI (means ± SD)	8.63 ± 5.40
Drugs	
Current prednisone dosage (mean± SD, mg)	13.11 ± 10.75
Antimalarials (current), n (%)	50 (50.0)
Methotrexate (current), n (%)	8 (8.0)
MMF (current), n (%)	18 (18.0)
CYC (ever), n. (%)	8 (8.0)
AZT (ever), n. (%)	34 (34.0)
Anti-ds-DNA +ve n. (%)	32 (32.0)

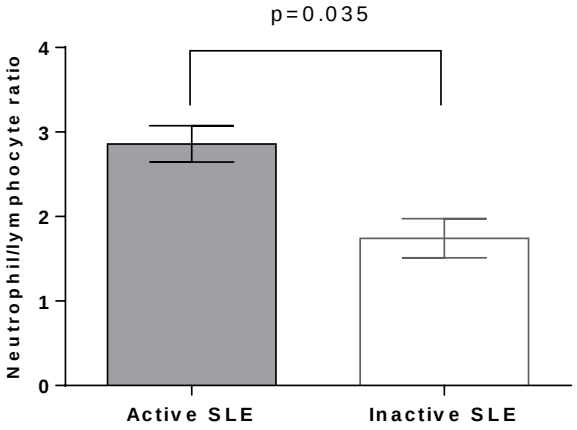

Figure 1: Mean values of NLR in active SLE patients and inactive SLE

The NLR was a valid fair test to differentiate between active and inactive SLE(area under the curve (AIC)=0.70, p=0.007). At the optimum cutoff value o≥ 2.19, the accuracy was 65% with sensitivity 63.5%, specificity 73.3%, and PPV at pretest 50% was 70.4% and PPV at pretest 90% was 95.5%. and the NPV at 10% was 94.8%.

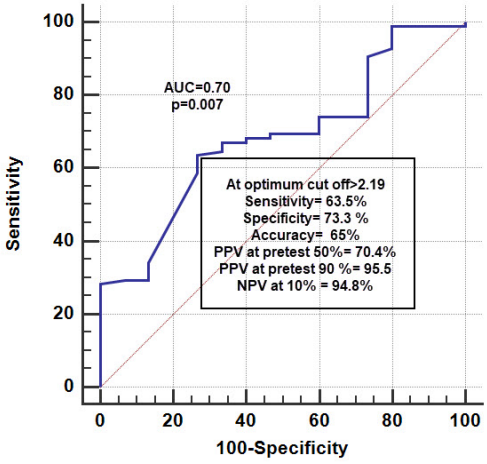

Figure2: ROC curve of neutrophil/Lymphocyte ratio showing the optimum cut off value that differentiate Active SLE from inactive SLE.

In addition, there was no statistical significant correlation between baseline characteristics of the patients (age, sex, BMI, positive smoking history, duration of the disease, preednisolon, hydoroxychloroquin, mycophenolate, and cyclophosphamide intake) with the NLR.as in Table2.

Table2: Multiple linear regression analysis to show effect of baseline characteristics on NLR

Variables	Partial regression coefficient	p value
Age	.020	.413
sex	.535	.472
BMI	-.040	.369
Smoking history positive	2.103	.114
Duration of disease	-.008	.878
Prednisolon	.074	.921
hydroxychloroquin	-.085	.869
Mycophenolate mofetil	-1.973	.074
Cyclophosphmide	1.228	.265

NLR, neutrophil lymphocyte ratio; BMI, body mass index

DISCUSSION

This study assessed NLR as a test to differentiate between active and inactive SLE and revealed that NLR was significantly higher in active SLE patients compated with the inactive SLE patients and It was a fair valid significant test that can diffrenentiate between active and inactive SLE. At the optimum cutoff value of ≥ 2.19, the accuracy was 65% with sensitivity 63.5%, specificity 73.3%, and PPV at pretest 50% was 70.4% and PPV at pretest 90% was 95.5%. and the NPV at 10% was 94.8%. There was no significant effect of baseline characteristics of patients in the NLR. This indicate that no effect of confounders on the result.

The high NLR in active SLE may be explained by the lower lymphocyte in active SLE compared to the inactive one.

Similar findings were reported by other studies Abd-Elhafeez et al reported that Neutrophil Lymphocyte Ratio (NLR) can be used as activity marker in active lupus patients [13].

Amaylia et al. **[14]** observed that NLR was significantly higher in SLE than normal subjects. Also Lixiu et al. **[15]** found that NLR is independently associated with SLE, and showed a significant increase in NLR in Lupus nephritis patients Furthermore, Baodong et al. **[16]** demonstrated that NLR was increased in SLE and positivity correlated with CRP, ESR and SLEDAI. They also observed that NLR was increased in lupus nephritis in comparison to SLE without nephritis. They stated that NLR could reflect inflammatory response and disease activity in SLE patients. On the other hand, Yunxiu et al. **[17]** reported that NLR was increased in SLE patients in comparison to control. They also reported that NLR was increased in active group in comparison to non-active group. Farouk HM et al showed that NLR could reflect inflammatory response and disease activity and disease damagein SLE patients [18].

The current study has some strong points over the previous study. It is the first study that measured the diagnostic accuracy and predictive value of NLR as a test to differentiate active lupus from inactive one. Also our sample was larger than previous studies.

The main limitation of the study is small sample size and being a cross sectional study in a single center. This can be solved by a larger multicenter prospective study. However, this is the first study in Iraq that assessed NLR as a test for SLE disease activity. NLR is cheap, quick and easily measurable and can be promising cheap markers to follow up disease activity.

In conclusion, NLR was a significant valid fair test to differentiate active SLE from the inactive one. Also NLE was an independent significant predictor of disease activity.

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