Neutrophil Lymphocyte Ratio And Platelet Lymphocyte Ratioassociated With Disease Activity In Patients With Systemic Lupus Erythematosus

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Abstract: Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with no well-known cause. The search for simple laboratory indicators is essential to assess the disease activity of the SLE. Currently, the Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) are widely used as markers of the inflammation.
Methods: A cross-sectional analytic study involving 35 patients who met the criteria by Systemic Lupus International Collaborating Clinics (SLICC) 2012 was conducted during August 2019 until June 2020. The samples were obtained from outpatients and inpatients of the Rheumatology Clinic at WahidinSudirohusodo hospital and its collaborating hospitals. The data of the value of neutrophils, lymphocytes, platelets and disease activity were collected using the Mexican Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI).
Results: Of 35 patients with SLE, all were women aged 18-51 years. The result shows that there is a significant relationship between NLR and MEX-SLEDAI scores (p <0.000). Also, PLR is significantly associated with MEX-SLEDAI scores (p <0.000).

Conclusion: NLR and PLR were considerably associated with the degree of disease activity in patients with SLE.

Keywords: Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), MEX-SLEDAI, disease activity, Systemic Lupus Erythematous (SLE).

1. INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease withno well-known cause. SLE has a broad clinical presentation covering almost all organs and tissues. In the United States (US), the prevalence is estimated at 51 per 100,000 people. Even though the exact number of patients with SLE in Indonesia is still unclear, it is estimated to be the same or even greater than that in the United States, with approximately 1,500,000 people (SLE Indonesia Foundation, 2012). The epidemiological data of SLE in all regions of Indonesia is stillunavailable.[1,2]

The search for simple laboratory indicators is essential for assessing the disease activity of SLE. Currently, the Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) are widely used as markers of inflammation. In patients with systemic inflammation, there is a marked change in the number of leucocytes which is generally characterized by neutrophilia and lymphopenia, whereas lymphopeniaoccurs in nearly 93% of cases of SLE. Neutrophils and lymphocytes play a role in the pathogenesis of SLE through the role of T and B cells. [3-6]This study aims to identify the NLR and PLR associated with SLE disease activity.

2. METHOD

An analytical study with a cross-sectional designwas conducted.The primary data were obtained from outpatients and inpatients who were newly diagnosed with SLE at WahidinSudirohusodo Hospital, its network, and rheumatism clinic in Makassar from August 2019 to June 2020. The inclusion criteria of this study were the patients with SLE who were newly diagnosed and willing to participate in the study. Meanwhile, the exclusion criteria for SLE patients were those who had received corticosteroid or immunosuppressant therapy and SLE patients with infection.

The 2012 Systemic Lupus International Collaborating Clinics (SLICC) was employed in the diagnosis of SLE classification criteria, while for SLE disease activity, we used the Mexican Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI). Data analysis was performed using the Statistical Package for Social Science (SPSS) version 22. The statistical analysis was performedusing descriptive statistical calculations with frequency distribution, followed by Pearson's Correlation and Anova test. The result of statistical test was significant if the p value was<0.05. The results are displayed in the form of tables, narration and pictures.

3. RESULTS AND DISCUSSIONS

Of the 35 subjects, all were women aged 18-51 with a mean age of 29.8 ± 8.8 years. The lowest level of neutrophils was 1952.00 and the highest was 8118.90 with a mean of 5124.37. The lowest platelet content was 101 000 and the highest was 453 000 with a mean of 262428.57. The lowest lymphocyte level was 288.00 and the highest was 1320.18 with a

mean of 782.21. The NLR value ranged from 1.25 to 21.06 with a mean of 5.37 ± 4.02. PLR values ranged from 124.93 to 652.05 with a mean of 244.26 ± 113.44. The MEX-SLEDAI score ranged from 1-21 with a mean of 8.63 ± 5.04 (Table 1). In the analysis of disease activity, the grade of mild SLE was found in 10 subjects (28.57%), and moderate SLE was found in 13 subjects (37.14). In fact, the severe SLE was found in 12 subjects (34.29%) (Table 2).

Table 1. The Statistics of Descriptive Variables (n=35)

Variables	Minimum	Maximum	Mean	SD
Neutrophils	1952,00	8118,90	5124,37	1671,75
Platelet	101000	453000	262428,57	92629,97
Limphocyt	288,00	2901,00	1320,18	782,21
NLR	1,25	21,06	5,37	4,02
PLR	124,93	652,05	244,26	113,44
MEX SLEDAI	1	21	8,63	5,04

SD: Standard of Deviation

Table 2.The Distribution ofSLE Categories of Grade (n=35)

Variables		N	%
Disease Activity	Mild	10	28,57
	Moderate	13	37,14
	Severe	12	34,29
	Total	35	100,0

This study involved 35 subjects with all of them female. This is in accordance with the results of a study conducted by Li et al which explained that female subjects had a proportion of over 90% and data from the European League Against Rheumatism (EULAR) which stated that female patients were nine times more likely to have SLE. than men.[1,7] These findings could be attributed to the estrogenic hormone facilitating humoral response which can lead to increased B cell proliferation and antibody production.[8] In addition, this study also showed that the age range of the subjects studied was in the range of 18-51 years with mean age 29.8 ± 8.8 years. This is also consistent with EULAR data showing that SLE patients have an onset of disease between the ages of 16-55 years.[7]

In this study, the mean NLR was 5.37 ± 4.02 and the mean PLR was 244.26 ± 113.44. Qin et al in 2016 also obtained a mean NLR of 3.61 ± 2.04 and a mean PLR of 155.64 ± 91.69 which increased when compared to control subjects.[9]This can be attributed to SLE where there is a systemic inflammatory response. In this inflammatory response, there will generally be changes in the number of leukocyte subtypes, especially a decrease in neutrophil and lymphocyte levels.[10]

Table 3. NLR and PLR associated with MEX SLEDAI score (n=35)			
Variables	Statistics	MEX SLEDAI	
NLR	R	0,882	
	P	0,000	
	N	35	
PLR	R	0,948	
	P	0,000	
	N	35	
r= Pearson's Correlation Coefficient			

This study correlated the NLR and PLR values with LES disease activity based on the MEX SLEDAI score (Table 3). The results showed that there was a significant positive correlation between NLR and MEX-SLEDAI scores (p <0.000). This illustrates that the higher the NLR value, the higher the MEX-SLEDAI score (Figure 1). In addition, there was also a significant positive correlation between NLR and MEX SLEDAI score (p <0.000), where the higher the PLR, the higher the MEX SLEDAI score (Figure 2).
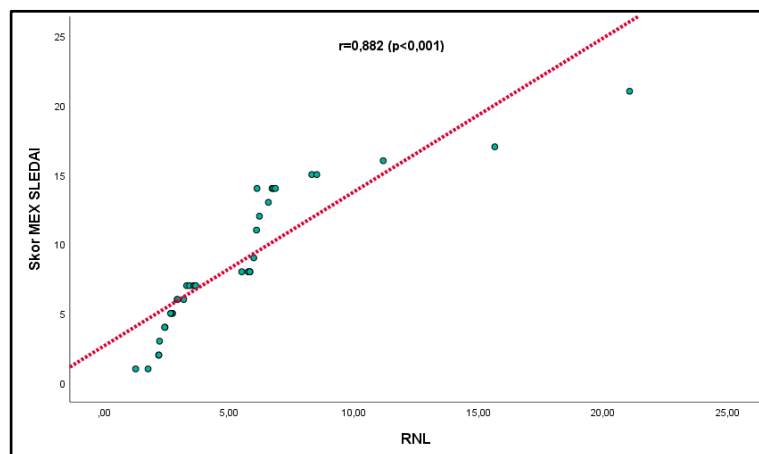

Figure 1. NLR associated with MEX SLEDAI

The level of leukocyte subtypes in the blood is one of the markers of the inflammatory response, where the lymphocyte levels are always decreased in autoimmune diseases, besides that, there is often a decrease in platelet levels in SLE patients, so it can be said that the Neutrophil Lymphocyte Ratio (NLR) and the Platelet Lymphocyte Ratio (PLR) can be used as a marker of the inflammatory response.[9] Wu et al. Conducted NLR and PLR studies on SLE disease activity using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). The study involved 116 samples of SLE patients and 136 control samples with significantly improved NLR and PLR results compared to the control group.[11]
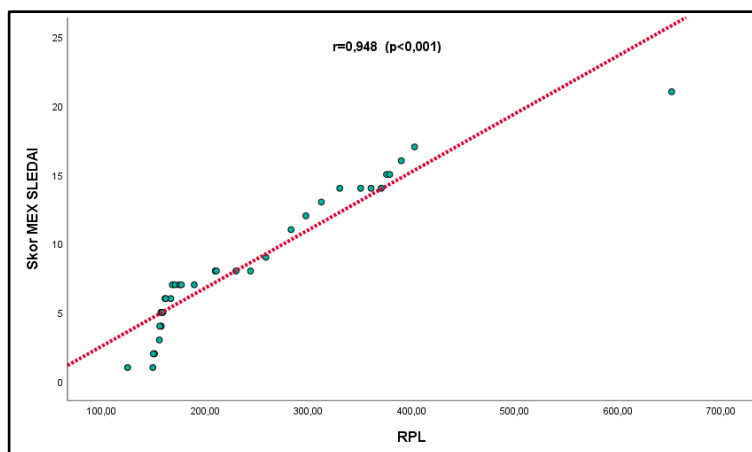
Figure 2. NLR was assicoated with MEX SLEDAI

A meta-analysis study conducted by Ma et al, where nine studies were included in the research comparing the relationship between NLR and SLEDAI scores, found a positive relationship (p <0.001), while six studies comparing the relationship between LPR and SLEDAI scores also revealed a positive correlation (p <0.001) .[12]It is well-known that cytokines have a significant role in the pathogenesis of inflammatory diseases, including SLE. Neutrophils and Platelets are involved in the formation of cytokines that will trigger the activation of neutrophils and platelets. Several recent studies have also shown that leukocytes and their subtypes are very useful in predicting inflammatory processes.[11]

When compared with other autoimmune inflammatory arthritis diseases such as Rheumatoid Arthritis (AR), it was found that the relationship between NLR and PLR on AR disease activity was found. Uslu et al conducted a study on NLR and PLR on disease activity in AR involving 104 AR patients and 51 control samples. The result showed that NLR and PLR increased significantly in the active group of patients based on the Disease Activity Score included 28 joints (DAS28).[13]

Fu et al also conducted a study on NLR and PLR on disease activity in AR using a retrospective study involving 128 AR patients. 78 control samples showed that NLR and PLR had a positive correlation with AR disease activity as assessed using the Disease Activity Score including 28 joints (DAS28) .[14]Erre et al. who conducted a meta-analysis of 13 NLR and 8 PLR studies on RAfound that NLR and PLR were significantly associatedwiththeoccurrenceof RA.[15] Thus, NLR and PLR can be used as markers of inflammation associated with RA disease activity.

Similar findings are also found on psoriatic arthritis studies. Kim, et al. who conducted NLR and PLR studies on psoriasis and psoriatic arthritis patients stated that NLR and PLR were strong predictors of psoriatic arthritis especially in patients with psoriasis.[16]Asahina et al. also performed a study of patients with psoriatic arthritis who were administered with biological therapy for 12 months. After the therapy, the outcome on NLR and PLR were obtained in short.[17]This is in line with the suggestion in this study that NLR and PLR can be used as markers to assess systemic inflammation in patients with psoriasis.

4. CONCLUSION

There is a significant relationship between NLR and PLR on the grades of disease activity in patients with SLE.

5. REFERENCES

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