Original Article

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Correlation of Platelet to Lymphocyte Ratio and C-Reactive Protein to Albumin Ratio with MEX-SLEDAI Scores in Patients with Systemic Lupus Erythematosus

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Abstract

Background: One of the methods used to assess systemic lupus erythematosus (SLE) disease activity is the Mexican systemic lupus erythematosus disease activity index (MEX-SLEDAI) score. Markers of SLE disease activity such as anti-dsDNA antibodies, complement, and anti C1q have limitations in terms of sensitivity and specificity. In rural areas where these markers are not available, simpler alternative markers are valuable. This study aimed to explore markers related to SLE disease activity based on the platelet to lymphocyte ratio (PLR) and C-reactive protein albumin ratio (CAR) using the MEX-SLEDAI score.

Methods: This was a cross-sectional study using a correlational analytical design. Data collection was carried out retrospectively using secondary data taken from medical records of patients with SLE treated at Dr. Hasan Sadikin General Hospital Bandung, Indonesia in 2019–2021 and the Laboratory Information System (LIS). The data was analyzed using the Spearman rank correlation test.

Results: Of the 51 participants, 92% were female with median MEX-SLEDAI scores of 9. The median value of PLR and CAR were 247.07 and 2.01, respectively. The CAR showed a moderate positive correlation ($r=0.563$, $p<0.001$), whereas the PLR showed no correlation ($r=0.023$, $p>0.05$) with the MEX-SLEDAI score.

Conclusions: MEX-SLEDAI score has a moderate positive correlation with CAR, suggesting that CAR may be used as a marker in assessing disease activity in adult patients with SLE.

Keywords: C-reactive protein albumin ratio, Mexican systemic lupus erythematosus disease activity index, platelet to lymphocyte ratio, relapse, systemic lupus erythematosus

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Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by increased production and deposition of antibodies, accompanied by complement activation that leads to damage to cells and tissues.[1,2] Tissue damage in various organs of the body in SLE has a wide range of impacts, including involvement in the skin, mucous membranes, heart, joints, blood, lungs, kidneys, immunity, and central nervous system. This disease is difficult to observe due to the nature of its episodic remission and relapse, and it carries a high risk of mortality. Therefore, the assessment of SLE disease activity is necessary to evaluate the severity of the disease and to monitor therapy.[3,4]

Several studies have suggested that clinical manifestations in SLE patients can be used to observe disease activity, including the Mexican Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI) score method. This index is a tool to assess the severity of disease activity based on clinical and laboratory features, and it is widely used in clinical practice for monitoring and evaluating therapy in SLE patients.[3] This

method was initiated by Guzman in 1992 with the aim of simplifying SLEDAI and reducing its implementation costs while still maintaining the quality of the information obtained. The advantage of using MEX-SLEDAI assessment is that it does not require the examination of complement parameters which can be quite expensive.[3,5] The MEX-SLEDAI score is an assessment of the severity of disease activity and is calculated from ten days prior to the onset of clinical symptoms until the time of examination, with a value range of 0–32. A high MEX-SLEDAI score is also associated with poor clinical outcomes in patients with SLE.[3,6]

The existing laboratory parameters, such as erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) are not specific to SLE and may be influenced by other factors. The European League Against Rheumatism (EULAR) recommends the use of anti-dsDNA antibodies, complement, and anti C1q as powerful tools for predicting disease flares; however, these markers have limitations in terms of sensitivity and specificity. Also not all laboratories carry outhave these examinations, especially in rural areas.[7] Therefore, there is a need to develop new markers for assessing disease activity in SLE, encompassing the utilization of simpler parameters such as platelets, lymphocytes, and inflammatory markers.[8] The scientific knowledge about the role of platelets in the immune system is rapidly advancing. Platelet to lymphocyte ratio (PLR) is one of the inflammation indices in routine blood tests related to inflammatory response markers, activity, or prognosis of inflammatory diseases. Thus, PLR is considered to have the potential to be a biomarker of disease activity in lupus nephritis.[9] SLE patients with nephritis complications had higher PLR values compared to SLE patients without nephritis. This finding may support PLR as a biomarker that can be used to describe SLE disease activity. Higher PLR values were found in patients with SLE compared to healthy subjects, and the SLEDAI score assessed a positive correlation between PLR values and SLE disease activity. Therefore, this study will examine the correlation between PLR values and MEX-SLEDAI scores.[10–12]

C-reactive protein is an acute-phase reactant and is overexpressed in autoimmune diseases such as SLE. However, CRP values are not specific and only indicate inflammation over a short period and can be influenced by various factors. The albumin synthesis rate is directly influenced by the severity of acute inflammation, making albumin categorized as a negative acute-phase protein.[13] Additionally, C reactive protein (CRP) to Albumin Ratio (CAR) is a new laboratory indicator that can be used as a parameter to describe the activity of the inflammatory process.14 Until now, there have been no studies on the value of CAR in relation to disease activity in SLE patients. This study aimed to determine the correlation between each parameter (PLR and CAR) with the MEX-SLEDAI score.

Methods

This study was a cross-sectional study using a correlational analytical design. Data collection was carried out retrospectively using secondary data taken from the Laboratory

Table 1 Characteristics of Research Sample (n=51)

Characteristics	n (%)	Median (min–max)
Age (years)		**28 (18 – 44)**
Gender, n(%)		
Male	4 (7.8%)	
Female	47 (92.2%)	
Laboratory Results		
WBC (uL)		5,450 (3,490–9,450)
Platelets (uL)		168,000 (124,000–256,000)
Total lymphocytes (uL)		590 (350–970)
CRP (mg/dL)		2.83 (0.74–10.93)
Albumin (g/dL)		1.9 (1.36–2.52)
PLR		274.07 (165.06–472.18)
CAR		2.01 (0.33–6.40)
MEX-SLEDAI Score		9 (5–14)

Note: WBC=Whole blood cell; CRP=C-reactive protein; PLR= Platelet to lymphocyte ratio, CAR=C-reactive protein albumin ratio

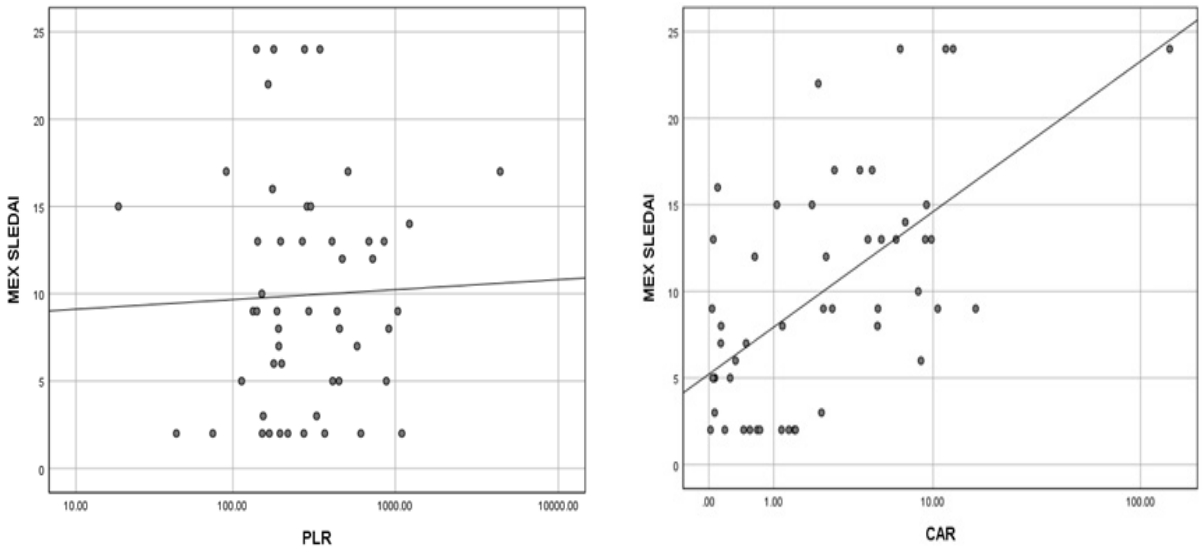

Figure 1 Scatterplot of PLR and CAR against MEX-SLEDAI score

Information System (LIS) and medical records of patients with SLE treated at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia from January 2019 to December 2021. The study population consisted of patients diagnosed with SLE based on the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) . This study obtained approval from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung with letter number LB.02.01/X.6.5/223/2022.

The inclusion criteria for this study were adult SLE patients aged ≥18 years hospitalized at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, had a MEX-SLEDAI score obtained from clinical assessment during hospitalization, patients underwent quantitative hematology, albumin, and CRP parameter examinations on days 1 to 3 of hospitalization. Meanwhile, the exclusion criteria were SLE patients with known malignancy, pregnant patients, and patients who had received platelet and albumin transfusions.

Patient characteristics data were presented in terms of age and gender. Laboratory data that were normally distributed were presented as mean±SD, and data that were not normally distributed were presented as median (minimum and maximum values).

The Spearman Rank test was employed to test the correlation of PLR and CAR values with MEX-SLEDAI scores. The criteria were significant if the p-value <0.05. The minimum size of the sample was calculated using the formula for non-paired numerical comparative sample testing.[7]

Results

From the calculation of the minimum sample size required (45 subjects), 51 subjects were obtained who met the research criteria. The analysis results showed that there was a very weak and non-significant correlation between PLR and MEX-SLEDAI score (r=0.023, p=0.437). There was a moderate and significant positive correlation between CAR and MEX-SLEDAI score (r=0.563, p<0.001), meaning that the higher the CAR, the higher the MEX-SLEDAI score (Figure 1).

Table 2 Correlation test of PLR and CAR with MEX-SLEDAI score

	MEX-SLEDAI score	
	Coefficient r	p-value
PLR	0.023	0.437
CAR	0.563	<0.001*

Note: *=Spearman rank correlation

Discussion

In this study, a very weak and insignificant correlation was found between PLR and MEX-SLEDAI score. Another study reveals that PLR does not correlate with the SLEDAI score.15 This can occur because the PLR ratio can be affected by many factors, a including different population compared to other studies, a history of anti-inflammatory drug therapy, which can suppress the production and release of lymphocytes in the bone marrow, and corticosteroid treatment, which can cause acute lymphopenia. In addition, patients with a history of methotrexate treatment may experience lymphopenia even though treatment has been stopped.[15–17] The total white blood cell count indirectly affects the PLR value, where lymphocytes are a type of white blood cell.

Furthermore, C-reactive protein plays a role in the immune complex by activating complement, opsonization, and phagocytosis in SLE. C-reactive protein is used to assess the inflammatory condition, as its production is stimulated by interleukin 6, which is a proinflammatory cytokine. Inflammation decreases the concentration of albumin by reducing the rate of albumin synthesis in the liver, accelerating the rate of catabolism, and in more severe inflammatory conditions, it can cause leakage of albumin from blood vessels.[18] Hypoalbuminemia is often found in patients with active SLE, and albumin levels in patients with lupus nephritis are lower than in patients without lupus nephritis.[19] In addition, C-reactive protein and albumin are often used to describe the activity of inflammation. A study states that CAR is a better inflammation marker than CRP alone.[11] This study found a relationship between CAR and MEX-SLEDAI score. Another study states that while CRP is elevated during the active stage of SLE, it either remains normal or shows only moderate elevation except in cases with lupus serositis or lupus nephritis.[20] In systemic inflammation, albumin levels decrease, and acute phase reactant levels increase. Therefore, there is an association between hypoalbuminemia and CRP levels. Other studies have reported that the value of CAR is similar to patient report outcomes (PRO), and its advantage is that it can eliminate the patient's perspective in filling out heterogeneous PRO, so that CAR values can provide objective information. Additionally, it can be used in conditions with many patients to save time, avoid variation in physician assessment, and does not require experienced personnel to perform the examination.[11,21,22]

Limitations of this study include that the results in this study do not represent the entire population of patients with relapsed SLE . This cross-sectional study may limit the significance of PLR values. The MEX-SLEDAI score, which is a measure of the severity of relapse, is subjective based on clinical assessment and this is unavoidable. The history of infection in this study are not excluded considering patients with SLE are highly susceptible to infection, which is unavoidable as well. In addition, this study did not specifically investigate disease duration, history of steroid treatment, and details of organ involvement; which could affect the values of some measured PLR and CAR parameters.

In conclusion, there is a moderate positive correlation between CAR and MEX-SLEDAI scores and statistical significance. Further studies on the relationship between PLR and inflammatory diseases using prospective study designs with repeated measurements of laboratory parameters are recommended.

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