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Correlation Between Serum Malondialdehyde Levels and Disease Activity in Patients with Mild to Moderate Systemic Lupus Erythematosus

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Abstract

Systemic lupus erythematosus (SLE) is characterized by persistent inflammation and oxidative stress, which contribute to the progression of the disease. Lipid peroxidation is indicated by malondialdehyde (MDA). The objective of this investigation was to evaluate the correlation between serum MDA levels and disease activity in patients with mild to moderate systemic lupus erythematosus (SLE). This investigation was a cross-sectional correlation analysis that employed baseline data from adult patients with systemic lupus erythematosus who were receiving conventional treatment. Spearman's correlation was employed to determine the relationship between serum MDA levels and disease activity, which was evaluated using the MEX-SLEDAI score. The study encompassed 38 patients with mild to moderate SLE. The MEX-SLEDAI score was 3 (range 2–7), and the median serum MDA concentration was 1.42 µmol/L (range 0.90–1.99). Spearman's correlation analysis demonstrated a moderately positive correlation between serum MDA levels and MEX-SLEDAI scores ($r = 0.415$, $p = 0.010$), indicating that elevated oxidative stress is associated with increased disease activity in SLE patients. A considerable positive correlation between serum malondialdehyde levels and disease activity is statistically significant in patients with mild to moderate systemic lupus erythematosus (SLE). These results support the existence of oxidative stress in the pathophysiology of lupus and suggest that MDA may serve as a potential biomarker for disease monitoring.

Keywords: Systemic Lupus Erythematosus**,** Malondialdehyde**,** Disease Activity**,** MEX-SLEDAI

1. Introduction

Systemic lupus erythematosus (SLE) is a classic example of a systemic autoimmune disorder marked by diverse clinical manifestations, involvement of multiple organ systems, and the presence of various autoantibodies. Despite the fact that SLE can affect both sexes across various age categories, it primarily affects women of reproductive age (20–40 years), with a female-to-male ratio of approximately 9:1. The health data from 2016 in Indonesia reported 2,166 hospitalized cases of SLE, of which 550 resulted in mortality.[1,2]

Both human and animal studies have shown a link between increased disease activity in systemic lupus erythematosus (SLE) and elevated oxidative stress, which contributes to organ damage.[3–7] Oxidative stress denotes an imbalance between the production and elimination of reactive oxygen intermediates (ROIs), which are highly reactive molecules generated by enzymatic cellular processes. These molecules are involved in the signaling pathways of cell death and are significant in the pathogenesis of SLE. The increased oxidative stress noted in SLE patients is thought to stem from interactions between autoantigens and autoantibodies, as well as mitochondrial dysfunction in T cells. Peroxynitrite has been identified as a reactive oxygen intermediate that induces lipid peroxidation and DNA damage. Lipid peroxidation in cellular structures, including mitochondria, lysosomes, and membranes, results in the production of reactive aldehydes such as malondialdehyde (MDA). These compounds

not only contribute to ongoing oxidative damage but are also significantly associated with increased disease activity in systemic lupus erythematosus (SLE).[8,9]

The involvement of oxidative stress in the pathogenesis and progression of systemic lupus erythematosus, along with the potential of malondialdehyde (MDA) as a reliable biomarker for lipid peroxidation, suggests that examining its correlation with disease activity could provide important insights for clinical monitoring. This study aimed to assess the relationship between serum MDA levels and disease activity, as indicated by the MEX-SLEDAI score, in patients with mild to moderate SLE.

2. Methods

This observational, cross-sectional study sought to assess the correlation between serum malondialdehyde (MDA) levels and disease activity in patients with mild to moderate systemic lupus erythematosus (SLE). Adult patients aged 18 to 65 years with a confirmed diagnosis of systemic lupus erythematosus (SLE), as per the 2019 EULAR/ACR classification criteria, were recruited from the Outpatient Clinic, Department of Internal Medicine, Dr. Mohammad Hoesin General Hospital, Palembang, from November 2024 to March 2025. Participants with severe disease activity, active infections, pregnancies, malignancies, or other autoimmune disorders were excluded from the study.

Demographic and clinical data were recorded, including age, sex, disease duration, comorbidities, and current medications. Disease activity was assessed using the Mexican adaptation of the Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI). Serum malondialdehyde (MDA) concentrations were measured using high-performance liquid chromatography (HPLC) with detection of thiobarbituric acid-reactive substances (TBARS). Blood samples were collected in the morning after a fasting period, subjected to centrifugation, and analyzed within two hours.

The Shapiro-Wilk test was utilized to assess the distribution of the data. Given the non-normal distribution of MDA levels and MEX-SLEDAI scores, the results are presented as median values. Spearman's rank correlation test was utilized to examine the association between serum MDA levels and disease activity. A p-value less than 0.05 is considered statistically significant. Statistical analyses were performed using SPSS version 26. The research received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine at Universitas Sriwijaya and Dr. Mohammad Hoesin General Hospital in Palembang, Indonesia (Approval No. DP.04.03/D.XVIII.06.08/ETIK/239/2024).

3. Results

The sample population's baseline characteristics are summarized in Table 1. The analysis comprised 38 participants diagnosed with mild-to-moderate systemic lupus erythematosus (SLE). The predominant demographic of participants was female (94.7%), with an average age of 33.13 ± 10.49 years. A majority of individuals (76.3%) experienced an illness duration of under five years. None were diagnosed with diabetes mellitus, however 26.4% exhibited concomitant hypertension. According to body mass index, 31.6% of participants were categorized as obese (BMI >25 kg/m^2).

The baseline oxidative stress level, assessed by serum malondialdehyde (MDA), had a mean of 1,41 ± 0,32 µmol/L, while the median MDA value was 1.42 µmol/L (range: 0.90–1.99 µmol/L). Disease activity, measured using the MEX-SLEDAI score, had a mean of 3.32 ± 1.27 with a median of 3 (range: 2–7).

To examine the association between oxidative stress and disease activity in SLE, a

Spearman correlation test was conducted between baseline MDA levels and MEX-SLEDAI scores. The results, as shown in Table 2, demonstrated a statistically significant positive correlation between MDA concentration and disease activity score (r = 0.415, p = 0.010).

Table 1. Baseline Characteristics of Subjects

Variable	Frequency (n) / Mean ± SD	Percentage (%) / Median (min-max)
Age (years)	33.13 ± 10.49	33.50 (17-57)
Gender		
Male	2	5.3
Female	36	94.7
Duration of SLE		
<5 years	29	76.3
≥5 years	9	23.6
Diabetes Mellitus		
Present	0	0
Absent	38	100
Hypertension		
Present	10	26.4
Absent	28	73.6
Body Mass Index		
Non obese (≤25)	26	68.4
Obese (>25)	12	31.6
MDA *baseline*	1.41 ± 0.32	1.42 (0.90-1.99)
MEX-SLEDAI *baseline*	3.32 ± 1.27	3 (2-7)
Methylprednisolone Dosage		
Not administered or up to ≤4 mg/day	34	89.5
>4 mg/day	4	10.5
MMF Dosage		
Not administered or 360 mg/day	37	97.4
720 mg/day	1	2.6
MMA Dosage		
Not administered or 500 mg/day	37	97.4
1000 mg/day	1	2.6
Methotrexate Dosage		
Not administered or ≤5 mg/week	33	86.8
>5 mg/week	5	13.2
Cyclosporine Dosage		
Not administered or 25 mg/day	35	92.1
50 mg/day	3	7.9
Hydroxychloroquine Dosage		
Not administered or 100 mg/day	11	28.9
200 mg/day	27	71.1

Table 2. Correlation between Malondialdehyde concentration and MEX-SLEDAI

Variable	MEX-SLEDAI	
Malondialdehyde	r = 0.415**	p = 0.010*

* Spearman correlation test (the p-value is significant when p < 0.05)

** When r = 0.00-0.19, the correlation is very weak; r = 0.20-0.39 indicates a weak correlation; r = 0.40-0.59 signifies a moderate correlation; r = 0.60-0.79 reflects a strong correlation; r = 0.80-0.99 denotes a very high correlation; and r = 1 represents a perfect correlation.

4. Discussion

This study found a higher proportion of female participants compared to males, reflecting the well-established pattern that SLE predominantly affects women. Several factors are believed to underlie this gender difference, including hormonal, genetic, and epigenetic mechanisms. Estrogen, which is more prevalent in women, is known to enhance B-cell activation and stimulate antibody production—both of which contribute to autoimmune responses. Genetically, women possess two X chromosomes, and certain genes located on the X chromosome, such as TLR7, are thought to increase susceptibility to autoimmune diseases. Moreover, epigenetic modifications—changes in gene expression influenced by environmental and hormonal factors—may also play a significant role in driving the development of autoimmune conditions.[10–15]

In this study, the majority of SLE patients were within the productive age group, with a mean age of 33.56 years. This finding aligns with existing literature indicating that SLE is more prevalent in young adults, particularly women of reproductive age. More specifically, the onset of SLE most commonly occurs between the ages of 31 and 34. The higher levels of estrogen during this period are thought to increase susceptibility to autoimmune diseases, including SLE.[16–18]

In the present study, the mean baseline serum MDA concentration was 1.41 µmol/L, with a median value of 1.42 µmol/L. This median level is notably higher than that reported by Paz *et al*. Elevated serum

MDA, a marker of oxidative stress, has been consistently identified in SLE patients and is linked to various clinical manifestations. In a comparative study involving 80 individuals with SLE and 80 healthy controls, MDA levels were significantly higher among the SLE group. These elevated levels have shown correlations with disease activity, as measured by the SLEDAI score, and tend to be more pronounced in patients presenting with neuropsychiatric symptoms, vasculitis, or positive anti-DNA antibodies. Nevertheless, no significant difference in MDA concentrations was observed between patients with and without irreversible organ damage.[19,20]

Regarding disease activity assessment, the MEX-SLEDAI was employed instead of the SLEDAI-2K because of its practicality in outpatient and resource-limited settings. The MEX-SLEDAI excludes serological parameters such as complement and anti-dsDNA levels, which are not always readily available, yet it has been validated as a reproducible and reliable tool for assessing mild-to-moderate disease activity. Although SLEDAI-2K remains the most widely accepted index internationally, the use of MEX-SLEDAI in this study provides a feasible and contextually appropriate approach for clinical monitoring in developing regions.[21]

SLE is associated with impaired adaptive immunity and a loss of tolerance to self-antigens. Its onset and progression require immune cell involvement, highlighting the central role of autoimmune reactivity. Studies in humans and mouse models have shown that oxidative stress occurs alongside T cell dysfunction, involving mitochondrial hyperpolarization, increased ROS production, and excessive use of intracellular antioxidants like glutathione.[22,23]

Oxidative stress induces mitochondrial hyperpolarization, marked by increased membrane potential and impaired ATP binding, leading to disrupted electron transport and greater electron leakage, which further enhances ROS production.[24] MDA levels reflect the extent of oxidative damage in SLE patients. Initially, MDA serves as a marker of oxidative stress. Beyond that, it contributes to DNA damage by reacting with

nucleosides such as deoxyguanosine and cytidine, forming mutagenic compounds like M1G. These interactions can lead to point mutations, frameshift mutations, strand breaks, and trigger apoptosis.[25,26]

This study has several acknowledged limitations. Firstly, while MDA serves as a marker of oxidative stress, the underlying mechanisms are multifaceted and involve additional biomarkers that were not assessed in this research. Superoxide dismutase is essential for antioxidant defense, catalyzing the transformation of superoxide radicals into oxygen and hydrogen peroxide, while glutathione peroxidase aids by promoting the oxidation of glutathione in reaction to endogenous hydroperoxides. Additional research is necessary to elucidate the exact functions of these enzymes in the pathophysiology of SLE.

5. Conclusion

This study demonstrates a positive correlation between serum MDA levels and disease activity in individuals with systemic lupus erythematosus (SLE). The findings confirm the role of oxidative stress in the origin and progression of systemic lupus erythematosus (SLE). Assessing MDA levels may provide additional understanding of disease activity and could serve as a potential biomarker in clinical assessment. Further research is required to examine its predictive relevance and application in guiding therapeutic strategies.

6. Acknowledgment

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