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The Correlation of Neutrophil-to-Lymphocyte Ratio with LupusQoL in Systemic Lupus Erythematosus Patients

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ABSTRACT

Background: SLE is a chronic autoimmune disease with diverse clinical manifestations depending on disease activity. Clinical manifestations, disease activity, and adverse drug reactions can affect quality of life. The LupusQoL questionnaire assesses the disease's impact on eight quality of life domains. The Neutrophil-to-Lymphocyte Ratio (NLR) is an inflammatory biomarker that correlates with SLE disease activity. **Objective:** This research aims to determine the correlation between NLR and various domains of the LupusQoL questionnaire in SLE patients. **Methods:** A total of 32 SLE patients were purposively selected in this 2024 observational study. NLR was based on blood counts from the past 4 weeks, while HRQoL was assessed via LupusQoL. Pearson correlation was used for analysis. **Result:** The mean NLR was 6.50 (1.3–29.43). LupusQoL showed the lowest score in fatigue (58.85). Pearson analysis revealed a moderate inverse correlation between NLR and the planning domain of LupusQoL (p= 0,022). NLR shows no statistically significant correlation with physical health, pain, intimacy, burden to others, emotional health, body image, or fatigue in SLE patients. **Conclusion:** Higher NLR is correlated with lower planning domain HRQoL in SLE patients and vice versa.

Keywords: Neutrophil-to-Lymphocyte Ratio (NLR), Quality of Life, LupusQoL, Systemic Lupus Erythematosus (SLE).

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is often referred to as the "disease of a thousand faces" due to the wide range of manifestations associated with this condition. SLE is a chronic autoimmune rheumatic disease that causes systemic inflammation and affects multiple organs.[1] The incidence and prevalence of SLE vary depending on ethnicity, race, location, gender, and age. Globally, the incidence of SLE is estimated to be approximately 5.14 cases per 100,000 population, with an annual diagnosis rate of 0.40 million

individuals. In the Asia-Pacific region, the incidence ranges from 0.9 to 3.1 cases per 100,000 population, while the prevalence is reported to be between 4.3 and 45.3 cases per 100,000 population. Specific data on SLE prevalence in Indonesia remain unavailable. According to the Lupus Foundation of America, most individuals are diagnosed with SLE between the ages of 15 and 44, and 90% of patients are women. The prevalence rate among women is reported to be 78.73 per 100,000, compared to 9.26 per 100,000 among men.[2]

The exact cause of Systemic Lupus Erythematosus (SLE) remains unclear; however, genetic, hormonal, and environmental factors are known to play significant roles in its etiopathogenesis. Genetic predispositions, such as the presence of HLA-DR2, HLA-DR3, and deficiencies in classical complement pathway components (C1q, C1r, C2, C4), increase the risk of SLE by impairing the clearance of cellular debris and disrupting B-cell tolerance. Additionally, the contribution of the X chromosome and the role of estrogen in enhancing immune activity and cytokine release, such as IL-1, have been recognized. Environmental factors, including ultraviolet (UV) light exposure, certain medications (e.g., procainamide, hydralazine), silica exposure, viral infections, smoking, and consumption of foods containing canavanine, further elevate risk by influencing cellular apoptosis, DNA demethylation, and immune responses.[3,4] Moreover, vitamin D deficiency has also been implicated in the mechanisms underlying SLE development.[5] The primary immunological disturbance in Systemic Lupus Erythematosus (SLE) involves the formation of autoantibodies triggered by self-antigens derived from apoptotic cells. These antigens are presented by antigen-presenting cells (APCs) and B cells to T cells, which subsequently activate B cells to produce pathogenic autoantibodies. Impaired clearance of immune complexes and apoptotic cells leads to chronic inflammation, characterized by increased pro-inflammatory cytokines such as IFN, TNF-α, and IL-17, along with reduced levels of IL-2 and TGF-β, which are essential for maintaining immune tolerance.[3,4] Excessive neutrophil activation generates neutrophil extracellular traps (NETs), contributing to neutrophilia, while T-cell dysfunction and loss of immune tolerance result in lymphopenia.[6,7] These mechanisms drive inflammation, irreversible tissue damage, and a wide range of clinical manifestations. Disease severity escalates with the number of affected organs.[8, 9]

The neutrophil-to-lymphocyte ratio (NLR) is a practical, cost-effective, and easily accessible hematological parameter used to reflect the balance between innate (neutrophil) and adaptive (lymphocyte) immune responses in pathological conditions.[10] NLR has been employed as an inflammatory indicator in various

diseases, including cardiovascular conditions, infections, cancer, sepsis, and COVID-19.[11,12,13] Specific NLR values are indicative of disease severity: local infections (≥5–<10), systemic infections (≥10–<13), sepsis (≥13–<15), and septic shock (≥15).[14] In sepsis patients, an NLR >13.2 is closely associated with a higher risk of mortality, with a mean NLR of 24.96 observed in cases of sepsis-related deaths within the first 24 hours.[15,16] COVID-19 patients often present with lymphopenia, which impacts NLR values.[17] For instance, COVID-19 patients with mild symptoms typically have an NLR <3.13, while those with an NLR >11.38 are predicted to be at a higher risk of mortality.[18,19] Additionally, NLR has been utilized to monitor pneumonia severity, the onset of preeclampsia, and obesity, though the cut-off values vary across studies.[20,21,22] Research by Wang L et al. demonstrated that NLR significantly correlates with inflammatory responses and disease activity in SLE.[23] Similarly, a study by Soliman WM et al. found that NLR values in SLE patients were significantly higher than those in control groups and showed a positive correlation with the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). This highlights the strong relationship between NLR values and SLE disease activity levels.[24]

According to research by Miguel et al., the neutrophil-to-lymphocyte ratio (NLR) can serve as a prognostic marker in bronchiectasis, particularly concerning severe exacerbations.[25] Higher NLR values are associated with an increased likelihood of exacerbations. Miguel et al. also identified a relationship between NLR and quality of life, with higher NLR values correlating with a more significant decline in the quality of life for patients with bronchiectasis.[25] Similarly, a study conducted by Rias et al. found a link between NLR values and quality of life in patients with type 2 diabetes mellitus. Higher physical activity levels combined with lower NLR values positively impacted patients' quality of life.[26] Furthermore, Zhao et al. reported that reducing NLR levels in lung cancer patients could improve their quality of life.[27]

The World Health Organization (WHO) defines quality of life as an individual's perception of their position in life within the context of their cultural environment and the value systems in which they live. From a medical perspective, there is a specific term for quality of life related to health, known as *health-related quality of life* (HRQoL). This concept aligns with the WHO's definition of health as "a state of complete physical, mental, and social well-being." HRQoL reflects an individual's response to the illness they experience. The level of HRQoL is assessed based on the patient's self-evaluation of the disease's impact and treatment on their physical, psychological, and social functioning, as well as the side effects caused by the treatment.[28]

Several instruments are available to assess health-related quality of life (HRQoL). Depending on the assessment's purpose, HRQoL instruments are categorized into two types: generic and specific. Specific instruments are typically used to evaluate the quality of life in patients with severe and chronic illnesses. In this study, the *LupusQoL* instrument was employed as a specific tool to assess the quality of life in patients with Systemic Lupus Erythematosus (SLE). *LupusQoL* evaluates the quality of life across eight domains: physical health, pain, planning, intimate relationships, dependence on others, emotional health, body image, and fatigue.[29]

METHODS

This study employed an analytical observational method with a cross-sectional approach. Sampling was conducted using a purposive sampling technique, resulting in a total of 32 participants. The study was carried out from August 2024 to November 2024. Inclusion criteria included patients with Systemic Lupus Erythematosus (SLE) undergoing treatment at Raden Mattaher General Hospital. Exclusion criteria included patients without complete or legible medical records or those unwilling to participate as respondents. Ethical approval was obtained from the ethics committee of Raden Mattaher General Hospital (No: S.223/SPE/XII/2024). All participants received detailed explanations about the study, provided informed consent, and agreed to participate as respondents.

Data collected from SLE patients included medical records to determine age and gender characteristics, the most recent complete blood count (conducted within the past four weeks) to obtain NLR values (absolute neutrophil count divided by absolute lymphocyte count), and quality of life data assessed per domain using the LupusQoL questionnaire. Once data were collected, univariate and bivariate analyses were performed. Univariate analysis described the frequency of variables, including age, gender, NLR values, and scores for each LupusQoL domain, presented in distribution tables. Bivariate analysis evaluated the correlation between NLR values and quality-of-life domains in LupusQoL. The Shapiro-Wilk test was used to assess data normality, and since the data followed a normal distribution, Pearson's correlation test was applied to examine the relationship between the two variables. The analyses were conducted using the Statistical Package for Social Sciences (SPSS).

RESULTS

Based on the data collection from 32 samples, the distribution of characteristics such as NLR values, and quality of life scores (assessed per domain) are presented in**Table 1**.

Table 1. Distribution of Research Subject Characteristics

Characteristic (n = 32)	Value (Mean ± SD)
Neutrophil-to-Lymphocyte Ratio (NLR)	6.50 ± 7.03
Health-Related Quality of Life (LupusQoL score (range: 1–100))	
Physical Health	64.16 ± 18.98
Pain	60.93 ± 26.30
Planning	66.92 ± 25.44
Intimacy	78.51 ± 25.64
Burden to others	58.85 ± 30.00
Emotional Health	61.19 ± 24.60
Body Image	69.37 ± 27.23
Fatigue	54.68 ± 23.33

The average NLR value for the patients was 6.50 (SD 7), with a range from 1.3 to 29.43. Quality of life for SLE patients was assessed using the LupusQoL questionnaire, which includes 8 domains. The highest possible score for each domain is 100, and the lowest score is 0. The closer the score is to 100, the better the quality of life, while the closer it is to 0, the poorer the quality of life. The average scores for each domain were as follows: physical health 64.16, pain 60.93, planning 66.92, intimate relationships 78.51, dependence on others 58.85, emotional health 61.19, body image 54.68, and the lowest average score was found in the fatigue domain, with a mean score of 54.68.

The quality of life impacted by SLE is outlined across several domains. Based on the statistical tests performed, the results in **Table 2** show that only the planning domain had a significant correlation with NLR values, with a p-value of 0.022. Since the significance value (sig. 2-tailed) ≤ 0.05, this indicates a statistically significant relationship between NLR and the planning domain. The correlation coefficient between NLR and the planning domain was 0.404, indicating a moderate relationship. The negative value of the correlation coefficient suggests that the relationship between NLR and the planning domain of quality of life is inverse. Therefore, as NLR increases, the quality of life in terms of planning for SLE patients tends to decrease, and vice versa. On the other hand, other domains, such as physical health, pain, intimate relationships, dependence on others, emotional health, body image, and fatigue, did not show significant relationships with SLE according to the statistical analysis results.

Table 2. Relationship Between Neutrophil-to-Lymphocyte Ratio (NLR) and Quality of Life Domains Based on LupusQoL in Patients with Systemic Lupus Erythematosus

***Health-Related Quality of Life Domains* (n = 32)**	***NLR***	
	r	***p-Value***
Physical Health	*-0,143*	*0,434*
Pain	*-0,125*	*0,496*
Planning	*-0,404*	*0,022*
Intimacy	*-0,302*	*0,093*
Burden to others	*-0,287*	*0,111*
Emotional Health	*-0,214*	*0,239*
Body Image	*-0,106*	*0,565*
Fatigue	*-0,020*	*0,912*

DISCUSSION

In this study, the average NLR for SLE patients was 6.5 (SD ±7), with a median of 3.73, a minimum of 1.3, and a maximum of 29.43. These results are similar to those found by Aldakhakhny S et al., where the mean NLR was 6.1 with an SD of ±2.1.[30] This study's findings are also in line with research by Han et al., which reported a median NLR value of 3.4.[31] The increase in NLR in SLE is attributed to neutrophilia resulting from inflammation and lymphopenia due to anti-lymphocyte antibodies attacking CD8+ T cells, triggering apoptosis, impairing lymphopoiesis, and sequestrating lymphocytes. This mechanism reflects the disease activity of SLE. According to a study by Soliman WM et al., the NLR in SLE patients was significantly higher compared to the control group. The NLR value in SLE patients was well correlated with increased disease activity, as assessed using the SLEDAI.[24] Similarly, studies by Aldakhakhny S et al., Firizal et al., and Han et al. found a significant correlation between NLR and disease activity assessed using SLEDAI. This indicates that NLR can be used as an inflammatory biomarker to assess disease activity in SLE patients.[30,32,31,33]

This study used the LupusQoL questionnaire to assess the quality of life of SLE patients across 8 domains: physical health, pain, planning, intimate relationships, dependence, emotional health, body image, and fatigue. A score of 100 indicates very good quality of life, while a score of 0 indicates very poor quality of life. The physical health domain for 32 SLE patients had an average score of 64.16. Due to the impact of SLE, 11 patients occasionally required assistance for moderate physical tasks, while the majority did not need help with light activities. The physical limitations caused by lupus reduce patient independence, leading to dependence on others, difficulties climbing

stairs, and a decrease in the speed of daily activities.

The average score for the pain domain in SLE patients was 60.90. Patients with scores ≤25.00 reported significant disruption in their activities due to pain, particularly in the joints and muscles. This pain often causes difficulty sleeping, late nights, and a lack of restful sleep. Some patients reported experiencing pain almost daily, which impedes mobility, daily activities, and participation in social events.

SLE patients with an average score of 25.00 in the planning domain often find it difficult to attend social events or complete tasks as they would like due to their unpredictable health condition. They also report experiencing difficulty in carrying out tasks. On the other hand, patients with a score of 100 do not face challenges in attending events or participating in social activities. The average score for the planning domain was 66.92. Similar findings were reported in a study by McElhone et al., which indicated that planning difficulties in SLE patients are caused by unstable health conditions, fatigue, decreased emotional health, and physical limitations.[34]

The intimacy domain had the lowest average score in SLE patients, which was 0.00. The low scores were particularly observed in patients who were unmarried. These patients reported a decreased interest in romantic relationships due to concerns about their illness. Conversely, patients with scores between 75.00 and 100.00 remained interested in forming relationships. Among the 15 married respondents, they were able to maintain their relationships. This finding aligns with research by Li-Wei Zhu et al., where 279 SLE patients in China, who were married, continued to maintain good relationships with their partners.[35]

In the domain of burden to others, the average score was 58.85. One patient had the lowest score of 8.33, feeling dependent on family due to the SLE they suffered from, needing assistance with daily tasks, and worrying about causing stress or anxiety for their family. The higher the score, the less dependence on family or relatives. For the emotional health domain of SLE patients, the average score was 61.19. Patients with scores ≤ 50 experienced anxiety, anger, and concern about their health due to lupus. Conversely, patients with scores between 75 and 100 rarely experienced emotional disturbances and were more optimistic about their health.

The average score for the body image domain in SLE patients was 69.37. Some patients felt self-conscious due to physical changes caused by SLE or medication side effects. Some used makeup, masks, or more covered clothing to conceal flare-ups or scars on their faces or bodies. However, patients with scores ≥ 50 felt more positive about their weight changes, considering them as improvements in appearance or health, especially after taking corticosteroids.

Some believed that even healthy individuals could gain or lose weight, so they did not feel embarrassed about weight changes caused by medication side effects.

Fatigue is a common symptom experienced by SLE patients, with an average fatigue score of 54.68. Patients with lower scores reported more disturbing fatigue affecting their activities. Some patients mentioned sleep disturbances due to fatigue. Pain disrupted their quality of sleep at night, and fatigue made them feel the need to sleep earlier. However, some found it difficult to sleep even after lying down for a long time, and this caused them to feel still tired when waking up in the morning.

This study examined the correlation between the Neutrophil-Lymphocyte Ratio (NLR) and quality of life domains in SLE patients based on the LupusQoL questionnaire. The results revealed a significant correlation between NLR values and the planning domain, with a significance value of 0.022 ($p = 0.022$). SLE patients reported that their disease activity interfered with their ability to plan activities. They found it difficult to plan future activities due to the uncertainty of SLE disease activity, which can suddenly worsen. The correlation test results indicated that as the NLR value increased, the score in the planning domain decreased. These findings are consistent with the study by Papachristodoulou et al., which also identified an impact of NLR on the planning domain, although differences were observed regarding the relationship between NLR and other domains.[36]

CONCLUSION

Based on the results and discussion of the study on the relationship between the Neutrophil-to-Lymphocyte Ratio (NLR) and quality of life domains assessed by LupusQoL in 32 SLE patients at the Internal Medicine Polyclinic of RSUD Raden Mattaher, Jambi Province, a moderate inverse correlation was found between NLR values and the planning domain, indicating that as NLR increases, the health-related quality of life score in the planning domain tends to decrease.

RECOMMENDATIONS

Future studies are recommended to use larger sample sizes to enhance accuracy, compare Neutrophil-to-Lymphocyte Ratio (NLR) values with SLEDAI scores or control groups to determine the cut-off value, explore cost-effective yet relevant inflammatory parameters, and assess the quality of life in SLE patients using instruments such as QLICD-SLE (V2.0), SLE QOL, and L-QOL.

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