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Prognostic nutritional index as predictor: Assessing disease activity in Juvenile Systemic Lupus Erythematosus (Non-Nephritic)

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ABSTRACT

Background and Objectives. The Prognostic Nutritional Index (PNI) is a widely utilized indicator to reflect patients' nutritional status, which is closely associated with the development of autoimmunity, chronic inflammation, and poor prognosis for autoimmune disease. This study aims to determine the correlation between PNI and disease activity (SLEDAI scores) in Juvenile Systemic Lupus Erythematosus (JSLE) patients.

Materials and Methods. This analytic observational retrospective study employed Spearman's Correlation to determine the association between JSLE disease activity and PNI. Medical record data of JSLE patients, covering their SLEDAI scores, albumin levels, and lymphocyte levels, were collected from 2018 to 2023. The disease activity was based on SLEDAI scores and classified into mild (0-5), moderate (6-12), and severe (>12) categories. Meanwhile, patients' nutritional status was assessed by their PNI scores.

Results. This analytic observational retrospective study employed Spearman's Correlation to determine the association between JSLE disease activity and PNI. Medical record data of JSLE patients, covering their SLEDAI scores, albumin levels, and lymphocyte levels, were collected from 2018 to 2023. The disease

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Conclusions. There was no correlation between electrolyte of blood and stool of intestinal stoma with location and resection of intestinal.

Keywords: children, JSLE, nutritional status, PNI, SLEDAI

Abbreviations:

ACR: American College of Rheumatology

CONUT: Controlling Nutritional Status

EULAR: European Alliance of Associations for Rheumatology

JSLE: Juvenile Systemic Lupus Erythematosus

LMIC: Low- and middle-income countries

NRI: Nutritional Risk Index

PNI: Prognostic Nutritional Index

SLE: Systemic Lupus Erythematosus

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

SLICC: Systemic Lupus International Collaborating Clinics

WBC: White Blood Cells

INTRODUCTION

Juvenile Systemic Lupus Erythematosus (JSLE) is a chronic autoimmune condition in children and adolescents that leads to inflammation and multi-system impairment. This disease is usually diagnosed before the age of 18 and affects about 15-20% of SLE patients[1,2]. JSLE often presents with more severe symptoms than adult-onset lupus, significantly impacting the patient's growth, development, and quality of life [3].

The incidence of JSLE ranges from 0.36 to 2.5 cases per 100,000 children, with a prevalence rate of 1.89-34.1 per 100,000 children [1,2]. Low- and middle-income countries (LMICs) have higher rates of SLE in the majority of their ethnic groups [4].

To date, the mechanisms of SLE have not been fully understood. While the evaluation of SLE disease activity can utilize various indices, including the Systemic Lupus Erythematosus Disease Activity-2000 (SLEDAI-2K), these assessment methods have several limitations such as observer inconsistencies and administrative burdens [5,6]. Managing the diverse symptoms of SLE in clinical settings remains challenging, thereby highlighting the need for new, easily measurable biomarkers for detecting its disease activity.

On the other hand, PNI uses total lymphocyte count and serum albumin levels to assess the nutritional and immunological status of a patient [7]. In chronic diseases like JSLE, a higher PNI score indicates better nutritional and immune status, which is associated with a more favorable prognosis [8]. The objective of this study is to observe the connection between PNI and SLEDAI scores to evaluate the potential of PNI to predict disease activity in JSLE.

MATERIALS AND METHODS

This retrospective observational study was carried out at the Pediatric Department of General Academic Hospital Dr. Soetomo Surabaya, with the subjects being children aged 1 month to 18 years who had been diagnosed with JSLE in 2018-2023 based on ACR 1997, SLICC 2012, or EULAR/ACR 2019 criteria. Meanwhile, this study excluded patients with hematologic

diseases, kidney diseases with proteinuria, and/or hepatology-related diseases, as well as patients with incomplete data.

In this study, the laboratory results of whole blood tests, albumin levels, and SLE disease activity were collected. Based on the SLEDAI score, disease activity was divided into mild (0-5), moderate (6-12), and severe (>12) categories. Patients' nutritional status was assessed by PNI score, and the confounding variables in this study were the presence of complications and therapy.

RESULTS

This study examined 57 patients, 6 males and 51 females, who met the inclusion criteria. These research subjects were between the ages of 4 and 17 (12.7 ± 2.8). The majority of the research subjects were female. Among these 57 cases, 35 were classified as mild, 18 as moderate, and 4 as severe based on the SLEDAI scores of the patients, which measure their disease activity. For each disease activity category, the average age of the research subjects was 13 years old (mild), 12 years old (moderate), and 10 years old (severe). (**Figure 1**).

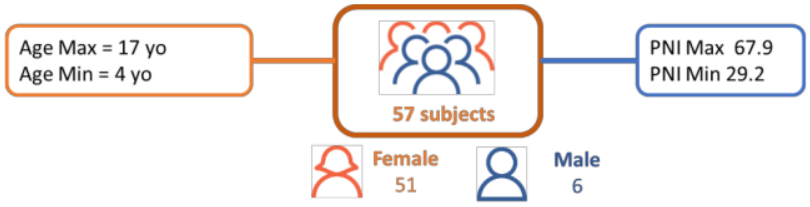

Figure 1. Demographic data of the research subjects

In this study, several laboratory examinations were also carried out and the results were grouped by disease activity level based on patients' SLEDAI scores. The albumin test results showed that the average albumin level of patients with mild disease was 3.7 g/dL, whereas that of patients with moderate and severe diseases was 3.5 g/dL. Meanwhile, the results of the leukocyte tests revealed a WBC of 8111 x 103/µl in the mild category, which progressively decreased to 4885 x 103/µl in the moderate category and increased to 6250 x 103/ µl in the severe category. The lab

results also found absolute lymphocyte counts of 1900 x 103/ µl, 930 x 103/ µl, and 1115 x 103/ µl in mild, moderate, and severe categories, respectively (**Table 1**).

Furthermore, according to patients' nutritional status and disease activity, it was found that subjects with a PNI score of 46.6 were in the mild category, those with a PNI score of 42 were in the moderate category, and those with a PNI score of 41.7 were in the severe category. The correlation test results indicated that the level of JSLE disease activity had a statistically significant correlation with PNI in the opposite direction (r =- 0.3; p = 0.007) (**Figure 2**).

Table 1. Basic characteristics of the research subjects

Parameter	SLEDAI SCORE		
	Mild (n=35)	**Moderate (n=8)**	**Severe (n=4)**
Age	13 (± 2.6)	12.7 (±2.5)	10.25 (±4.8)
Gender	f=34; m=1	f=16; m=3	f=4; m=0
Albumin (g/dL)	3.7 (±0.5)	3.5 (±0.7)	3.5 (±0.3)
WBC (10^3/ µl)	8111	4885	6250
Lymphocytes (10^3/ µl)	1900	930	1115
PNI	46.6 (±5.5)	42 (±11.1)	41.7 (±3.7)

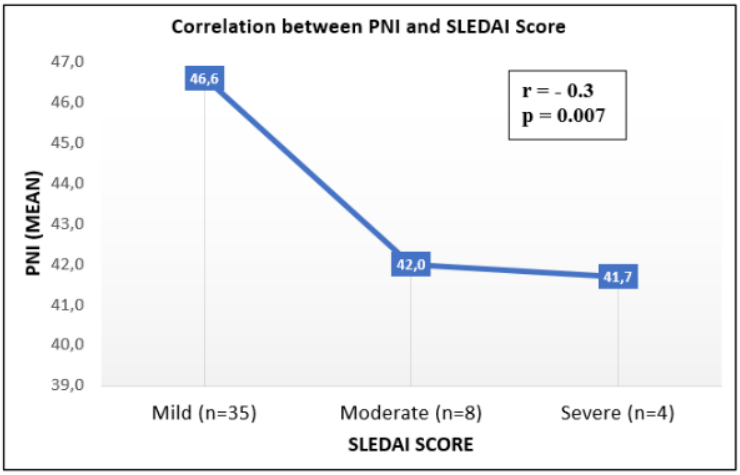

Figure 2. Correlation between nutritional status (measured by PNI score) and JSLE disease activity (measured by SLEDAI score)

DISCUSSION

JSLE is an autoimmune and inflammatory condition that causes substantial harm and impairment [9]. The mechanism of this disease differs between age groups due to various factors, such as family cohorts, uneven ethnic distribution, differences in specific clinical and laboratory characteristics in different age groups compared to adults, and more severe organ manifestations [3].

The diagnosis of JSLE can be made between the ages of 4 and 17 [3]. Approximately 10-20% of all individuals diagnosed with SLE experience symptoms before the age of 16, thus being categorized as having childhood-onset or juvenile systemic lupus erythematosus [9].

The subjects participating in this study were predominantly female. This confirms recent literature that JSLE is more common in females; there is a higher incidence of childhood-onset SLE in girls compared to boys, with a ratio of 3:1. This ratio increases to 9:1 after reaching puberty [10]. Likewise, the risk of adult-onset SLE is also higher in females as more women suffer from this condition than men. Although the exact reasons for the large difference in the incidence of this

disease in females and males remain unclear, it is believed that a complex interplay of hormonal, environmental, and genetic factors is involved [9].

As mentioned previously, the fundamental processes causing SLE remain unclear [9]. Numerous studies have investigated the association between individuals' nutritional status and immunity, where undernutrition is linked to immunosuppression and a higher vulnerability to infections. On the other hand, over-nutrition or excessive eating is correlated with chronic low-grade inflammation which increases the risk of and impacts the prognosis of autoimmune, cardiovascular, and metabolic diseases [11]. Typically, individuals with SLE have diverse medical interventions and may experience persistent exhaustion, mental health issues, and alterations in appetite, which can elevate the likelihood of malnourishment [12].

In this study, the correlation between subjects' disease activity (based on the SLEDAI score) and their immune nutritional status (based on the PNI score) was assessed. The analysis revealed that subjects with PNI scores of 46.6, 42, and 41.7 were classified as having mild, moderate, and severe disease activity, respectively. The correlation tests revealed a statistically significant inverse association between PNI and JSLE disease activity ($r = -0.3$; $p = 0.007$). Currently, studies that examine the relationship between PNI score and SLE disease activity remain very limited. The results of this present study align with the findings of a prior study by Ahn et al. [13] which indicate that PNI is a significant predictor of active SLE which is not influenced by other factors. In conjunction with prior research, this study demonstrates that PNI can be a valuable indicator for assessing disease activity in individuals with JSLE.

PNI, along with nutritional risk index (NRI) and controlling nutritional status (CONUT) score, has been used previously by Correa-Rodríguez et al. in their study to examine the clinical disease activity and damage in SLE patients. Their study employed the SLEDAI-2K to evaluate patients' disease activity and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) to measure the damage to the

patients' organs caused by the disease. In the clinical evaluation of SLE patients, both PNI and NRI can serve as useful indicators for identifying active SLE [8].

The results of the albumin tests taken in this study indicated that the average albumin level of patients with mild disease activity was 3.7 g/dL, while that of patients with moderate and severe disease activities was 3.5 g/dL. Extensive research has been conducted on the relationship between low levels of albumin in the blood (hypoalbuminemia) and disease activity in SLE. As a protein synthesized by the liver, albumin can be affected by several factors, including inflammation and kidney function, which may be compromised in individuals with SLE. Lupus nephritis, a prevalent and serious sign of SLE, frequently causes proteinuria, which is the excessive accumulation of proteins in the urine, particularly albumin. The loss of protein through the kidneys directly leads to hypoalbuminemia in affected patients. There is a significant relationship between the severity of lupus nephritis and the amount of protein in the urine. This correlation is also linked to disease activity and can result in significantly reduced levels of albumin [14,15]. Furthermore, a reduction in the synthesis of albumin in the liver may result from elevated inflammatory cytokine levels in those with active SLE. This is a part of the acute-phase response, during which the body prioritizes the synthesis of acute-phase proteins over albumin. In addition, inflammation can cause a rise in blood vessel permeability, which allows albumin to leak into the surrounding tissues [16]. Decreased serum albumin levels have been found to be significantly correlated with higher SLEDAI scores, suggesting that hypoalbuminemia may serve as a marker to monitor disease activity in individuals with SLE [17].

The leukocyte tests carried out in this study found the highest leukocyte count of 8111 x 103/μl in the mild category, which significantly decreased in the moderate and severe categories according to the classification of SLEDAI scores. This trend is also demonstrated in the measurement of absolute lymphocyte count. Previous studies have indicated a negative correlation between absolute lymphocyte count and disease activity in SLE [18,19]. Despite being one of the standard laboratory variables for SLE diagnostic criteria, both the original SLEDAI score and the

modified SLEDAI score (SLEDAI-2K) still exclude lymphopenia [16,20,21]. Therefore, in the evaluation of SLE disease activity, the seemingly insignificant but highly substantial impact of lymphopenia may not be well reflected by the SLEDAI-2K score. Hence, PNI may be a valuable indicator for improving the assessment of SLE activity with the SLEDAI-2K [13].

CONCLUSION

This study discovers a correlation between JSLE disease activity (SLEDAI) and PNI, emphasizing the importance of improving patient's nutritional status in managing JSLE severity.

Limitations include the single-center design and single PNI test. Further research with larger samples, multi-center design, and controls for confounding factors are necessary for a more comprehensive understanding.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this study.

AUTHOR'S CONTRIBUTIONS

Author's contributions: Conceptualization, I.L.S., Z.H., A.E.; methodology, I.L.S., Z.H., A.E.validation, I.L.S., Z.H., A.E.; formal analysis, I.L.S.; investigation, I.L.S., Z.H., A.E.; resources, I.L.S., Z.H.; data curation, I.L.S. and Z.H.; writing – original draft preparation, I.L.S.; writing – review and editing, I.L.S., Z.H., A.E.; visualization, I.L.S..; supervision, Z.H. and A.E.; project administration, Z.H.; funding acquisition, I.L.S., Z.H., A.E..

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