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RESEARCH ARTICLE

Correlation of AISI and PLR as Systemic Inflammatory Markers with Hospitalization Duration in Pediatric Typhoid Fever Patients

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Abstract:

Introduction: Typhoid fever remains a major public health problem in developing countries, including Indonesia, with a high incidence among children requiring hospitalization. Simple systemic inflammatory markers such as the Aggregate Index of Systemic Inflammation (AISI) and Platelet Lymphocyte Ratio (PLR) are increasingly studied because they can be calculated from routine blood tests and may serve as clinical indicators. **Method**: This retrospective cross-sectional study involved 57 pediatric patients with typhoid fever at PKU Muhammadiyah Sampangan Hospital, Surakarta, who met the inclusion and exclusion criteria. Data were analyzed using the Kolmogorov–Smirnov test for normality and the Spearman correlation test to evaluate associations between variables. **Result** : The results showed no significant correlation between AISI and the length of hospitalization ($p = 0.994$; $p > 0.05$) or between PLR and the length of hospitalization ($p = 0.320$; $p > 0.05$). **Discussion**: These findings indicate that AISI and PLR have no prognostic value in predicting hospitalization duration in pediatric typhoid fever patients. Further studies with larger sample sizes, prospective designs, and the inclusion of additional inflammatory biomarkers are needed to validate and strengthen these findings.

Kata Kunci: Typhoid fever, Pediatric, AISI, PLR, Inflammatory markers, Hospitalization duration

INTRODUCTION

Typhoid fever remains one of the major health problems in developing countries, particularly in Africa, the Eastern Mediterranean, Southeast Asia, and the Western Pacific. According to WHO data, the global incidence of typhoid fever is estimated to reach 9 million cases annually, resulting in approximately 110,000 deaths per year. The risk of typhoid is higher among populations without access to clean water and adequate sanitation, with children being the most vulnerable group (1). This disease continues to be a significant public health

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concern, especially in developing countries, including Indonesia. The incidence of typhoid fever in children remains high and often requires hospitalization (2).

The clinical manifestations of typhoid fever in children vary, ranging from gradually rising fever, gastrointestinal disturbances such as nausea, vomiting, diarrhea, or constipation, to severe complications like gastrointestinal bleeding or intestinal perforation if not properly managed. This disease can trigger a systemic inflammatory response in the body. Inflammation is a protective response to infection or injury; however, excessive or prolonged inflammation may worsen the patient's condition and prolong recovery time (3).

In recent years, there has been increasing attention toward accessible and cost-effective systemic inflammatory markers. Two of these are the Aggregate Index of Systemic Inflammation (AISI) and the Platelet-Lymphocyte Ratio (PLR). AISI is an index that combines several components of the complete blood count, namely neutrophils, monocytes, platelets, and lymphocytes, calculated with the formula (Neutrophils × Monocytes × Platelets) / Lymphocytes. AISI has been shown to be a valuable prognostic indicator for various inflammatory conditions and diseases, providing a comprehensive reflection of systemic inflammatory status (4,5). Meanwhile, PLR is the ratio of platelet count to lymphocyte count (Platelets / Lymphocytes). PLR has also been recognized as an informative systemic inflammatory marker, indicating shifts in immune and inflammatory responses to infection (6,7). Both can be easily calculated from routine blood tests available in most healthcare facilities.

Several studies have demonstrated that AISI and PLR are elevated in various infectious and inflammatory conditions such as sepsis, pneumonia, COVID-19, and certain oncological cases. Increased values of AISI and PLR indicate a massive systemic inflammatory response, which generally correlates with more severe clinical conditions and longer hospitalization (8,9). However, studies specifically investigating the correlation of AISI and PLR with the length of hospitalization in pediatric typhoid fever patients remain very limited, particularly in Indonesia. These parameters may serve as early assessment tools for risk stratification, aiding clinicians in making decisions regarding close monitoring, the need for aggressive interventions, or predicting hospitalization duration. Furthermore, the optimal use of routine laboratory data will enhance cost efficiency and patient care, particularly in advanced healthcare facilities.

Based on this background, this study aims to evaluate the correlation between AISI and PLR values with the length of hospitalization in pediatric patients with typhoid fever at a teaching hospital, as an innovative effort to improve the quality of early clinical assessment.

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METHOD

This study will employ an observational analytic research design with a cross-sectional, retrospective approach. This design was chosen to analyze the relationship between the independent variables (Aggregate Index of Systemic Inflammation/AISI and Platelet-Lymphocyte Ratio/PLR at the beginning of hospitalization) and the dependent variable (length of hospitalization of pediatric typhoid fever patients) based on existing medical record data. The study will be conducted at PKU Sampangan Hospital, Surakarta. Data collection will take place from August 2025 to September 2025, with ethical clearance No. 5832/B.2/KEPK-FKUMS/VIII/2025.

The data used will be derived from the medical records of pediatric typhoid fever patients hospitalized between January 2024 and December 2024. The inclusion criteria are patients under 18 years old diagnosed with typhoid fever based on clinical criteria and positive S. typhi IgM serology. Eligible patients must also have complete medical records containing full blood count data (neutrophils, monocytes, platelets, lymphocytes) within the first 24–48 hours of hospitalization, along with length of stay data. Exclusion criteria include patients with comorbidities affecting systemic inflammation, those who had received specific antibiotics prior to hospital admission, or those discharged against medical advice.

The formula used to calculate the Aggregate Index of Systemic Inflammation (AISI) is (monocytes × neutrophils × platelets) / lymphocytes, while the formula for the Platelet-Lymphocyte Ratio (PLR) is platelets / lymphocytes. Descriptive analysis will be used to describe the characteristics of the subjects. The Kolmogorov–Smirnov normality test will be applied to assess data distribution, and the correlation between AISI and PLR with the length of hospitalization will be analyzed using Spearman's correlation test.

RESULT

The baseline characteristics of the study subjects are presented in Table 1, including age, sex, nutritional status, hemoglobin, leukocyte count, platelet count, absolute neutrophil count, absolute monocyte count, absolute lymphocyte count, PLR, AISI, and length of hospitalization. Based on the inclusion and exclusion criteria, a total of 57 patients were enrolled in the study.

Bivariate analysis in Table 2 was performed using Spearman's correlation test to examine the relationship between PLR and AISI levels with the length of hospitalization in pediatric typhoid fever patients. This test was applied because PLR and AISI data were not normally distributed. The correlation analysis showed no significant relationship between AISI and length of hospitalization ($p = 0.994$, $p > 0.05$), as well as between PLR and length of hospitalization ($p = 0.320$, $p > 0.05$).

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Tabel 1. Baseline Characteristics of Study Subjects

Variabel	Hasil
Age (month)	79 (7-206) [b]
0-12 month	3 (5%)
1-<5 year	17 (30%)
5-<7 year	11 (19%)
7-<12 year	7 (12%)
12-<18 year	19 (34%)
Gender	
Man	29 (49%)
Woman	28 (51%)
Nutritional status (BMI/Age)	
Underweight	8 (14%)
Normal	42 (74%)
Overweight	7 (12%)
Hb (g/dl%)	13,10 ± 1,65[a]
WBC ($10^3/mm^3$)	6,07 (1,14 – 26,38)[b]
Platelet($10^3/mm^3$)	206 (10 – 517) [b]
Low (<150x10^3)	11 (19%)
Normal(150-450x10^3)	44 (77%)
High (>450x10^3)	2 (3%)
Absolute Netrophil Count ($10^3/mm^3$)	3,38 (0,48 – 21,94 [b])
Absolute Monocyte Count ($10^3/mm^3$))	0,57 ± 0,39 [a]
Absolute Limphocyte Count ($10^3/mm^3$)	1,7 (0,10 – 8,17) [b]
PLR	131,22 (15,94 – 1350,98)[b]
AISI	175,86 (7,58 – 7708,39) [b]
Hospitalization duration(days)	2 (2 – 5) [b]

Note : a= rate and SD, b= median (min-max), PLR=Platelet Limfosit Ratio, AISI= Aggregate Index of Systemic Inflammation, g-gram, dl=deciliter, mm=milimiter

Table 2. Bivariate analysis

Parameter	r-value	p-value
AISI	-0.01	0.994
PLR	0.134	0.320

DISCUSSION

This study included 57 pediatric patients who were clinically diagnosed with typhoid fever and had a tubex tf® result of more than 4 positive, ranging in age from 7 months to 17 years. The case distribution indicated that the 12–<18 years age group had the highest prevalence, accounting for 34% of all patients. This proportion was greater compared to other age groups. A study by Britto et al. (2017) reported that pediatric typhoid cases increase with age, with children over 9 years contributing 41% of all cases (10). A similar pattern was observed in Indonesia, based on a retrospective study in Jakarta from 2017 to 2023, which confirmed the high prevalence of typhoid fever in children and adolescents. The high incidence among adolescents may be attributed to increased mobility, the habit of eating outside the home, and greater independence in food choices, all of which contribute to the risk of consuming food contaminated with *Salmonella typhi* (11,12).

The distribution of typhoid fever cases by sex in this study showed a relatively balanced proportion between male and female children, suggesting that sex does not serve as a distinguishing factor in the prevalence of typhoid fever in the pediatric population. This finding is consistent with the study by Rasul et al. (2017) in Pakistan, which reported no significant difference in incidence between boys and girls (13). A systematic review by Boakye O. et al. (2025), which included data spanning from 1928 to 2024, revealed mixed results regarding gender-based susceptibility to typhoid fever. The relationship between sex and susceptibility appears inconsistent and

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likely influenced by a combination of biological, social, and environmental factors (14).

Based on nutritional status (BMI-for-age), the majority of pediatric patients with typhoid fever in this study were in the normal category, with 42 children (74%). Meanwhile, 8 children (14%) were undernourished, and 7 children (12%) were overweight. This distribution shows that although most patients had normal nutritional status, typhoid fever can still occur across all categories. A similar phenomenon was reported in Indonesia, emphasizing that adequate nutrition does not guarantee full protection against infection(15). Epidemiological studies in endemic regions demonstrate that while malnutrition increases susceptibility to infection through impaired immunity, high environmental exposure to *Salmonella typhi* means that well-nourished children continue to account for most cases, reflecting their predominance in the general pediatric population (16,17).

The association of PLR with length of hospitalization has been observed in pediatric asthma cases (18). However, in this study, correlation analysis revealed that the relationship between PLR and hospitalization duration in pediatric typhoid fever patients was not significant ($p = 0.320$; $r = 0.134$), as shown in the correlation test table. A p-value greater than 0.05 indicates no statistically significant correlation. This suggests that variations in hospitalization duration in typhoid fever are not influenced by changes in PLR.

PLR has been recognized as a simple, inexpensive, and informative inflammatory marker that can be used to assess systemic inflammatory status in various diseases. Numerous studies have demonstrated its prognostic value in conditions such as malignancies, cardiovascular diseases, autoimmune disorders, and infections. For example, elevated PLR has been linked to disease severity and poor prognosis in patients with COVID-19, sepsis, and multiple types of cancer (5,6).

The results of this study showed no correlation between AISI ($p = 0.994$; $r = -0.01$) and the length of hospitalization in pediatric typhoid fever patients. AISI is a novel inflammatory indicator derived from the complete blood count, integrating neutrophils, monocytes, lymphocytes, and platelets. It has been reported to outperform PLR, MLR, NLR, N/LP, NPR, NMR, and NMLR in providing a comprehensive representation of blood cell dynamics and systemic inflammatory status, while also being cost-effective and readily available (7). AISI reflects the role of innate immunity, represented by monocytes, neutrophils, and platelets, as well as adaptive immunity, represented by lymphocytes (19).

This finding is in line with a study by Gurpinar A. et al. (2025) on the relationship between the Systemic Immune Inflammation Index (SII) and AISI in sepsis

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patients, which found no significant difference (p = 0.224) between the control group and patients (20). This may be attributed to the complexity of the AISI formula, which involves four hematological parameters in pediatric populations, where variability is higher than in adults, and reference values differ by age (21). As an acute infectious disease, typhoid fever may also exhibit a different inflammatory response pattern compared to chronic diseases in which AISI has been shown to be effective.

CONCLUSION

This study demonstrated that among 57 pediatric patients with typhoid fever, the highest case distribution was observed in the adolescent age group, with a predominance of normal nutritional status, and no significant differences based on sex. Correlation analysis confirmed that PLR and AISI were not associated with the length of hospitalization, indicating that neither parameter can yet be considered a reliable predictive indicator in pediatric typhoid fever. The duration of hospitalization may be more strongly influenced by the timeliness and appropriateness of antibiotic therapy, which plays a critical role in controlling bacterial load and reducing systemic inflammation. Future research is recommended to include a larger sample size, a prospective design, the addition of other inflammatory biomarkers, and analysis of antibiotic treatment patterns to achieve a more comprehensive understanding of the relationship between hematological and clinical factors with hospitalization duration.The content of conclusion should clearly state the result of correlated objective (and may also possible with future direction).

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