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Association of SII and AISI in patients with sepsis: A retrospective study

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Abstract

Sepsis, a life-threatening dysregulated immune response to infection, necessitates reliable biomarkers for early risk stratification and prognosis. Sepsis occurs when bacteria that cause an infection the body's overwhelming inflammatory reaction to an infection leads to extensive tissue injury, organ dysfunction, and can be deadly if not promptly addressed. This study investigates the role of Systemic immune-inflammation index (SII), Systemic inflammatory response index (SIRI) and Aggregate Index of Systemic Inflammation (AISI) score in patients with sepsis. This retrospective study included 127 patients diagnosed with sepsis between November 2023 and March 2024. Neutrophil, lymphocyte and platelet levels statistically significant differences were observed in between the groups ($p<0.0001$). However, inflammatory indices calculated for the study groups did not show significant differences in terms of SII, SIRI, AISI ($p<0.05$). This study highlights SII and AISI as accessible, cost-effective biomarkers for assessing systemic inflammation and predicting adverse outcomes in sepsis. This research also emphasizes the predictive significance of SII and AISI, which are straightforward and regularly measured biomarkers. Further prospective studies are warranted to validate these findings and explore their utility in dynamic monitoring of sepsis progression.

Keywords: Sepsis, aggregate index of systemic inflammation, systemic immune-inflammation index, systemic inflammatory response index

Introduction

Sepsis represents a critical condition where the body's extensive inflammatory response to an infection results in widespread tissue damage, organ failure, and can ultimately be fatal if not treated [1]. Although medical care has improved, sepsis continues to pose a significant global health threat, with substantial rates of illness and death. It is estimated that sepsis affects millions of people worldwide each year, contributing to one in five deaths globally [2]. The pathophysiology of sepsis is complex and involves an interplay between microbial invasion, the host's immune response, and systemic inflammation [3]. Systemic inflammation, a hallmark of sepsis, is characterized by the widespread activation of the immune system, resulting in the release of pro-inflammatory cytokines and other mediators [4]. This exaggerated immune response is intended to control the infection but often leads to a dysregulated state, where excessive inflammation damages host tissues. The disruption of the immune balance can result in septic shock, characterized by severe hypotension and inadequate blood flow to vital organs [5]. The precise mechanisms underlying sepsis and systemic inflammation are not fully understood, but it is known that both innate and adaptive immune responses play crucial roles.

Cells involved in the body's first line of immune defense recognize and respond to pathogens through pattern recognition receptors (PRRs) like Toll-like receptors (TLRs) [6]. Upon activation, these cells release cytokines, which amplify the inflammatory response and recruit additional immune cells to the site of infection. However, in sepsis, this response becomes excessive and systemic, leading to widespread tissue damage, endothelial dysfunction, and a cascade of coagulation abnormalities. In recent years, research has focused on identifying biomarkers and therapeutic targets for sepsis and systemic inflammation, with the aim of improving diagnosis, prognosis, and treatment outcomes [7]. Early recognition and prompt management of sepsis are

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critical, as timely intervention can significantly reduce the risk of organ failure and improve survival rates. Despite these efforts, effective treatment remains a challenge, highlighting the need for a deeper understanding of the underlying molecular and cellular mechanisms driving sepsis and systemic inflammation. Lately, several studies have been conducted with the inflammatory indexes [8-14]. Systemic immune-inflammation index (SII) provides a comprehensive reflection of the body's immune status. SII has shown promise as a prognostic indicator, particularly in predicting patient outcomes and guiding treatment strategies in sepsis and other inflammatory conditions [8].

Systemic inflammatory response index (SIRI) levels indicate a heightened inflammatory response, suggesting that the immune system is under significant stress or that a systemic inflammatory response is ongoing. Researchers have investigated SIRI as a possible indicator for predicting outcomes in a range of illnesses including infections, sepsis, cardiovascular diseases, and malignancies. It provides valuable insights into the balance between pro-inflammatory and anti-inflammatory forces within the body, aiding in the assessment of disease severity and patient prognosis [15]. Aggregate Index of Systemic Inflammation (AISI) aims to capture the aggregate effect of different inflammatory cells and platelets, which play crucial roles in both inflammation and coagulation [16]. High AISI values are indicative of an enhanced inflammatory state and have been associated with poorer clinical outcomes across different conditions.

SII, SIRI, and AISI are valuable hematologic indices that provide insights into the systemic inflammatory response by integrating the roles of different blood cell types. These indices have shown potential as prognostic markers in various clinical settings, including sepsis, cancer, and cardiovascular diseases. Our research seeks to evaluate the prognostic significance of the SII, SIRI, and AISI scores in sepsis patients.

Material and Methods

Our retrospective study included a group of 127 patients diagnosed with sepsis who were hospitalized in the Intensive Care Unit of Ordu University Training and Research Hospital between November 2023 and March 2024, and a control group of 394 patients who had no growth in blood cultures, no signs of infection, and no diagnosis of sepsis. Age, gender, White blood cell count (WBC), neutrophil count (NEU), lymphocyte count (LYM), monocyte count (MON), platelet count (PLT), and blood culture results were evaluated from the hospital information system. The SII, SIRI and AISI were calculated respectively as follows: platelets x (neutrophils/lymphocytes), (neutrophils x monocytes)/lymphocytes and Neutrophil count × Monocyte count x Platelet count/Lymphocyte count. The research adhered to the principles outlined in the Declaration of Helsinki. For laboratory evaluations, the initial hemogram data were documented at the same time as the blood culture growth in patients admitted to the intensive care unit.

Hematological parameters were analyzed using an automatic analyzer Sysmex XN 1000 (Sysmex Corporation, Kobe, Japan). Sepsis diagnosis was made with an increase of at least two points or more in the Sequential Organ Failure Assessment (SOFA) scoring system. The study was approved by the Ordu University Ethics Committee (12.07.2024-91).

Statistical Analyses

Statistical analyses were performed using the MedCalc (version 20.009; Ostend, Belgium) statistical package program. Numbers and percentages were used for categorical variables in the statistical description of the data. In the evaluation of numerical data, the Kolmogorov-Smirnov test was used to determine whether the groups were normally distributed. The Mann Whitney U test was used for pairwise comparison of the groups. Logistic regression analysis was performed for modeling of the study and was shown in a table. The study group analyzed with the reference group in the logistic regression table was expressed as "…". The odds ratio (OR) was given with a 95% confidence interval. The significance level was taken as $p<0.05$ in the interpretation of the results.

Results

In this study, a total of 521 individuals were involved, 394 healthy controls with an average age of 68.3±20.4 and 127 Sepsis patients with an average age of 56.4±30.7. The groups did not exhibit any significant differences in age or gender. (Table 1). Neutrophil, lymphocyte and platelet levels statistically significant differences were observed in between the groups ($p<0.0001$, Table 2). However, no significant differences were observed in the inflammatory indices regarding SII, SIRI, or AISI. In the logistic regression model applied for the study, as PLT level increases, the risk of patients developing sepsis decreases [OR: 0.997 (0.994-1.000), P=0.039]. According to the modeling, although not statistically significant, the risk of developing sepsis decreases as neutrophil, monocyte and lymphocyte values increase. The risk of developing sepsis increases with increasing age and female gender.

Table 1. Demographic information of the study groups

		Control			Patient		
		n	%		n	%	
Gender	Male	210	53.3		61	48.0	
	Female	184	46.7		66	52.0	
		n	Mean	SD	n	Mean	SD
Age (year)		394	56.46	30.74	127	68.31	20.39

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Table 2. Comparison of the blood parameters of the study and control groups

	Groups											
	Control					Patient						P-value
	N	Median (95% CI)			25P	75P	N	Median (95% CI)			25P	75P	
Neutrophil (10^9/L)	394	9.18	8.77	9.78	6.02	13.5	127	8.72	7.72	9.39	5.18	13.25	0.302
Monocyte (10^9/L)	394	0.815	0.761	0.859	0.560	1.14	127	0.600	0.530	0.690	0.370	0.868	<0.0001*
Lymphocyte (10^9/L)	394	1.39	1.26	1.50	0.86	2.32	127	0.84	0.70	1.00	0.48	1.54	<0.0001*
Platelet (10^9/L)	394	244.2	229.9	254.0	176.9	301.0	127	196.4	178.2	219.2	116.0	265.9	<0.0001*
SII	394	1336.3	1191.3	1574.7	701.9	2646.1	127	1682.1	1227.4	2224.3	840.0	4148.4	0.058
SIRI	394	4.265	3.94	5.448	2.24	9.48	127	6.28	4.058	7.47	1.96	10.8	0.462
AISI	394	1055.9	939.1	1160.8	510.5	2308.0	127	983.6	671.2	1323.3	338.4	2337.2	0.224

*Significant difference at <0.05 level according to Mann-Whitney U test, CI: confidence interval, SII: systemic inflammatory index (neutrophil x platelet/ lymphocyte count), SIRI: systemic inflammatory response index (neutrophil × monocyte/ lymphocyte count) and AISI: aggregate index of systemic inflammation (neutrophil × platelet x monocyte/lymphocyte count)

Discussion

Sepsis is a critical condition that arises from an abnormal immune reaction to an infection, remains a significant cause of morbidity and mortality in critically ill patients. Early recognition of sepsis and prediction of the severity of the inflammatory response are essential for timely intervention and improved outcomes. Over the years, various biomarkers and indices have been proposed to assess systemic inflammation in sepsis, with the aim of improving clinical decision-making and prognostication. Among these, the SII, the SIRI, and the AISI have garnered attention as potential tools for clinical use.

Our study indicates that neutrophil, lymphocyte and platelet levels statistically significant differences were observed in between the study subjects (p<0.0001, Table 2). However, inflammatory indices did not show disparity differences in terms of SII, SIRI, AISI. Moreover, PLT level increases, the risk of patients developing sepsis decreases [OR: 0.997 (0.994-1.000), P=0.039, Table 3]. In this research, we have shown the predictive value of the SII and AISI, an easily obtainable and commonly used biomarker. This research illustrates the predictive value of SII and AISI, which are straightforward and commonly obtained biomarkers.

In the study conducted by Jang et al. on patients undergoing haemodialysis with catheter-related bloodstream infection (CRBSI), the SIRI value was significantly higher. In the group with infections compared to the non-infected group. Following antimicrobial therapy, the SIRI value was found to be significantly lower in CRSBI patients. They hypothesized that SIRI serves as a new and effective marker for the early detection of CRBSI in haemodialysis patients [17].

In another study conducted by Liu et al. to assess the prognostic accuracy of the SII in combination with the quick Sequential Organ Failure Assessment (qSOFA) criteria for predicting 28-day mortality in sepsis [18]. In observational design by Yang et al. to examine the role of preoperative SII they found that After multivariable adjustments, patients with an SII greater than 1792.19 showed a significantly increased risk of developing sepsis post-surgery. Morover, they found no association between preoperative SII and postoperative sepsis.

They hypothsized that SII was identified as potential risk factor for sepsis following surgery [19]. In the study conducted by Zinulle and her colleagues on patients with Idiopathic Pulmonary Fibrosis they demonstrated that the predictice capacity of the SII, SIRI and AISI. They showed that the survival rates between the two groups, categorized by their AISI values, showed a notable difference [20]. Another study conducted by Xiu et al. on hypertension patients, they indicated that elevated AISI levels showed a significant correlation with cardiovascular mortality among individuals with hypertension. The authors concluded that higher AISI levels are strongly linked to an levated risk of cardiovascular mortality and may serve as an early warning sign of unfavorable outcomes [16].

Mangalesh et al.'s study to predict systemic sepsis mortality using the inflammation index has shown that SII is a suitable parameter that can be used in addition to clinical sepsis scores to improve the accuracy of patient assessment [21]. They concluded that SII had independent and comparable prognostic accuracy compared to the SOFA score. Morover, they hypothsized rhat the SII may be used in addition to clinical sepsis scores to improve the accuracy of assessments. In another study by Shuyan et al. investigating the relationship between systemic inflammation response index and mortality in sepsis and its prognostic significance, increased systemic inflammatory response was associated with mortality in female patients with sepsis [22]. They concluded that elevated SIRI was associated with an increased risk of mortality in sepsis. SIRI is an independent prognostic biomarker of mortality in sepsis. The potential for using these indices in clinical practice is promising, particularly due to their simplicity and accessibility. All three indices rely on routine laboratory values that are commonly available in clinical settings, making them cost-effective tools for assessing the inflammatory state of septic patients. Additionally,

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they provide a quantitative measure that can complement clinical judgment, helping clinicians identify high-risk patients who may benefit from more aggressive intervention or monitoring.

However, there are significant limitations to their clinical utility. First, these indices, while reflective of systemic inflammation, do not provide a comprehensive picture of the pathophysiological processes underlying sepsis. Sepsis involves complex interactions between pro-inflammatory and anti-inflammatory mediators, immune cells, and the endothelium, which are not fully captured by simple indices. Second, the variability in cut-off values and the lack of standardization across studies limit their generalizability. Finally, these indices are static measures and may not reflect dynamic changes in the inflammatory response over time, which is crucial in the management of septic patients.

Conclusion

While SII, SIRI, and AISI show promise as tools for predicting inflammatory responses in patients with sepsis, their application in medical practice is currently restricted by several factors, including variability in reference values, lack of dynamic assessment, and the complexity of sepsis pathophysiology. Upcoming studies ought to concentrate on the validation of these indices in larger, more diverse populations and their integration with other clinical and biomarker data to improve their predictive accuracy.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
Ethical approval and ethics committee permission for this study were obtained from Ordu University Medical Faculty Clinical Research Ethics Committee with the decision number 12.07.2024-91.

References

1. Cecconi M, Evans L, Levy M, et al. Sepsis and septic shock. Lancet. 2018;392:75-87.
2. Ackerman MH, Ahrens T, Kelly J, et al. Sepsis. Crit Care Nurs Clin North Am. 2021;33:407-18.
3. Huang M, Cai S, Su J. The pathogenesis of sepsis and potential therapeutic targets. Int J Mol Sci. 2019;20:5376.
4. Nedeva C. Inflammation and cell death of the innate and adaptive immune system during sepsis. Biomolecules. 2021;11:1011.
5. Esposito S, De Simone G, Boccia G, et al. Sepsis and septic shock: new definitions, new diagnostic and therapeutic approaches. J Glob Antimicrob Resist. 2017;10:204-12.
6. Kawai T, Akira S. Toll-like receptors and their crosstalk with other innate receptors in infection and immunity. Immunity. 2011;34:637-50.
7. Liu D, Huang SY, Sun JH, et al. Sepsis-induced immunosuppression: mechanisms, diagnosis and current treatment options. Mil Med Res. 2022;9:56.
8. Jiang D, Bian T, Shen Y, et al. Association between admission systemic immune-inflammation index and mortality in critically ill patients with sepsis: a retrospective cohort study based on MIMIC-IV database. Clin Exp Med. 2023;23:3641-50.
9. Xia Y, Xia C, Wu L, et al. Systemic immune inflammation index (SII), system inflammation response index (SIRI) and risk of all-cause mortality and cardiovascular mortality: a 20-year follow-up cohort study of 42,875 US Adults. J Clin Med. 2023;12:1128.
10. Zinellu A, Paliogiannis P, Mangoni AA. Aggregate index of systemic inflammation (AISI), disease severity, and mortality in COVID-19: a systematic review and meta-analysis. J Clin Med. 2023;12:4584.
11. Akbulut Yağcı B, Erdal H. Can pan-immune inflammation value and systemic inflammatory response index be used clinically to predict inflammation in patients with cataract. ACAM. 2023;14:1064-7.
12. Erdal H, Günaydın FE. Are pan-immune inflammation-value, systemic inflammatory response index clinically useful to predict in patients with chronic spontaneous urticaria?. Ann Clin Anal Med. 2023;14:897-900.
13. Genç ŞÖ, Erdal H. Evaluating hematological inflammatory markers as predictors of preeclampsia. Clin.Exp.Obstet.Gynecol. 2024;51:163.
14. Günaydın FE, Erdal H. Is there a relationship between systemic immune-inflammatory indices and asthma?. ACAM. 2023;14:840-3.
15. Wang RH, Wen WX, Jiang ZP, et al. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Front Immunol. 2023;14:1115031.
16. Xiu J, Lin X, Chen Q, et al. The aggregate index of systemic inflammation (AISI): a novel predictor for hypertension. Front Cardiovasc Med. 2023;10:1163900.
17. Yang J, Wang H, Hua Q, et al. Diagnostic value of systemic inflammatory response index for catheter-related bloodstream infection in patients undergoing haemodialysis. J Immunol Res. 2022;2022:7453354.
18. Liu C, Wu X, Deng R, et al. Systemic immune-inflammation index combined with quick sequential organ failure assessment score for predicting mortality in sepsis patients. Heliyon. 2023;9:e19526.
19. Yang J, Ran T, Lin X, et al. Association between preoperative systemic immune inflammation index and postoperative sepsis in patients with intestinal obstruction: a retrospective observational cohort study. Immun Inflamm Dis. 2024;12:e1187.
20. Zinellu A, Collu C, Nasser M, et al. The aggregate index of systemic inflammation (AISI): a novel prognostic biomarker in idiopathic pulmonary fibrosis. J Clin Med. 2021;10:4134.
21. Mangalesh S, Dudani S, Malik A. The systemic immune-inflammation index in predicting sepsis mortality. Postgrad Med. 2023;135:345-51.
22. Ru S, Luo Y. The association and prognostic value of systemic inflammatory response index with short and long-term mortality in patients with sepsis. Medicine (Baltimore). 2023;102:e33967.