Research Article / Araştırma Makalesi

Prognostic Value of Systemic Immune-Inflammation Index (SII), Platelet-Lymphocyte Ratio (PLR) and Neutrophil-Lymphocyte Ratio (NLR) in Predicting Mortality in Pneumosepsis Patients in Intensive Care Unit

Yoğun Bakım Ünitesinde Pnömosepsis Hastalarında Mortaliteyi Öngörmede Sistemik İmmün-İnflamasyon İndeksi (SII), Trombosit-Lenfosit Oranı (PLR) ve Nötrofil-Lenfosit Oranının (NLR) Prognostik Değeri

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Abstract

Background: This study aims to evaluate the prognostic value of Systemic Immune-Inflammation Index (SII), Platelet-Lymphocyte Ratio (PLR) and Neutrophil-Lymphocyte Ratio (NLR) to predict mortality in patients with pneumosepsis in the intensive care unit (ICU).
Materials and Methods: The study was conducted retrospectively and clinical data of patients diagnosed with pneumosepsis were analyzed. Age, gender, comorbidities, length of stay (LOS) in the ICU, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, SII, PLR, NLR values and prognoses were obtained from patient files and hospital records system.
Results: A total of 68 patients were included in the study. 60.3% of the patients were male and 39.7% were female. The mean age of deceased patients was statistically significantly higher than that of discharged patients ($p = 0.016$). In the study, 22 patients were discharged and 46 patients died. While the mean SII value was 464.05±107.31 in the discharged group, this value was 845.53±111.04 in those who died ($p<0.001$). Similarly, the PLR value was 88.14 ± 10.66 in those discharged and 114.89±12.97 in those who died ($p<0.001$). The NLR value was 3.5 ± 0.86 in the discharged group and 6.73±0.84 in the deceased group ($p<0.001$).
Conclusions: This study reveals that SII, NLR and PLR indices are important and reliable indicators for predicting mortality in pneumosepsis patients in the ICU.

Keywords: Systemic immune-inflammation index, Platelet/lymphocyte ratio, Neutrophil/lymphocyte ratio, Pneumosepsis, Intensive care unit

Öz

Amaç: Bu çalışma, pnömosepsis tanısı almış hastalarda yoğun bakım ünitesinde mortaliteyi öngörmek amacıyla Sistemik İmmün-İnflamasyon İndeksi (SII), Trombosit-Lenfosit Oranı (PLR) ve Nötrofil-Lenfosit Oranı'nın (NLR) prognostik değerini değerlendirmeyi amaçlamaktadır.
Materyal ve Metod: Çalışma retrospektif olarak gerçekleştirilmiş ve pnömosepsis tanısı almış hastaların klinik verileri analiz edilmiştir. Hastaların yaşı, cinsiyeti, eşlik eden hastalıkları, yoğun bakımda kalış süresi, Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skoru, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi II (APACHE II) skoru, SII, PLR, NLR değerleri ve prognozları hasta dosyaları ve hastane kayıt sisteminden elde edilerek kaydedilmiştir.
Bulgular: Çalışmaya toplam 68 hasta dahil edilmiştir. Hastaların %60,3'ü erkek, %39,7'si kadındır. Hayatını kaybeden hastaların yaş ortalaması, taburcu edilen hastalara kıyasla istatistiksel olarak anlamlı şekilde daha yüksek bulunmuştur ($p = 0,016$). Çalışmada 22 hasta taburcu edilirken, 46 hasta hayatını kaybetmiştir. Taburcu edilen grupta ortalama SII değeri 464,05±107,31 iken, hayatını kaybedenlerde bu değer 845,53±111,04 olarak tespit edilmiştir ($p<0.001$). Benzer şekilde PLR değeri taburcu edilenlerde 88,14 ± 10,66, hayatını kaybedenlerde ise 114,89±12,97'dir ($p<0.001$). NLR değeri ise taburcu edilen grupta 3,5±0,86 hayatını kaybeden grupta 6,73±0,84 olarak bulunmuştur ($p<0.001$).
Sonuç: Bu çalışma, yoğun bakım ünitesindeki pnömosepsis hastalarında SII, NLR ve PLR indekslerinin mortaliteyi öngörmede önemli ve güvenilir göstergeler olduğunu ortaya koymaktadır.

Anahtar Kelimeler: Sistemik immün-inflamasyon indeks**,** Trombosit/lenfosit oranı, Nötrofil/lenfosit oranı, Pnömosepsis, Yoğun bakım ünitesi

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Introduction

Sepsis is a life-threatening organ dysfunction caused by the host's response to infection. Sepsis and septic shock are major global health concerns, affecting millions and causing high mortality rates worldwide. Early diagnosis and treatment within the first hours of sepsis onset significantly improve the survival chances of the patient (1–3).

Pneumonia is defined as an acute infectious process in the lung parenchyma and represents the most common cause of infection-related mortality globally. It also contributes significantly to morbidity, particularly in critically ill patients with comorbidities, potentially leading to sepsis and septic shock (4,5). Pneumonia is a primary cause of sepsis. Research indicates that pneumonia-induced sepsis is associated with higher mortality rates compared to sepsis from other infection sources (6).

For sepsis patients, identifying biomarkers that predict mortality, facilitating early diagnosis and treatment, and exploring factors that yield favorable clinical outcomes are critical (7, 8).

The Systemic Immune-Inflammation Index (SII), a novel biomarker based on platelet, lymphocyte, and neutrophil counts, was introduced in 2014 (9). The Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR), additional inflammatory biomarkers, may serve as indicators of sepsis onset. A hematological profile can also be employed to assess therapy response and detect early signs of infection. Sepsis is one of the conditions in which PLR and NLR are utilized as predictive indices (10).

Our study aimed to evaluate the utility of SII, PLR, and NLR in predicting pneumosepsis mortality.

Materials and Methods

This retrospective study was approved by the Ethics Committee of Health Sciences University Diyarbakır Gazi Yaşargil Training and Research Hospital (Approval no: 2024/187). The study was conducted in accordance with the Declaration of Helsinki. Our study included patients admitted to the ICU between January 2018 and February 2020 and diagnosed with pneumosepsis. Patients who were older than eighteen years of age, clinically, laboratory and radiologically diagnosed with pneumosepsis and whose data were not missing were included in the study. Patients who were younger than 18 years of age, who were not diagnosed with pneumosepsis and whose data were incomplete were excluded (Figure 1).

Patient demographics (age, gender), comorbidities, length of stay (LOS) in the ICU, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, SII, PLR, NLR values, and prognoses (discharged or deceased) were recorded from patient files and hospital records.

Scoring systems are important tools used to predict disease severity and mortality in intensive care patients, including patients with sepsis. They are also useful for standardizing research in ICUs and comparing the quality of patient care. The APACHE II scoring system is one of the most widely used systems in the world. The APACHE II system consists of three parts: the acute physiology score, age, and chronic health assessment. In this way, the acute and chronic health status of the patient is evaluated (11). The SOFA scoring system is used to diagnose and predict outcomes for patients with sepsis in the ICU. The SOFA scoring system calculates a severity score using straightforward measurements of major organ dysfunctions without considering any parameters related to the patient's chronic health status (12).

The SII was calculated as follows: SII = neutrophil count (10^9/L) × platelet count (10^9/L) / lymphocyte count (10^9/L) (9).

The diagnosis of sepsis was established according to the Sepsis-3 criteria, and pneumonia was diagnosed based on the American Thoracic Society guidelines (13,14).

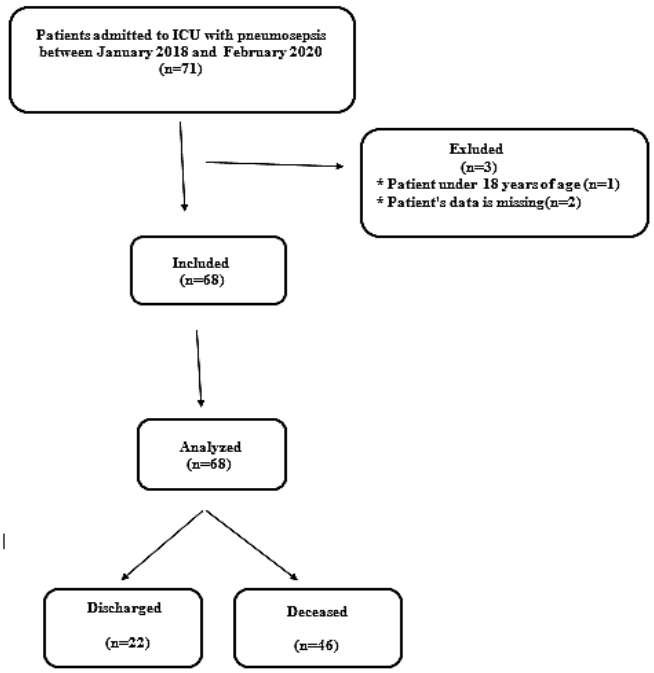

Figure 1. Flow chart showing patient flow

Statistical Analysis

Statistical analyses were performed using SPSS software version 22.0 (SPSS Inc., Chicago, IL). Descriptive statistics of continuous variables were expressed as mean and standard deviation, and categorical variables were expressed as frequency (n) and percentage (%). Student's t test or Mann-Whitney U test was applied for comparisons of continuous variables between groups, depending on whether the data conformed to normal distribution. Chi-square test and Fisher's exact test were used to compare categorical variables between groups. ROC analysis was performed to evaluate SII, PLR, NLR and other parameters in predicting mortality in pneumosepsis. Multivariate logistic regression analysis was performed to identify factors associated with mortality. A value of $p<0.05$ was accepted as the limit of statistical significance.

Results

Of the 68 patients, 60.3% were male and 39.7% were female. Twenty-two patients were discharged, while 46 died. The average age of discharged patients was 54.82±8.17 years, while the average age of deceased patients was 61.24±10.81 years. This difference was statistically significant (p = 0.016). The LOS ICU was 14.18±6.12 days for discharged patients and 22.37±15.48 days for deceased patients. This difference was also statistically significant (p = 0.019) (Table 1).

Table 1. Demographic characteristics of the patients

	All patients (n = 68)	**Discharged (n = 22)**	**Deceased (n = 46)**	***p* value**
Gender (n %)	41 (60.3%) Male 27(39.7%) Female	13(59.1%) Male 9(40.9%) Female	28(60.9%) Male 18(39.1%)Female	0.901
Age (years)	59.16 ± 10.42	54.82 ± 8.17	61.24 ± 10.81	0.016
Comorbidities				
Hypertension	21(30.8%)	6 (27.2%)	15 (32.6%)	0.065
Diabetes	14(20.5%)	8 (36.4%)	6 (13%)	<0.001
Neurological disease	7 (10.3%)	2 (9.1%)	5 (10.9%)	0.832
Chronic pulmonary diseases	17 (25%)	5 (22.7%)	12 (26.1%)	0.371
Cardiac disease	16 (23.5%)	6 (27.2%)	10 (21.7%)	0.365
Chronic kidney diseases	15 (22.1%)	4 (18.2%)	11 (23.9%)	0.062
Chronic liver disease	9 (13.2%)	3 (13.6%)	6 (13%)	0.901
Malignancy	4 (5.9%)	1 (4.5%)	3 (6.5%)	0.633
LOS ICU	19.72±13.7	14.18±6.12	22.37±15.48	<0.001
SOFA	8.94±3.22	5.18±1.92	10.74±1.88	<0.001
APACHE II	27.84±9.37	19.64±4.48	31.76±8.53	<0.001
PLR	106.1±17.57	88.14±10.66	114.89±12.97	<0.001
NLR	5.69±1.74	3.5±0.86	6.73±0.84	<0.001
SII	722.11±210.28	464.05±107.31	845.53±111.04	<0.001

n: Number of patients. %: Percentage. SOFA: Sequential Organ Failure Assessment. APACHE II: Acute Physiology and Chronic Health Evaluation II. LOS: Length of stay. ICU: Intensive care unit. NLR:Neutrophil-Lymphocyte Ratio. PLR: Platelet-Lymphocyte Ratio. SII: Systemic Immune-Inflammation Index

In the discharged group, the mean SII was 464.05 ± 107.31, while it was 845.53 ± 111.04 in the deceased group (p<0.001). The PLR was 88.14 ± 10.66 in the discharged group and 114.89 ± 12.97 in the deceased group (p<0.001). The mean NLR was 3.5 ± 0.86 in the discharged group and 6.73 ± 0.84 in the deceased group (p<0.001).

The results of multivariate logistic regression analysis of the variables associated with mortality in the study are presented in Table 2.

The ROC analysis results for SII, PLR, and NLR parameters in predicting mortality in pneumosepsis are presented in Figure 2, while the ROC analysis results for age, LOS ICU, SOFA score, and APACHE II score are shown in Figure 3.

Table 2. Multivariate logistic regression analyses to examine the association between mortality and statistically significant variables of the study

	***p* value**	**HR**	**95% CI**	
			Lower	**Upper**
SOFA	<0.001	1.085	1.007	1.196
APACHE II	<0.001	1.052	1.015	1.198
LOS ICU	<0.001	1.053	1.008	1.062
PLR	<0.001	1.001	1.000	1.002
NLR	<0.001	1.060	1.034	1.083
SII	<0.001	1.004	1.001	1.007

SOFA: Sequential Organ Failure Assessment. APACHE II: Acute Physiology and Chronic Health Evaluation II. LOS: Length of stay. ICU: Intensive care unit. PLR: Platelet-Lymphocyte Ratio. NLR:Neutrophil-Lymphocyte Ratio. SII: Systemic Immune-Inflammation Index. HR: Hazard ratio. 95% CI: 95% Confidence interval.

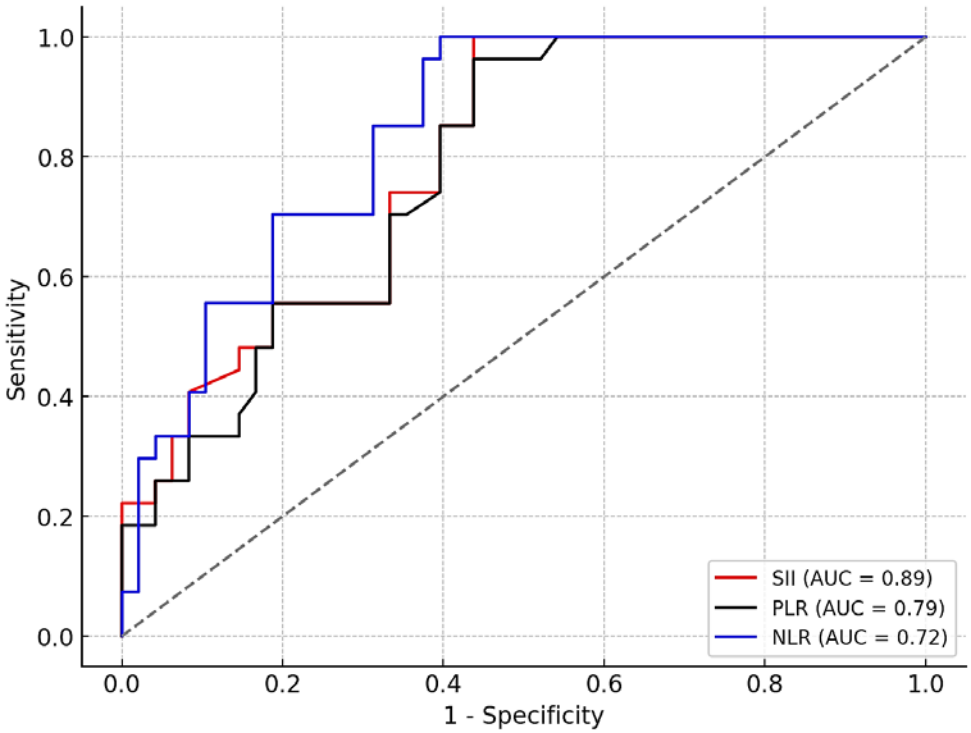

Figure 2. Comparison of the effects of SII, PLR, and NLR values on mortality using ROC curves and AUC values

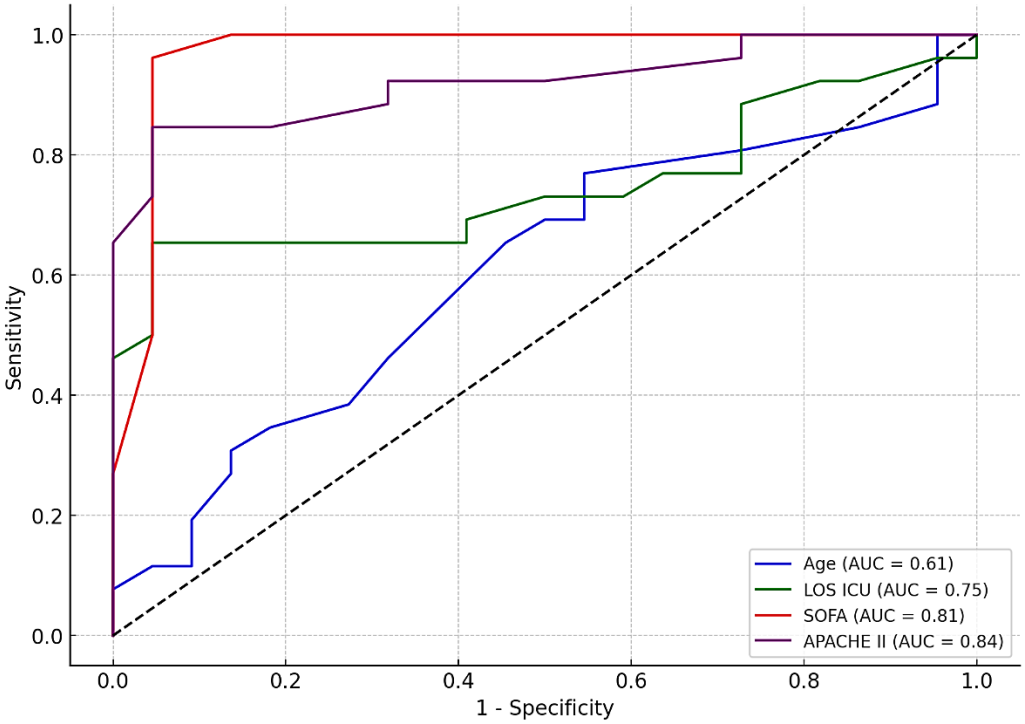

Figure 3. Comparison of the effects of Age, LOS ICU, SOFA score, and APACHE II score on mortality using ROC curves and AUC values

Discussion

The Systemic Immune-Inflammation Index (SII) has been defined as a prognostic biomarker for various diseases, as it reflects the balance of inflammatory, immune, and thrombotic pathways in patients by combining three predictive indicators. Initially, it was identified as a prognostic indicator in patients with resected hepatocellular carcinoma, based on early studies (9).

In a study of 242 patients (128 with sepsis, mean age 70.1 years and 114 without sepsis, mean age 69.7 years), the mean SII was 4444.06×10^9 in patients with sepsis and 3013.94×109^9 in patients without sepsis(15). A statistically significant correlation between SII and sepsis was shown. Mangalesh et al. reported that among 267 patients with sepsis, the SII, PLR, and NLR values were statistically significant in the discharged and deceased patient groups (16). Another study showed that inflammatory parameters, such as SII and NLR, are associated with disease severity and can potentially serve as important risk factors in the progression of COVID-19 (17). In our study, the SII, PLR, and NLR values were statistically significant in predicting mortality in pneumosepsis patients and were consistent with findings in the literature.

In this study of 16,007 individuals from a cohort of critically ill patients with sepsis in the MIMIC database, the results of the analysis showed a J-shaped relationship between SII and short-term mortality, with low and high levels associated with an increased hazard. The SII level with the lowest 28-day mortality risk was 774.46×10^9/L. Therefore, a lower SII theoretically indicates that the body may be impaired by severe inflammation or myelosuppression and may generally be associated with a poor prognosis(18). In our study, elevated SII was found to be associated with mortality in pneumosepsis patients and these results are consistent with other literature supporting the use of SII as a prognostic indicator in sepsis patients.

The SII has also been used to evaluate clinical outcomes in various types of cancer, predict mortality in patients with infective endocarditis, estimate respiratory failure in Guillain-Barré syndrome, and assess mortality risk in acute or subacute sinus vein thrombosis (19–22).

To lower the morbidity and mortality linked to sepsis, risk stratification is crucial for directing early identification and treatment. Because of their relative accessibility and the availability of hemogram data, NLR and PLR have long been utilized as predictors of morbidity and mortality in cardiovascular illnesses, malignancies, and sepsis. NLR levels have been found to be higher in sepsis and septic shock in a number of investigations (16). Similarly, our study observed that high NLR and PLR levels were associated with mortality in pneumosepsis patients, supporting the prognostic value of these biomarkers.

One study reported that the NLR outperformed conventional infection indicators in predicting bacteremia (23). Numerous investigations have documented the effectiveness of the NLR in predicting severity and mortality in critically ill and septic patients (24). The prognostic significance of the PLR and NLR in SARS-CoV-2 infections has been clarified in recent studies (25). PLR is also utilized to predict sepsis mortality, illness severity, and diagnosis (26). The results of our investigation, which associate mortality in pneumosepsis patients with elevated NLR and PLR levels, are consistent with findings from previous research.

Limitations

The primary limitations of this study include its retrospective design and its limited sample size. As a retrospective study, this research may be prone to missing data, which could restrict the generalizability of the results. Additionally, the limited sample size hinders the ability to draw broader conclusions about the population. Therefore, larger and more diverse prospective studies are required to produce more reliable and generalizable results.

Conclusion

This study demonstrates that inflammatory biomarkers, particularly the SII, NLR, and PLR, play a significant role in predicting mortality in pneumosepsis patients. These biomarkers are easily accessible and reliable indicators for determining the prognosis of pneumosepsis patients in the ICU. Future studies should evaluate and validate the potential use of these biomarkers for monitoring treatment responses in larger patient populations.

Ethical Approval: *The Diyarbakır Gazi Yaşargil Training and Research Hospital Ethics Committee gave its approval for the study to be conducted (Approval no: 2024/187).*

Author Contributions:
Concept: K.U., H.T.
Literature Review: K.U., H.T.
Design : K.U., H.T.
Data acquisition: K.U.
Analysis and interpretation: K.U., H.T.
Writing manuscript: K.U., H.T.
Critical revision of manuscript: K.U., H.T.

Conflict of Interest: *The authors have no conflicts of interest to declare.*

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