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Neutrophil-to-Lymphocyte Ratio and Acute Kidney Injury in Patients with Sepsis Admitted to Intensive Care Unit

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ABSTRACT

Acute Kidney Injury (AKI) is a common complication in patients with sepsis and contributes to high morbidity and mortality. Early detection of AKI remains challenging because conventional biomarkers have several limitations. The Neutrophil-to-Lymphocyte Ratio (NLR) is an easily obtainable inflammatory marker with potential value in identifying patients at risk of AKI; however, previous studies have reported inconsistent findings. This study aimed to analyze the association between the neutrophil-to-lymphocyte ratio (NLR) and the incidence of acute kidney injury (AKI) in septic patients admitted to the intensive care unit (ICU). This observational analytical study employed a retrospective design using medical record data from 75 septic patients. The mean NLR was significantly higher in patients with AKI than in those without AKI (27.57 vs. 13.66; p < 0.001). Receiver operating characteristic (ROC) analysis identified an optimal NLR cut-off value of 14.45 for predicting AKI, with a sensitivity of 72.7%, a specificity of 81.0%, and an area under the curve (AUC) of 0.788. These findings indicate that a higher NLR is significantly associated with the incidence of AKI among septic patients in the ICU. Therefore, NLR may serve as a useful inflammatory marker to support the early identification of AKI in patients with sepsis.

1. INTRODUCTION

Acute Kidney Injury (AKI) is one of the most frequent and serious complications in patients with sepsis, particularly those admitted to the intensive care unit (ICU) (Zarbock et al., 2023). The incidence of AKI among critically ill patients ranges from 16% to 67%, depending on the diagnostic criteria used, and sepsis remains the leading cause of AKI in this population (Samoni et al., 2023; Wang, Sun and Liu, 2023). The development of AKI in septic patients is associated with substantially increased morbidity and mortality, prolonged ICU and hospital length of stay, greater need for renal replacement therapy, higher healthcare costs, and an increased risk of progression to chronic kidney disease (CKD) and end-stage kidney disease. Despite advances in critical care management, septic AKI continues to be associated with poor clinical outcomes, highlighting the importance of early identification of patients at risk (Pickkers et al., 2021).

In Indonesia, sepsis is a common cause of critical illness requiring intensive care and remains associated with high mortality among ICU patients. Acute kidney injury (AKI) frequently complicates the clinical course of sepsis and is associated with worse clinical outcomes, including increased mortality and prolonged hospitalization (Jonny et al., 2020; Hotabilardus and Anggraeni, 2025). Early diagnosis of AKI remains challenging. Serum creatinine, which is currently the most widely used biomarker for diagnosing AKI, generally increases only after significant kidney injury has already occurred, limiting its usefulness for early detection (Bufkin, Karim and Silva, 2024). Although several novel urinary and serum biomarkers have demonstrated promising diagnostic performance, their high cost and limited availability restrict routine

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implementation in clinical practice, particularly in resource-limited healthcare settings (Zhou, Tang and Hu, 2026). Therefore, there is an urgent need for a simple, inexpensive, and widely available biomarker that can facilitate the early identification of AKI in septic patients.

The neutrophil-to-lymphocyte ratio (NLR), calculated from a routine complete blood count, has emerged as a readily available marker of systemic inflammation (Zahorec, 2021; Buonacera et al., 2022; Islam, Satici and Eroglu, 2024). During sepsis, activation of the innate immune response induces neutrophilia through the release of inflammatory cytokines, while stress-induced apoptosis and redistribution of lymphocytes result in lymphopenia. Consequently, the NLR increases markedly and reflects the intensity of the systemic inflammatory response. Excessive inflammation contributes to endothelial dysfunction, microvascular impairment, oxidative stress, and tubular cell injury, all of which play central roles in the pathogenesis of sepsis-associated AKI. Therefore, elevated NLR values may reflect the inflammatory processes involved in the development of AKI among septic patients.

Several studies have demonstrated an association between elevated NLR and the occurrence of AKI in patients with sepsis. Patients who developed AKI consistently showed significantly higher NLR values than those without AKI. However, the reported diagnostic performance of NLR has varied considerably across studies. Previous investigations have reported different optimal cut-off values ranging from approximately 10 to 17, with substantial variation in sensitivity and specificity. These inconsistencies may be attributable to differences in study populations, disease severity, patient characteristics, diagnostic criteria for AKI, and clinical settings. Consequently, although NLR shows promise as an inflammatory marker associated with AKI, its clinical utility has not yet been established consistently across different populations.

This variability highlights an important research gap. Current evidence has not established a universally applicable NLR threshold for identifying AKI in septic patients, and limited evidence is available from Indonesian populations. Differences in demographic characteristics, comorbidities, healthcare systems, and patterns of sepsis management may influence the diagnostic performance of NLR. Therefore, validation of NLR in different clinical settings is necessary before it can be considered a reliable adjunctive biomarker for identifying septic patients at risk of AKI. The present study was conducted to evaluate the association between the neutrophil-to-lymphocyte ratio and the incidence of acute kidney injury among patients with sepsis admitted to the ICU at Ibnu Sina Hospital. In addition, this study aimed to determine the optimal NLR cut-off value and evaluate its diagnostic performance within the local patient population. The findings are expected to provide additional evidence regarding the clinical value of NLR as a simple, inexpensive, and readily available inflammatory marker for supporting the early identification of AKI in septic patients, particularly in resource-limited healthcare settings.

2. METHOD

This analytical observational study employed a retrospective design to evaluate the association between the neutrophil-to-lymphocyte ratio (NLR) and the incidence of acute kidney injury (AKI) among patients with sepsis admitted to the Intensive Care Unit (ICU) of Ibnu Sina YW-UMI Hospital, Makassar, Indonesia. Medical records of patients admitted between August 2024 and the end of the study period (until the required sample size was achieved) were reviewed. The study protocol was approved by the Health Research Ethics Committee with ethical approval number UMI012601026.

The study population consisted of all adult patients (≥18 years) diagnosed with sepsis according to the Sepsis-3 criteria, defined as suspected or documented infection accompanied by an increase in the Sequential Organ Failure Assessment (SOFA) score of ≥2 points, who were admitted to the ICU during the study period. Total sampling was applied. Patients were included if they had complete blood count results obtained at ICU admission, complete renal function data, and complete medical records. Patients with pre-existing chronic kidney disease, hematological or immunological disorders affecting leukocyte counts, referral from another hospital without

baseline laboratory data, incomplete medical records, or death within 24 hours of ICU admission were excluded.

The independent variable was the neutrophil-to-lymphocyte ratio (NLR), calculated by dividing the absolute neutrophil count by the absolute lymphocyte count obtained from the first complete blood count performed upon ICU admission. The dependent variable was the occurrence of AKI, diagnosed according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, namely an increase in serum creatinine of ≥0.3 mg/dL within 48 hours, an increase in serum creatinine to ≥1.5 times the baseline value within 7 days, or urine output <0.5 mL/kg/hour for at least 6 hours. Baseline serum creatinine was determined using the most recent pre-admission creatinine value available in the medical records. Patients without sufficient baseline creatinine data to classify AKI were excluded from the analysis.

Data extraction was performed using a standardized data collection form by the research team after obtaining permission from the hospital. The collected variables included demographic characteristics, complete blood count results, serum creatinine levels, urine output, and other clinical information required for AKI classification. Medical records were reviewed to ensure data completeness and consistency before analysis. Records with incomplete essential variables were excluded; therefore, no imputation for missing data was performed. Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation, whereas non-normally distributed variables are presented as median and interquartile range (IQR). Categorical variables are expressed as frequencies and percentages.

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal NLR cut-off value for identifying AKI using the Youden Index. Based on the identified cut-off value, NLR was categorized into high and low groups. The association between categorized NLR and AKI was evaluated using the Chi-square test or Fisher's Exact test when the assumptions of the Chi-square test were not satisfied. Statistical significance was defined as a two-sided p-value <0.05. Because of the retrospective design and limited sample size, multivariable logistic regression analysis was not performed. Therefore, the findings of this study should be interpreted as demonstrating an association between NLR and AKI rather than an independent predictive effect..

3. RESULT AND DISCUSSION

Result

Characteristics of the Respondents

Univariate statistical tests are used to examine the frequency distribution of each variable in the study. These tests aim to provide an overview of the data distribution based on the number and percentage of respondents in each variable category. The results of the univariate analysis are presented in the following table.

Table 1. Distribution of Respondent Characteristics

Characteristics	Frequency	Percentage (%)
Age		
18–44 years	16	21.3%
45–59 years	18	24.0%
60–74 years	30	40.0%
75 years and older	11	14.7%
Gender		
Male	44	58.7%
Female	31	41.3%

Next, the 45–59 age group consisted of 18 people (24.0%), followed by the 18–44 age group with 16 people (21.3%), and the ≥75 age group with 11 people (14.7%). These results indicate that the majority of respondents in this study were in the older age group (≥60 years). By gender, the majority of respondents were male, totaling 44 people (58.7%), while female respondents numbered 31 (41.3%). These data show that the proportion of male respondents was higher than that of female respondents in this study.

Table 2. Distribution of Research Variables

Research Variables	Total Frequency	Low NLR	High NLR
AKI	33 (44%)	23(30.7)	10 (13.3%)
Non-AKI	42 (56%)	7 (9.3%)	35 (46.7%)
Total	75 (100%)	30 (40%)	45 (60%)

Based on Table 2, the distribution of respondents according to the occurrence of Acute Kidney Injury (AKI) shows that out of a total of 75 respondents, 33 respondents (44%) experienced AKI and 42 respondents (56%) did not experience AKI (non-AKI). These results indicate that the majority of respondents in this study did not experience AKI. Based on the Neutrophil–Lymphocyte Ratio (NLR) category, 30 respondents (40%) had a low NLR, and 45 respondents (60%) had a high NLR. In the AKI group, the majority of respondents had a low NLR, namely 23 respondents (30.7%), while 10 respondents (13.3%) had a high NLR. Conversely, in the non-AKI group, the majority of respondents had a high NLR, namely 35 respondents (46.7%), while 7 respondents (9.3%) had a low NLR

Table 3. Differences in *Neutrophil–Lymphocyte Ratio* Regarding the Incidence of

	N	Mean	Data Normality Test	Mann-Whitney Test
Non-AKI	42	13.66	0.000	0.000
AKI	33	27.57	0.003	

Based on Table 3, the group of patients with Acute Kidney Injury (AKI) had a mean Neutrophil–Lymphocyte Ratio (NLR) of 27.57, while the non-AKI group had a mean NLR of 13.66. These results indicate that the mean NLR in AKI patients was higher than in non-AKI patients. The results of the normality test showed that the NLR data in the non-AKI group had a significance value of 0.000 and in the AKI group, 0.003. Since both significance values were less than 0.05 ($p < 0.05$), it can be concluded that the NLR data in both groups were not normally distributed. Therefore, the difference was analyzed using the Mann–Whitney test. The Mann–Whitney test yielded a significance value of 0.000 ($p < 0.05$), indicating a statistically significant difference in the Neutrophil–Lymphocyte Ratio between the AKI and non-AKI patient groups. Thus, it can be concluded that the Neutrophil–Lymphocyte Ratio is associated with the occurrence of Acute Kidney Injury, where patients with AKI have significantly higher NLR values compared to non-AKI patients. These findings indicate that an elevated NLR, as a marker of systemic inflammation, may play a role in the occurrence of AKI in the studied patients.

Table 4. Neutrophil–Lymphocyte Ratio Cut-off Values for the Incidence of Acute Kidney Injury in Sepsis Patients

NLR Cut-off	Sensitivity	Specificity	Youden Index
12.35	0.879	0.619	0.498
12.45	0.818	0.619	0.437
13.04	0.758	0.643	0.401
13.47	0.727	0.714	0.441
13.85	0.727	0.786	0.513
14.45	0.727	0.810	0.537

14.83	0.697	0.810	0.507
15.61	0.697	0.833	0.530

The ROC analysis results showed an AUC value of 0.788 (95% CI: 0.684–0.891; p<0.001), indicating that the NLR has good discriminatory ability in predicting AKI in patients with sepsis. Based on the Youden index calculation, the optimal NLR cutoff value was determined to be 14.45, with a sensitivity of 72.7% and a specificity of 81.0%. This indicates that patients with an NLR value ≥14.45 have a higher risk of developing AKI compared to patients with an NLR value <14.45.

Discussion

The present study demonstrated a statistically significant association between the neutrophil-to-lymphocyte ratio (NLR) and the incidence of acute kidney injury (AKI) among patients with sepsis admitted to the Intensive Care Unit (ICU). Patients who developed AKI had significantly higher NLR values than those without AKI, and receiver operating characteristic (ROC) analysis showed that an NLR cut-off value of 14.45 provided good discriminatory performance for identifying AKI. These findings suggest that an elevated NLR is associated with the occurrence of AKI in septic patients and support the potential role of NLR as an adjunctive inflammatory marker for the early identification of patients at increased risk of renal complications. However, because of the retrospective observational design, these findings should be interpreted as demonstrating an association rather than a causal relationship.

The observed association is biologically plausible considering the pathophysiology of sepsis-associated AKI. Sepsis induces a dysregulated immune response characterized by excessive activation of neutrophils and suppression of lymphocyte-mediated adaptive immunity. This imbalance results in an increased NLR, reflecting the intensity of systemic inflammation. Activated neutrophils release pro-inflammatory cytokines, reactive oxygen species (ROS), proteolytic enzymes, and neutrophil extracellular traps (NETs), which contribute to endothelial injury, increased vascular permeability, and microvascular dysfunction. Simultaneously, inflammatory mediators such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and other cytokines promote oxidative stress and impair renal microcirculation, leading to tissue hypoxia, tubular epithelial cell injury, and decreased glomerular filtration. Therefore, elevated NLR values may reflect the underlying inflammatory processes associated with the development of AKI rather than directly causing kidney injury.

The findings of this study are generally consistent with previous investigations reporting that septic patients with AKI have significantly higher NLR values than those without AKI. Wei et al., (2023) reported that elevated NLR was associated with impaired renal function among septic patients, while Chen et al., (2022) found that higher NLR values were associated with AKI progression in critically ill patients. Similarly, Jaelani et al., (2023) demonstrated that patients with AKI had significantly higher NLR values than non-AKI patients, supporting the role of systemic inflammation in the development of renal dysfunction. The consistency of these findings strengthens the evidence that NLR reflects the inflammatory burden accompanying AKI in patients with sepsis.

Although the present findings are generally comparable with previous studies, differences remain regarding the optimal diagnostic cut-off value of NLR. In the present study, ROC analysis identified an optimal cut-off value of 14.45, whereas previous studies have reported cut-off values ranging from approximately 10.15 to 17.11. Such variability is expected because the optimal threshold is influenced by several factors, including differences in patient demographics, severity of sepsis, prevalence of AKI, timing of NLR measurement, ICU admission criteria, laboratory methods, and statistical approaches used for ROC analysis. Consequently, no universally applicable NLR cut-off has yet been established, and validation within different clinical populations remains necessary before widespread implementation in routine clinical practice.

Receiver operating characteristic analysis demonstrated an area under the curve (AUC) of 0.788, indicating good discriminatory ability for distinguishing septic patients with AKI from those without AKI. An AUC within this range suggests that NLR has acceptable diagnostic accuracy

and may be useful as an initial screening marker. Nevertheless, the discriminatory performance remains moderate and is insufficient to replace established diagnostic criteria such as the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. Therefore, NLR should be interpreted as an adjunctive biomarker and used together with clinical assessment, serum creatinine measurements, urine output monitoring, and other laboratory findings to improve the early recognition of AKI.

The present findings have important clinical implications. Because NLR is calculated from a routine complete blood count, it is inexpensive, readily available, and does not require additional laboratory testing. In critically ill patients with sepsis, an elevated NLR at ICU admission may help clinicians identify individuals who require closer monitoring of renal function, more frequent assessment of urine output and serum creatinine, careful optimization of hemodynamic status, avoidance of nephrotoxic medications, and timely nephrology consultation when indicated. Consequently, NLR may contribute to early risk stratification and support clinical decision-making in the management of septic patients.

Several factors should be considered when interpreting the findings of this study. The association between NLR and AKI may have been influenced by potential confounding variables, including age, baseline comorbidities, severity of sepsis, source of infection, use of vasopressor agents, fluid resuscitation strategies, and baseline renal function. Because only bivariate analysis was performed, the independent contribution of NLR could not be determined after adjustment for these potential confounders. Therefore, caution is warranted when interpreting NLR as an independent predictor of AKI, and the results should be regarded as evidence of an association rather than proof of causality.

This study has several strengths. AKI was diagnosed using the internationally accepted KDIGO criteria, ensuring standardized outcome classification. The study included all eligible sepsis patients admitted to the ICU during the study period using a total sampling technique, thereby minimizing selection bias. Furthermore, NLR was derived from routine laboratory examinations performed at ICU admission, making the findings readily applicable to daily clinical practice, particularly in resource-limited healthcare settings where advanced biomarkers may not be available.

Several limitations should also be acknowledged. First, the retrospective design precludes the establishment of causal relationships between NLR and AKI. Second, this was a single-center study with a relatively small sample size, which may limit the generalizability of the findings. Third, multivariable logistic regression analysis was not performed; therefore, the effects of potential confounding variables could not be controlled. Finally, other inflammatory biomarkers, such as C-reactive protein (CRP), procalcitonin, interleukins, or novel renal injury biomarkers, were not evaluated and may have provided additional information regarding the prediction of AKI.

Future prospective multicenter studies involving larger and more diverse patient populations are needed to validate the optimal NLR cut-off identified in this study. Multivariable analyses should also be performed to determine whether NLR independently predicts AKI after adjustment for relevant clinical confounders. Furthermore, future research should investigate whether combining NLR with established inflammatory or renal injury biomarkers can improve the accuracy of early AKI identification and facilitate more effective risk stratification among patients with sepsis admitted to the ICU.

4. CONCLUSION

This study demonstrated a statistically significant association between the neutrophil tolymphocyte ratio (NLR) and the incidence of acute kidney injury (AKI) among patients with sepsis admitted to the intensive care unit (ICU). Patients who developed AKI had significantly higher NLR values than those without AKI. Receiver operating characteristic (ROC) analysis identified an optimal NLR cut-off value of 14.45, with a sensitivity of 72.7%, a specificity of 81.0%, and an area under the curve (AUC) of 0.788 for identifying AKI. These findings suggest that the NLR may serve as a simple, inexpensive, and readily available inflammatory marker to support

the early identification of AKI in patients with sepsis. However, because of the retrospective observational design, the findings should be interpreted as demonstrating an association rather than a causal or independent predictive relationship.

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