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Neutrophil-to-Lymphocyte Ratio as a Diagnostic Predictor and Initial Management in Sepsis-Induced Acute Kidney Injury: A Systematic Review Based on Recent Studies

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ABSTRACT

Sepsis is a leading cause of Sepsis-Induced Acute Kidney Injury (SI-AKI) and contributes substantially to high morbidity and mortality among critically ill patients. The neutrophil-to-lymphocyte ratio (NLR) is a systemic inflammatory biomarker that is readily obtained from routine blood tests and has potential value as a diagnostic predictor and a basis for early management of SI-AKI. This systematic review aims to evaluate the role of NLR as a diagnostic predictor and a basis for early management in patients with SI-AKI based on recent studies. This study is a systematic review conducted in accordance with the PRISMA 2020 guidelines. A literature search was performed using PubMed and Google Scholar databases for articles published between 2021 and 2025. Included studies were original articles involving adult populations, assessing NLR as a parameter, and reporting outcomes related to SI-AKI. The methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Tool. A total of five observational studies met the inclusion criteria. Most studies demonstrated significantly higher NLR values in septic patients who developed SI-AKI compared with those who did not. Several studies also reported an independent association between elevated NLR and AKI progression as well as increased mortality. However, one study found no significant association between NLR and certain clinical outcomes, including the need for mechanical interventions and length of hospital stay. NLR has the potential to be used as an early diagnostic parameter and a risk stratification tool in SI-AKI.

Keywords: *inflammatory biomarker, neutrophil-to-lymphocyte ratio, sepsis, sepsis-induced acute kidney injury.*

INTRODUCTION

Sepsis is defined as organ dysfunction due to infection. Sepsis can lead to a variety of complications, including brain dysfunction, cardiomyopathy, liver dysfunction, coagulopathy, and AKI (Ziesmann & Marshall, 2018). Sepsis-Induced Acute Kidney Injury (SI-AKI) is an AKI condition that occurs in patients with sepsis. In this condition, the mechanism triggered by sepsis causes kidney damage directly (Hotabilardus & Anggraeni, 2025). Kidney Disease: Improving Global Outcomes (KDIGO) defines AKI as a condition that meets one of the following criteria: an increase in serum creatinine (SCr) of at least 0.3 mg/dL within 48 hours; an increase in SCr to ≥1.5 times baseline, known or suspected to have occurred in the previous 7 days; or a urine output volume of <0.5 mL/kg/hr for 6 hours (Pais, 2024).

More than 40% of patients with sepsis experience AKI as one of the most common complications. Moreover, the mortality rate for patients with AKI is higher than for those with AKI or sepsis alone (Pais, 2024; Pan et al., 2024). In the intensive care unit (ICU), sepsis causes about half of all AKI episodes. The mortality rate due to SI-AKI ranges from 50% to 60%. Furthermore, SI-AKI is an independent risk factor for high mortality in patients with sepsis and can contribute to the development of chronic kidney disease (Lendak et al., 2025). The prognosis of SI-AKI is worse than that of sepsis or AKI occurring separately (Hotabilardus & Anggraeni, 2025).

The diagnosis of SI-AKI can be established through reliable, fast, accessible, and cost-effective predictors of organ dysfunction progression (Bu et al., 2019; Caraballo & Jaimes, 2019; Lelubre & Vincent, 2018; Wei et al., 2023). However, the pathophysiological mechanism of SI-AKI development is not yet fully understood. The pathophysiology of AKI in sepsis is complex and multifactorial, involving intrarenal hemodynamic changes, endothelial dysfunction, infiltration of inflammatory cells in the renal parenchyma, intraglomerular thrombosis, and obstruction of the tubules due to necrotic cells and debris (Pan et al., 2024).

Current therapies remain non-specific and suboptimal, and the mortality rate due to AKI is still very high (Gameiro et al., 2020; Xie et al., 2022). Although hypoperfusion and hypovolemia are considered causes of SI-AKI, AKI has also been observed in normotensive patients (Hotabilardus & Anggraeni, 2025). Thus, a multifactorial injury theory—such as inflammation—is also suspected as a pathomechanism of AKI. Early identification of predictors for AKI is therefore essential for timely recognition and initiation of therapies (Lendak et al., 2025). Early identification and intervention in sepsis-induced AKI are crucial for improving disease prognosis and facilitating patient therapy (Pan et al., 2024).

However, serum creatinine levels are insufficient to diagnose kidney injury and recovery. White blood cells provide more informative insights, as they are essential for systemic inflammatory responses to severe infections, trauma, or shock. Neutrophils, lymphocytes, monocytes, eosinophils, and basophils are the types of leukocytes that can be distinguished through a complete blood count. The neutrophil-lymphocyte ratio (NLR) is a biomarker of systemic inflammation.

NLR is easy to obtain and calculate from a complete blood count. It reflects the balance between innate (neutrophil) and adaptive (lymphocyte) immune responses (Kowita et al., 2023). NLR is higher in patients with AKI than in non-AKI patients. It can also monitor AKI stages, as well as risks and mortality rates in AKI patients (Bustani, Gunawan, Karita, & Susiyadi, 2024). However, studies analyzing the role of NLR as a diagnostic parameter for SI-AKI remain very limited. Thus, this study aims to determine the role of NLR as a diagnostic and therapeutic parameter in SI-AKI patients based on previous studies.

METHOD

This study is a systematic review study used to determine the use of NLR as an early and therapeutic diagnostic predictor in patients with SI-AKI based on previous studies. The systematic review in this study was prepared based on the Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2020). The databases used in this study to search for related literature include PubMed and Google Scholar. The study used in this study is a study published between 2021 and 2025 regarding the use of NLR as an early and therapeutic diagnostic predictor in patients with SI-AKI.

The keywords used in this study included "Neutrophil lymphocyte ratio", "epsis-Induced Acute Kidney Injury", and "predictor", "diagnostic". Synonyms for each keyword were also used in this study to expand the search results in each study. Keywords are arranged by using the BOOLEAN operators "and" and "or" for each database. This study only includes studies published in English and can be accessed free of charge through a predetermined database.

The inclusion criteria in this study include that the research is an original article with a research sample of adult patients who are more than 17 years old, the research uses NLR

parameters, and is published in the last 5 years. The exclusion criteria in this study include a literature review study, do not clearly mention the role or analysis of NLR outputs, and cannot be accessed free of charge by researchers.

The assessment of the quality of the inclusion study in this study was carried out using the Joanne Bridge Instrument (JBI) to assess the quality of the study in each inclusion research. JBI is a tool used to evaluate the risk of bias in research based on the design of each study and studies with a percentage of risk of bias below 70% are excluded from this study.

Each inclusion study in this study was then extracted based on the author and year of publication, country, subject characteristics (age, gender, and sample size), and research output. All researchers performed data extraction independently. Each conflict will be resolved by discussion and decision on a mutually agreed option

RESULTS AND DISCUSSION

The results of the inclusion study screening based on the PRISMA *Flowchart* in this study are shown in figure 1. The results of the inclusion study extraction in this study are shown by the.

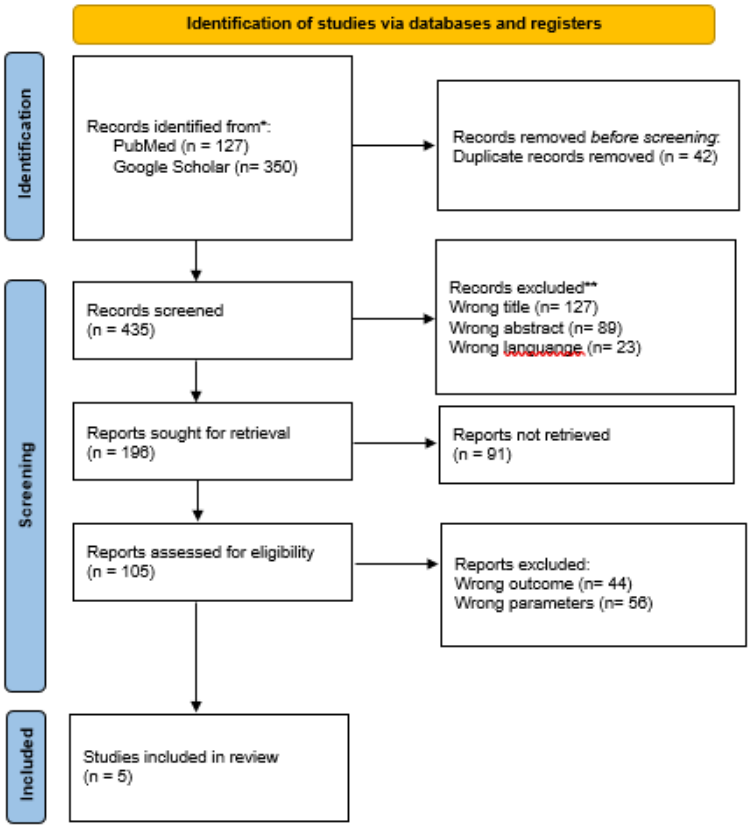

Figure 1. PRISMA *Flowchart*

The process of identifying and selecting studies in this systematic review is carried out in accordance with the guidelines of PRISMA 2020. Literature searches were conducted through two databases, namely PubMed and Google Scholar. From the search process, a total of 477 articles were obtained, consisting of 127 articles from PubMed and 350 articles from Google Scholar. A total of 42 duplicate articles were excluded before the screening stage,

leaving 435 articles for title and abstract screening. At this stage, 239 articles were excluded because they did not fit the research topic.

Reasons for exclusion include incongruity of the research topic (n = 127), irrelevant abstracts (n = 89), and inappropriate publication language (n = 23). A total of 198 articles were continued to the full text search stage. Of these, 91 articles were excluded because the full text could not be obtained, so 105 articles were assessed as thoroughly eligible. At the eligibility assessment stage, 100 articles were excluded for not meeting the inclusion criteria. Reasons for exclusion included irrelevant research outputs (n = 44) and inappropriate study parameters, including not assessing the ratio of neutrophils to lymphocytes (n = 56). A total of 5 studies met all inclusion criteria and were included in this systematic review.

Table 1. Research Inclusion Studies

Author (Year)	Research Design	Number of Samples	Research Results	JBI
Lendak et al. (2025)	Observational studies	257 sepsis patients (SI-AKI: 133; non SI-AKI: 124)	NLR was significantly higher in the SI-AKI group (p=0.002).	90%
Pan et al. (2024)	Retrospective studies	271 sepsis patients (SI-AKI: 112; non-SI-AKI: 159)	NLR differed significantly between the SI-AKI and non-SI-AKI groups (p=0.029).	85%
Xie et al. (2022)	Cross-sectional retrospektif	1,238 sepsis patients (SI-AKI: 507; non-SI-AKI: 731)	NLR was higher in the SI-AKI group than in the non-SI-AKI group (p=0.001).	85%
Wei et al. (2023)	Single-center retrospective study	413 patients with SI-AKI (low NLR: 206; NLR high: 207)	There was no significant difference in clinical outcomes between the NLR groups (p>0.05).	75%
Chen et al. (2021)	Population-based and multi-institutional retrospectives	10,441 ICU patients with stage 1–2 AKI	NLR is independently related to AKI progression and mortality; curve pattern J.	90%

Observational research conducted by Lendak et al. in 2025 in Serbia included 257 sepsis patients grouped based on the development of SI-AKI, including SI-AKI, n = 133; without SI-AKI, n = 124 aged more than equal to 18 years. This study showed that the NLR parameters differed significantly between the SI-AKI group and the non-SI-AKI group ($p<0.05$, $p = 0.002$), with higher NLR values in the SI-AKI group (Lendak et al., 2025).

A retrospective study conducted by Pan et al. in 2024 in Taiwan included 271 sepsis patients also grouped based on the development of SI-AKI, including SI-AKI, n = 112; without SI-AKI, n = 159. This study included patients enrolled in the prospective registry system of the ER between 1 January 2020 and 30 November 2020. This study included a sample of more than the same age as 20 years. This study showed that the NLR parameters differed significantly between the SI-AKI group and the non-SI-AKI group ($p<0.05$, $p = 0.029$), with a higher NLR value in the SI-AKI group (Pan et al., 2024).

A study conducted by Xie et al. in 2022 in China that is a study *cross-sectional* The retrospective included 1238 patients with SI-AKI at Xi'an Jiaotong University's First Affiliated Hospital. This study included patients aged 18 years and above. Patients in this study were also grouped based on the development of SI-AKI, including SI-AKI, n = 507; without SI-AKI, n

= 731. This study included a sample of more than the same age as 20 years. This study showed that the NLR parameters differed significantly between the SI-AKI group and the non-SI-AKI group ($p<0.05$, $p = 0.001$), with higher NLR values in the SI-AKI group (Xie et al., 2022).

A study conducted by Wei et al. in 2023 in China which is *single-center retrospective study* included 413 patients with SI-AKI in *West China Hospital of Sichuan University*. This study included patients aged 18 years and above. Patients in this study were also grouped based on their NLR levels, including low NLR, n=206 and high NLR, n=207. This study showed that there was no significant difference in the incidence of mechanical intervention, transfer to ICU, sepsis shock, or length of stay in both groups ($P>0.05$) (Wei et al., 2024).

The study conducted by Chen et al. published in 2021 was a population-based, multi-institutional retrospective study using the Chang Gung Research Database in Taiwan. This study included 10,441 adult patients who were admitted to the intensive care unit (ICU) with a diagnosis of stage 1 or 2 AKI. The ratio of neutrophils to lymphocytes (NLR) was measured at the time of the onset of AKI.

The main outcomes were composite progression of AKI to stage 3, the need for kidney replacement therapy, or mortality within 14 days. The results showed that NLR was independently related to AKI progression and intrahospital mortality after adjustment for confounding factors. Analysis *restricted cubic spline* shows a J-curve-shaped relationship, with the lowest risk of NLR values between 7–38. The relationship between NLR and clinical outcomes varies based on the reason for ICU admission. NLR is assessed as an easily obtainable clinical parameter and has the potential to be used for risk stratification in critical AKI patients (Chen et al., 2022).

Five inclusion studies in this study showed that NLR values increased in patients with SI-AKI. Pathophysiologically, NLR increases rapidly within 6 hours of physiological stress and shows an earlier response than total *white blood cell* (WBC) and a left-wing shift on the WBC differential analysis. NLR has been used to distinguish between mild and severe diseases as well as as as a prognostic marker. Patients with early-stage AKI and NLR < 7 or > 38 were associated with adverse events in hospital, including AKI progression and mortality, in the short term (Chen et al., 2022; Pan et al., 2024).

NLR is an indicator of systemic inflammatory response and plays an important role in the diagnosis and prognosis of sepsis. On the one hand, infection by pathogens stimulates neutrophils to secrete pro-inflammatory cytokines, regulatory cytokines, and chemokines, which cause varying degrees of organ damage. On the other hand, lymphocytes suppress the body's inflammatory response by secreting anti-inflammatory factors such as interleukin-10 (IL-10). Both of these things maintain the balance of the immune system. NLR is a common and easily accessible serological indicator that effectively responds to fluctuations in the condition of sepsis patients (Kowita et al., 2023).

The neutrophil-lymphocyte ratio (NLR), calculated from a complete blood count, is proposed as a surrogate indicator to reflect the relative relationship between the inflammatory response and immune status (Xiao et al., 2022). Increased NLR levels are associated with the development of S-AKI in sepsis patients and can be considered as a stratification of S-AKI risk (Xie et al., 2024). A higher NLR may indicate the development of severe inflammation in the patient. The relationship between NLR and the development of septic AKI is due to inflammatory functions in the pathophysiology of AKI (Kowita et al., 2023).

The ability of ΔNLR to predict the prognosis of septic AKI is better than other potential markers, such as Neu, Lym, WBC, PCT, PLT, and CRP, as well as NLR at hospital admission and NLR at diagnosis of septic AKI. Therefore, ΔNLR can be used as a prognostic biomarker for septic AKI patients. ΔNLR is used to indicate the dynamic change of NLR from its initial value (Wei et al., 2024). Although NLR has been reported to be able to predict the progression of AKI in sepsis, its sensitivity and specificity are limited to complex interactions between immune mechanisms, activation of inflammatory cascades, and disruption of coagulation pathways.

Furthermore, these interactions will result in microvascular dysfunction, leukocyte/platelet activation, and microthrombi formation, which ultimately leads to injury of renal tubule epithelial cells (Xiao et al., 2022). However, NLR can potentially be a tool for risk stratification, especially when considering its low cost and accessibility in a clinical setting with limited resources. NLR is superior due to its simplicity and broad accessibility, but it is less sensitive to accurately predict mortality risk in critically ill patients with AKI. Thus, the role may be complementary (Guedes et al., 2025).

CONCLUSION

A systematic review of recent observational studies reveals that neutrophil-to-lymphocyte ratios (NLR) consistently rise in sepsis patients progressing to Sepsis-Induced Acute Kidney Injury (SI-AKI), with higher NLR values significantly linked to SI-AKI incidence, kidney injury progression, and poorer clinical outcomes. As a simple, readily obtainable systemic inflammatory biomarker, NLR holds strong potential as an early diagnostic predictor and risk stratification tool to guide timely clinical decision-making and management in SI-AKI patients. However, its limitations in sensitivity and specificity preclude standalone use, necessitating combination with other clinical parameters and biomarkers for enhanced diagnostic and prognostic accuracy. For future research, prospective randomized controlled trials should prioritize determining optimal NLR cut-off values and integrating NLR into standardized SI-AKI management algorithms to validate its clinical utility.

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