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Comparison of Neutrophil-to-Lymphocyte Ratio (NLR) in Gram-Positive and Gram-Negative Bacteremia from Blood Specimens

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ABSTRACT

Bacteremia remains a significant cause of morbidity and mortality worldwide, with both Gram-positive and Gram-negative bacteria contributing to the disease burden. The neutrophil-to-lymphocyte ratio (NLR) has emerged as a simple, cost-effective biomarker for evaluating inflammation and infection severity. This study aimed to compare the NLR values between patients with Gram-positive and Gram-negative bacteremia confirmed by blood culture. An analytical observational cross-sectional study was conducted at Bayu Asih Purwakarta Hospital from January to July 2025. Data from patients with positive blood cultures and complete hematological profiles were included and analyzed using the Mann-Whitney U test. A total of 84 cases were studied, consisting of 42 Gram-positive and 42 Gram-negative bacteremia. The results showed a statistically significant difference in NLR values between the two groups ($p = 0.038$. These findings support the utility of NLR as a useful biomarker in differentiating types of bacterial infections in bacteremia cases. In conclusion, NLR may aid in early diagnosis and clinical decision-making for bacteremia management.

INTRODUCTION

Bacteremia is a type of infection that occurs in the bloodstream due to bacterial growth. Bacteremia infections occur due to several factors, such as nosocomial infections, infections acquired from the community or environment, and other comorbidities. Bacteremia is caused by bacterial infections Gram-positive or Gram-negative bacteria (Mastra et al., 2025; Putri & Sundari, 2022).

Notwithstanding the substantial advances in diagnosis and treatment that have been observed in recent decades, there is an absence of substantial evidence to support many of the diagnostic aspects. Bacteremia continues to be a major source of morbidity and mortality on a global scale (Alonso-Menchén et al., 2022; McNab et al., 2024). Nevertheless, numerous epidemiological and diagnostic aspects of bacteremia continue to be subjects of debate. A review of the extant literature reveals a paucity of homogeneous data regarding the evolution of its incidence and etiology over time. Furthermore, the findings of studies conducted to date have yielded conflicting results on certain pivotal issues. In addition, clinical guidelines offer little to no advice on certain aspects of blood culture analysis (Alonso-Menchén et al., 2022).

Bacteremia represents a considerable risk to health, primarily due to its frequently atypical presentation and its capacity to progress to sepsis and diseases continue to be a major problem (Kern & Rieg, 2020). Indonesia is a developing country where infectious diseases continue to be a major problem. The most common type of infection is

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bloodstream infection, which includes bacteremia. Bacteremia is a condition in which the blood contains live bacteria. This disease can develop into a complication, such as sepsis, It is conceivable that this may become one of the most prevalent causes of morbidity and mortality on a global scale if not treated immediately (Marwasyifa et al., 2025).

Sepsis may develop when the infection is resistant to the host's defenses, although not all bacteremia cases progress to sepsis (Marwasyifa et al., 2025). Sepsis and bacteremia are among the most significant causes of morbidity and mortality on a global scale. A delay in the diagnosis of these conditions, in conjunction with an inaccurate diagnosis, has been demonstrated to result in an elevated mortality rate (Jonathan et al., 2019). A comprehensive analysis of extant research findings has revealed that one of the fundamental principles that are indispensable for the efficacious management of sepsis is the timely and precise identification of individuals who are at high risk for mortality (Liu et al., 2016).

The identification of the pathogen that causes sepsis can be achieved through culturing the pathogen from either the patient's body specimen or the suspected source of infection that has the potential to develop into sepsis. (Sudiartha et al., 2020). Blood cultures are considered the gold standard for diagnosing bacterial sepsis. A definitive diagnosis of sepsis necessitates the isolation of bacteria from a blood culture. However, this approach is not feasible in many cases due to the prolonged nature of the process, which can take 48 to 72 hours, and its suboptimal sensitivity sepsis (Wang et al., 2024). In the domain of human medicine, the neutrophil-to-lymphocyte ratio (NLR) is a measure employed to evaluate inflammatory status and immune function. NLR has improved diagnostic accuracy over other biomarkers to detect bacteremia in patients admitted to the emergency room (Liu et al., 2016). NLR is a relatively more cost-effective parameter and easier to calculate because it only requires complete blood count results (Sudiartha et al., 2020).

An examination of the correlation between the neutrophil-to-lymphocyte ratio (NLR) in patients with sepsis and septic shock was conducted by Jonathan et al (2019) in their study. The study revealed a substantial discrepancy in the mean neutrophil-to-lymphocyte ratio (NLR) values among patients with Gram-positive bacterial infections and those with Gram-negative bacterial infections. Higher NLR values were observed in the former patient population. However, the study did not explain the origin of the specimens used for bacterial identification.

A more in-depth analysis is needed to address this research question and to determine the differences in NLR values In patients with confirmed Gram-positive and Gram-negative bacteremia, as indicated by the results of blood culture analysis. This study is expected to provide additional scientific evidence regarding the potential of the NLR as a simple yet meaningful parameter for aiding in the initial and differential diagnosis of bacterial infections and supporting faster, more accurate clinical decision-making in cases of sepsis.

MATERIALS/METHOD

This study employs an analytical observational study with a cross-sectional design, conducted at Bayu Asih Purwakarta Regional General Hospital. The research data were collected from the Bayu Asih Purwakarta Hospital laboratory during period from January 2025 to July 2025.

The study subjects were all patients who underwent blood culture examinations during that period. The inclusion criteria were patients with positive blood culture results and complete hematology test results obtained can be utilized to calculate the neutrophil-to-lymphocyte ratio (NLR). Patients with blood culture results that were considered contaminated or those with incomplete hematology data were excluded from the study. The sampling method employed was total sampling, which entails the inclusion of all patients meeting the predetermined inclusion criteria. A total of 84 blood specimens with positive cultures were analyzed in this study, comprising 42 cases of Gram-positive bacteremia and 42 cases of Gram-negative bacteremia.

Subsequently, blood specimens that exhibited positive results on the BACT/ALERT 3D incubator were subjected to Gram staining to ascertain the bacterial group, whether Gram-positive or Gram-negative. Subsequent identification was facilitated by utilizing the Vitek 2 Compact system. Complete hematology examinations were conducted using the Sysmex XN-550. The examination results yielded the absolute neutrophil and lymphocyte counts, which were subsequently utilized to calculate the neutrophil-to-lymphocyte ratio (NLR) employing the following formula:

$$NLR = \frac{\text{Absolute Neutrophil Count}}{\text{Absolute Lymphocyte Count}}$$

The statistical analysis was initiated with a preliminary assessment of normality. In instances where the distribution of data was found to be normal and its variance proved homogeneous, the independent t-test was employed. Conversely, in instances where the data distribution was deemed non-normal, the Mann-Whitney U test was employed.

RESULTS AND DISCUSSION

Normality Test

Results of the normality test to the distribution of neutrophil-to-lymphocyte ratio (NLR) values in the Gram-positive and Gram-negative bacteremia groups are presented in Table 1.

Table 1. NLR Normality Test Results

Variabel	Kolmogorov-Smirnov (Sig.)	Shapiro-Wilk (Sig.)
NLR Gram-Positive	0,000	0,000
NLR Gram-Negative	0,008	0,002

Note: a p-value < 0.05 indicates that the data distribution is not normal.

Based on the results of the Kolmogorov-Smirnov and Shapiro-Wilk tests, the NLR data distribution in both groups showed a significance value < 0.05. This indicates that the data does not adhere to a normal distribution, necessitating the utilization of a non-parametric statistical method, specifically the Mann-Whitney U test, to proceed with the comparison analysis between the two groups.

NLR Comparison Test

A Mann-Whitney test was employed to evaluate the difference in neutrophil-to-lymphocyte ratio (NLR) among patients with Gram-positive and Gram-negative bacteremia. The results of the analysis demonstrated a statistically significant difference, as presented in Table 2.

Table 2. Comparison Test of NLR in Gram-Positive and Gram-Negative Bacteria

	NLR
Mann-Whitney U	650.000
Wilcoxon W	1553.000
Z	-2.076
Asymp. Sig. (2-tailed)	0.038

The statistical analysis conducted using the Mann-Whitney test demonstrated a statistically significant difference in neutrophil-to-lymphocyte ratio (NLR) values between Gram-positive and Gram-negative bacteremia groups (U = 650, Z = -2.076, p = 0.038). A p-value of less than 0.05 signifies the presence of a statistically significant difference between two groups.

These results are consistent with the findings of the study by Sumardi et al (2021), which also demonstrated that the neutrophil-to-lymphocyte ratio (NLR) in Gram-positive infections was significantly higher than in Gram-negative infections in patients with sepsis (median NLR Gram-positive: 31.5 vs Gram-negative: 17.8; p = 0.001). This study lends further support to the use of NLR as a biomarker, with the capacity to differentiate between various types of bacterial infections.

Table 3. Minimum and Maximum NLR Values in Gram-Positive and Gram-Negative Bacteremia

Bacteria Type	Minimum NLR	Maximum NLR
Gram-Positive	4,22	47,50
Gram-Negative	1,24	31,33

The NLR range in Gram-positive bacteremia (4.22–47.50) is wider than in Gram-negative bacteremia (1.24–31.33). This finding suggests that the inflammatory response in Gram-positive infections tends to be higher. The minimum neutrophil-to-lymphocyte ratio (NLR) value in Gram-positive infections exceeds the normal range for healthy populations (generally <3–5), while in Gram-negative infections, values remain within the normal range.

From a clinical perspective, a high neutrophil-to-lymphocyte ratio (NLR) >10 has been demonstrated to be a significant predictor of mortality and the development of complications in patients with sepsis and bacteremia. Meta-analysis studies further demonstrate that an NLR >3–5 can serve as a reliable indicator of severe infection and inflammation (Forget et al., 2017; Islam et al., 2024).

Table 4. Comparison of Gram Types in ICU and Non-ICU Rooms

		Gram		
		Gram-Positive	Gram-Negative	Total
Room	ICU	15	10	25
	Non ICU	27	32	59
Total		42	42	84

A comparative analysis of Gram-positive and Gram-negative bacteremia cases reveals a higher incidence in the non-ICU ward (59 cases) compared to the ICU (25 cases). This discrepancy can be attributed to variations in capacity or the number of patient rooms between the ICU and non-ICU wards within the hospital. Within the intensive care unit (ICU), Gram-positive cases predominate (15 cases), while in the non-

ICU, Gram-negative cases are slightly more numerous (32 vs. 27). This finding suggests that, in both the ICU and non-ICU, both types of bacteria contribute equally to bacteremia cases (Tarigan et al., 2025).

The objective of this study is to make a comparison between the NLR values of patients with Gram-positive and Gram-negative bacteremia. The findings indicate a statistically significant discrepancy between the two groups, with Gram-positive patients exhibiting a tendency towards higher NLR ranges. These findings lend support to the hypothesis that the neutrophil-to-lymphocyte ratio (NLR) can serve as a biomarker, capable of differentiating between distinct types of bacterial infection in cases of bacteremia (Jonathan et al., 2019; Sumardi et al., 2021).

The substantial difference in the neutrophil-to-lymphocyte ratio (NLR) between Gram-positive and Gram-negative bacteria is attributable to disparities in the pathophysiology of the immune response. Gram-positive infections, such as Staphylococcus aureus, have been observed to elicit a more robust systemic inflammatory response, resulting in a heightened increase in the neutrophil-to-lymphocyte ratio (NLR) (Sumardi et al., 2021). Conversely, Gram-negative bacteria have also been observed to induce severe inflammation; however, the response to this infection can vary depending on the virulence of the bacterium and the immune status of the patient (Zhao et al., 2025).

This finding aligns with the conclusions of meta-analyses that have previously confirmed the reliability, affordability, and ease of use of the neutrophil-to-lymphocyte ratio (NLR) as a biomarker for the diagnosis and prognosis of bacterial infections (Chen et al., 2023).

CONCLUSIONS

The present study demonstrates that the neutrophil-to-lymphocyte ratio (NLR) is significantly higher in patients with Gram-positive bacteremia compared to those with Gram-negative bacteremia. These findings suggest that NLR is a valuable and accessible biomarker for distinguishing between Gram-positive and Gram-negative infections in bacteremia cases. The broader range of NLR observed in Gram-positive bacteremia reflects a stronger inflammatory response. Further research with larger multicenter populations is recommended to validate the clinical application of NLR as a diagnostic and prognostic tool in sepsis and bacteremia management.

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