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Diagnostic Utility of Neutrophil-to-Lymphocyte Ratio in Correlation with Procalcitonin Levels among Neonates with Suspected Sepsis

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Abstract: Neonatal sepsis remains a significant cause of morbidity and mortality globally, particularly in resource-limited settings. The gold standard blood culture is limited by delayed turnaround time and suboptimal sensitivity, necessitating rapid, reliable biomarkers such as the neutrophil-to-lymphocyte ratio (NLR) and procalcitonin (PCT). Objective: to investigate the correlation between NLR and PCT levels in neonates with suspected sepsis, and evaluate the feasibility of NLR as an early diagnostic tool alongside PCT. A cross-sectional study was conducted at Muhammadiyah Hospital, Palembang, Indonesia, from January to March 2024. Thirty neonates aged 0–28 days with clinical suspicion of sepsis were recruited by purposive sampling. NLR values were obtained from automated hematology analyzers, and PCT levels were measured using fluorescence immunoassay. Statistical analysis used Spearman's correlation, with $p < 0.05$ considered significant. The mean NLR was 3.99 (range: 2.3–6.2), and the mean PCT level was 5.72 ng/mL (range: 2.9–9.2 ng/mL). A significant positive correlation was observed between NLR and PCT ($r = 0.684$, $p < 0.001$), indicating that higher NLR values corresponded with elevated PCT levels. The study concludes that NLR shows a strong, statistically significant correlation with PCT in neonates with suspected sepsis. As a cost-effective and widely available marker, NLR can serve as an early screening tool, with PCT providing confirmatory value. However, the findings should be interpreted with caution due to the small sample size and single-center study design, which may limit the generalizability of the results.
Keywords: Correlation; lymphocyte; neutrophil; procalcitonin; sepsis.

INTRODUCTION

Neonatal sepsis is a severe systemic infection that occurs within the first 28 days of life and remains a major cause of morbidity and mortality worldwide, particularly in low- and middle-income countries. According to the World Health Organization (WHO, 2022), severe infections, including sepsis, account for approximately 15% of global neonatal deaths, with the burden disproportionately affecting regions with limited healthcare resources. In Indonesia, neonatal sepsis continues to be a significant contributor to infant mortality, with prevalence rates ranging from 8–20% depending on hospital setting (Putri et al., 2025); (Fadilah et al., 2022).

The vulnerability of neonates to sepsis is primarily due to their immature immune systems. Both innate and adaptive immune responses are underdeveloped, resulting in impaired pathogen clearance and rapid dissemination of bacteria (Ng et al., 2025). Clinically, neonatal sepsis is challenging to diagnose because signs are subtle and nonspecific—temperature instability, respiratory distress, lethargy, and poor feeding—that may overlap with other neonatal disorders (Salama & Tharwat,

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2023); (Hasibuan et al., 2024)

Blood culture, though considered the gold standard, has limitations such as low sensitivity and long turnaround time (Mubaraki et al., 2023; Liu et al., 2024). Consequently, the use of hematological and biochemical biomarkers has gained attention. The neutrophil-to-lymphocyte ratio (NLR) is inexpensive, derived from routine CBC, and reflects the balance between innate immune activation and lymphocyte suppression (Buonacera et al., 2022; Santhosh et al., 2025; Zhu et al., 2024). Procalcitonin (PCT) is highly specific for bacterial sepsis, rising within 2–4 hours of infection onset, peaking at 6–24 hours, and declining with successful treatment (Huang et al., 2023). Several studies have suggested that combining NLR and PCT improves diagnostic performance compared with using either marker alone. However, most of these studies were conducted in high-resource settings, and data from low- and middle-income countries, including Indonesia, remain scarce. Variations in neonatal immune response, infection patterns, and healthcare settings may influence biomarker behavior, underscoring the need for locally contextualized evidence. Therefore, this study aims to evaluate the correlation between NLR and PCT in Indonesian neonates with suspected sepsis to address this gap and provide data relevant to regional clinical practice (Singhal et al., 2024); (Ni et al., 2019); (Chen et al., 2023)

Although several studies have demonstrated that combining NLR with PCT improves the diagnostic accuracy of neonatal sepsis, most of these findings are derived from populations outside Indonesia. Considering possible regional variations in infection patterns and neonatal immune responses, locally contextualized evidence is essential. Therefore, this study aims to address this gap by examining the correlation between NLR and PCT in neonates with suspected sepsis at Muhammadiyah Hospital, Palembang, South Sumatra. The findings are expected to contribute to the development of cost-effective diagnostic strategies that are applicable in resource-constrained healthcare settings.

MATERIALS AND METHODS

This study employed a quantitative analytic approach with a cross-sectional design to evaluate the relationship between NLR and PCT levels in neonates with suspected sepsis. The research was conducted from January to March 2024 at the Clinical Laboratory and Neonatal Care Unit of Muhammadiyah Hospital, Palembang, Indonesia. Study Population and Sampling: The study population comprised neonates aged 0–28 days who presented with clinical signs suggestive of sepsis, such as temperature instability, respiratory distress, poor feeding, or lethargy. A purposive sampling technique was used to recruit. The sample size of 30 neonates was determined based on the minimum requirement for a correlation study. Using a power analysis ($\alpha = 0.05$, power = 0.80, and an expected correlation coefficient of $r = 0.5$ based on previous studies), the minimum sample size required was 26 subjects. To anticipate potential data loss or exclusion, we included 30 eligible neonates. Inclusion criteria included (1) clinical suspicion of sepsis by the attending neonatologist, (2) availability of complete blood count (CBC) and PCT results, and (3) parental or guardian consent. Exclusion criteria were neonates with (1) congenital hematological disorders, (2) major congenital anomalies, or (3) ongoing steroid or immunomodulatory therapy.

Data Collection: Venous blood samples (2–3 mL) were collected using sterile techniques by certified medical personnel. Complete blood count (CBC) analysis was performed using an automated hematology analyzer (Sysmex XS-800i), from which

absolute neutrophil and lymphocyte counts were obtained to calculate the NLR. For classification purposes, the reference limit for NLR was defined based on previously reported neonatal values (NLR < 2.0 considered normal), while PCT levels < 0.5 ng/mL were considered within the normal range according to the manufacturer's guidelines and published literature. PCT concentrations were measured using a fluorescence immunoassay (Finecare™ FIA Meter Plus, Wondfo Biotech) with validated commercial kits, following the manufacturer's instructions. Internal and external quality control procedures were conducted daily to ensure accuracy and reliability, and all instruments were regularly calibrated according to standard operating procedures (SOPs).

Data Analysis: Data were entered and analyzed using SPSS version 25. The Shapiro–Wilk test was applied to assess data normality. Given the non-parametric nature of the data, Spearman's rank correlation coefficient was used to determine the relationship between NLR and PCT. A p-value of less than 0.05 was considered statistically significant. Descriptive statistics (mean, standard deviation, range) were used to summarize continuous variables, and frequency distributions were used for categorical variables. Ethical Considerations: This study was reviewed and approved by the Health Research Ethics Committee of Universitas Muhammadiyah Palembang, with ethical clearance number No.000510/KEP IKesT Muhammadiyah Palembang/2024. Written informed consent was obtained from the parents or legal guardians of all participating neonates prior to data collection.

RESULTS AND DISCUSSION

The mean NLR was 3.99 (SD ± 1.04), ranging from 2.3 to 6.2, while the mean PCT concentration was 5.72 ng/mL (SD ± 1.88), ranging from 2.9 to 9.2 ng/mL (Table 1). According to previous studies, the normal NLR range in healthy neonates is typically < 2.0, and PCT levels < 0.5 ng/mL are considered within the physiological range. Based on these reference cut-offs, 73.3% of the neonates in this study exhibited elevated NLR values, and 86.7% had increased PCT concentrations, indicating a high likelihood of systemic inflammatory or infectious processes consistent with neonatal sepsis.

Table 1. Descriptive Statistics of NLR and PCT Levels in Neonates with Suspected Sepsis

Variable	Mean ± SD	Range	Median	High	Low
NLR	3.99 ± 1.04	2.3–6.2	3.95	73.3%	26.7%
PCT (ng/mL)	5.72 ± 1.88	2.9–9.2	5.80	100%	0%

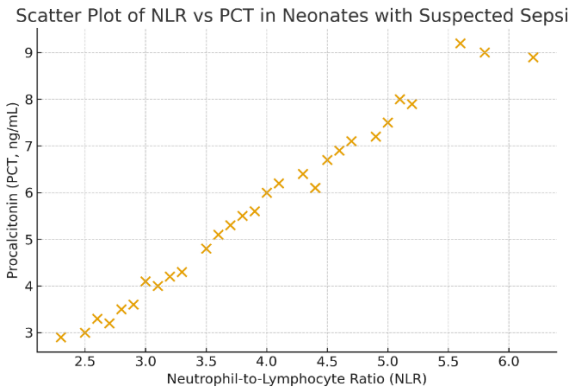

Figure 1. Scatter Plot of NLR vs PCT in Neonates with Suspected Sepsis

Table 2. Spearman Correlation Test between NLR and PCT

Variabel X (NLR)	Variabel Y (PCT)	Nilai Korelasi (r)	Sig. (p-value)
NLR	PCT	0.684	0.000

Correlation analysis using Spearman's rank test demonstrated a statistically significant positive correlation between NLR and PCT ($r = 0.684$, $p < 0.001$) (Table 2). This indicates that higher NLR values tend to be associated with higher PCT concentrations, suggesting that both biomarkers respond in parallel to the systemic inflammatory response triggered by bacterial infection. This finding highlights that both biomarkers reflect parallel but complementary pathways of the neonatal immune response to bacterial invasion. Elevated NLR indicates neutrophilia and lymphopenia, representing systemic inflammation and immune suppression, while elevated PCT levels reflect a host response to bacterial endotoxins and pro-inflammatory cytokines (Martinez et al., 2024; Qiu et al., 2024). Several studies corroborate our findings. Zhu et al. (2024) reported that NLR is a reliable prognostic marker in severe neonatal infections, while Wang et al. (2025) emphasized PCT's high specificity in diagnosing neonatal sepsis. A meta-analysis by Demirci et al. (2025) further demonstrated that PCT outperforms CRP in specificity for bacterial sepsis, but its diagnostic performance is enhanced when combined with hematological indices such as NLR. Similar evidence from Qiu et al. (2024) and Singhal et al. (2024) indicated that a dual-marker approach (NLR + PCT) can achieve diagnostic accuracies exceeding 85%, suggesting its utility in guiding early initiation of antibiotics and reducing unnecessary antimicrobial use.

In the Indonesian context, studies conducted at Dr. Soetomo General Academic Hospital, Surabaya, reported that NLR serves as a practical and cost-effective marker for early detection of neonatal sepsis in resource-limited settings (Purnomowati et al., 2025). Similarly, research at Haji Adam Malik General Hospital, Medan, demonstrated that both NLR and platelet-to-lymphocyte ratio (PLR) have significant diagnostic value in identifying neonatal sepsis (Hasibuan et al., 2024). These findings are consistent with our results and further highlight the potential of NLR and PCT as affordable and accessible diagnostic tools in developing countries, where advanced biomarkers may not be routinely available. By integrating local evidence, this study strengthens the applicability of the NLR–PCT correlation for neonatal sepsis diagnosis within the Indonesian healthcare setting.

Our findings carry important clinical implications, particularly for Indonesia and other resource-limited settings. While PCT is highly specific, its cost and limited availability restrict its routine use in district hospitals. In contrast, NLR can be calculated from a routine CBC test, which is widely available even in peripheral health facilities. Therefore, incorporating NLR as a frontline screening tool, followed by PCT confirmation when available, represents a cost-effective diagnostic strategy (Lakshmanan et al., 2025). This approach could support early diagnosis, rational antibiotic initiation, and antimicrobial stewardship, thereby reducing sepsis-related mortality and slowing the emergence of antibiotic resistance.

Another implication of our study is the potential role of NLR and PCT in disease monitoring and prognosis. Previous studies have shown that decreasing PCT levels are associated with clinical improvement and successful treatment response (Xu et al., 2022), while persistently high NLR correlates with poor outcomes in critically ill neonates (Tang et al., 2022). This suggests that serial monitoring of both markers can provide additional guidance for treatment duration, preventing prolonged or unnecessary antibiotic therapy, which is crucial in neonatal intensive care units

(NICUs). Despite its strengths, including being one of the first studies conducted in South Sumatra to evaluate the correlation between NLR and PCT, this research has limitations. The relatively small sample size and single-center design may limit generalizability. Moreover, confounding variables such as gestational age, birth weight, maternal infection history, and antibiotic exposure prior to admission were not fully controlled. Future multicenter studies with larger sample sizes are needed to establish population-specific cut-off values for NLR and PCT in diagnosing neonatal sepsis across different Indonesian regions. Integration of these biomarkers into clinical scoring systems such as the Neonatal Sequential Organ Failure Assessment (nSOFA) score could further refine diagnostic accuracy and risk stratification (Mearelli et al., 2020).

In summary, this study strengthens the evidence that NLR and PCT are complementary biomarkers in neonatal sepsis. The combined use of both markers could serve as a practical, cost-effective, and clinically meaningful diagnostic approach in resource-limited settings. Wider implementation of this dual-marker strategy has the potential to improve early recognition of sepsis, optimize antibiotic use, and ultimately reduce neonatal morbidity and mortality.

Clinically, integrating NLR into neonatal sepsis screening protocols may be particularly beneficial in resource-limited settings where access to PCT testing is restricted. In such contexts, NLR can guide early clinical decision-making and prompt initiation of empirical antibiotic therapy, while PCT, when available, can refine diagnostic accuracy and support antimicrobial stewardship. This study has several limitations, including a relatively small sample size, a single-center design, and the absence of adjustment for potential confounding variables such as gestational age, birth weight, and maternal infection history. These factors should be considered in future multicenter studies with larger cohorts to validate and generalize the findings. Future multicenter prospective studies with larger sample sizes are recommended to validate these findings and establish clinically relevant cut-off values for NLR and PCT in diagnosing neonatal sepsis.

CONCLUSION

NLR shows a statistically significant correlation with PCT levels in neonates with suspected sepsis. Their combined use can facilitate earlier diagnosis and treatment initiation, potentially reducing sepsis-related morbidity and mortality.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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