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ACCURACY OF PROCALCITONIN, C-REACTIVE PROTEIN, AND MEAN PLATELET VOLUME AS INFECTION MARKERS IN NEONATAL SEPSIS

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ABSTRACT
Neonatal sepsis remains a significant cause of morbidity and mortality, yet diagnosis is limited by nonspecific symptoms and delayed blood culture results. This study evaluated the diagnostic accuracy of procalcitonin (PCT), C-reactive protein (CRP), and mean platelet volume (MPV) as early biomarkers of neonatal sepsis. A retrospective cohort study was conducted in the Neonatology Unit of H. Adam Malik General Hospital, Medan, from January to December 2024. The sampling technique used is consecutive sampling. Of 346 neonates screened, 121 met the inclusion criteria and had concurrent PCT, CRP, MPV, and blood culture results. Clinical and laboratory data were extracted from electronic medical records. Diagnostic performance was assessed using sensitivity, specificity, predictive values, likelihood ratios, and ROC analysis. Among 121 neonates, 31.4% had positive blood cultures. MPV showed no significant difference between culture-positive and culture-negative groups ($p = 0.104$) and demonstrated limited discriminatory value (AUC 0.592). CRP was significantly associated with culture results ($p = 0.037$), showing high specificity (94.7%) but low sensitivity (30.0%) at $\geqslant$1 mg/L (AUC 0.624). PCT demonstrated the strongest performance, with significantly higher levels in culture-positive neonates ($p = 0.022$), sensitivity of 64.5%, specificity of 69.0%, and an AUC of 0.672. Diagnostic accuracy was 66.7% for PCT, 85.1% for CRP, and 55.4% for MPV. PCT provided the most balanced diagnostic utility for neonatal sepsis, while CRP served as a highly specific rule-in marker. MPV showed limited usefulness. Although these biomarkers contribute to early assessment, they are insufficient as standalone diagnostic tools and should be integrated with clinical evaluation and microbiological testing.

Keywords: C-reactive protein; infection; mean platelet volume; neonatal sepsis; procalcitonin

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INTRODUCTION

Neonatal sepsis is one of the leading causes of neonatal death. The diagnosis is clinically made or confirmed through a positive culture of sterile body fluid (Ershad et al., 2019). The World Health Organization estimated that neonatal sepsis accounts for 600,000 neonatal deaths, and 10% neonates need antibiotics (WHO, 2018). Sepsis is the leading cause of early neonatal death in Indonesia, accounting for 12% and 20.5% neonates aged 0-6 days and 6-28 days, respectively (Ministry of Health of the Republic of Indonesia, 2019). Its incidence rate is high in tertiary hospitals, 15.5% in Cipto Mangunkusumo Hospital and 24.6% in H. Adam Malik Hospital (Hasibuan, 2018). The diagnosis is challenging because of unspecific symptoms, and the gold standard examination, blood-culture, is time consuming and limited (Pusponegoro, 2016). Therefore, rapid biomarkers are necessary. Procalcitonin (PCT) increases in systemic bacterial infection with a sensitivity and specificity of 81% and 79%, respectively (Arowosegbe et al., 2016). C-reactive protein (CRP) increases through interleukin-6 (IL-6) mediated hepatic stimulation (Hisamuddin et al., 2015), while the inflammatory and coagulation changes in sepsis increase mean platelet volume (MPV), with sensitivity of 70–97% and specificity of 82–100% (Aydemir et al.,

2018). This study aimed to evaluate the accuracy of PCT, CRP, and MPV in neonatal sepsis to determine the best marker for accurate diagnosis of neonatal sepsis.

METHOD

This retrospective cohort was done in the Neonatology Unit of H. Adam Malik General Hospital, Medan, from January to December 2024, to determine the diagnostic accuracy of PCT, CRP, and MPV individually or in combination. The study population is neonatal sepsis patients based on electronic medical records, using consecutive sampling. The inclusion criteria were neonates who were admitted with a clinical diagnosis of neonatal sepsis, also having MPV, PCT, CRP, and blood culture examination simultaneously. The exclusion criteria were neonates with congenital disorders or incomplete electronic medical records. The minimum sample size was calculated using a diagnostic test formula with an expected sensitivity of 80%, an error margin of 15%, a neonatal sepsis prevalence of 24.6%, and an attrition of 10%. The sample size was 121 subjects with sampling technique used is consecutive sampling. The demographic data (sex, gestational age, chronological age, delivery methods, diagnosis, and length of stay), laboratory parameters (PCT, CRP, and MPV), and blood culture results were collected. The diagnostic performance for each marker was determined using sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and overall accuracy. The receiver operating characteristic (ROC) curve analysis was conducted to assess the ability of each marker to predict neonatal sepsis accurately.

RESULT

Baseline characteristic

The data were collected from electronic medical records from inpatients of the Neonatology Unit of H. Adam Malik General Hospital, Medan, from January to December 2024. This study included 121 of 346 eligible neonates who were selected through inclusion and exclusion criteria. Most participants were term neonates (53.7%), The clinical characteristic data and laboratory parameters were presented in Table 1.

Table 1.
The Baseline Characteristic and Laboratory Parameters of Neonates with Sepsis (n = 121)

Characteristics	Score
Sex, n (%)	
Boy	58 (47.9)
Girl	63 (52.1)
Gestational Age, n (%)	
Preterm	56 (46.3)
Term	65 (53.7)
Length of Stay, days (median, range)	12 (1–67)
Delivery Mode, n (%)	
Spontaneous	20 (16.5)
Sectio Caesarea	101 (83.5)
Clinical Outcomes, n (%)	
Deceased	32 (26.4)
Alive	89 (73.6)
Hemoglobin (g/dL), mean ± SD	13.74 ± 3.29
Hematocrit (%), mean ± SD	39.6 ± 9.46
Leukocyte ($\times 10^3/\mu L$), mean ± SD	14.05 (1.29–43.5)
Thrombocyte ($\times 10^3/\mu L$), median (range)	248 (12–868)
Neutrophil (%), median (range)	61.9 (2.4–90.6)
Lymphocyte (%), median (range)	25.9 (4.1–76.7)
NLR (Neutrophil-to-Lymphocyte Ratio), median (range)	2.53 (0.04–22.1)
PLR (Platelet-to-Lymphocyte Ratio), median (range)	75 (1.57–471.96)
MPV (Mean Platelet Volume), median (range)	10 (8–14.2)

The Correlation between MPV, CRP, and PCT with Blood Culture Result

Each infection marker has a different association degree with blood culture results (Table 2). There was no significant difference in MPV between positive and negative blood culture (10.25 vs. 9.9 fL, p = 0.104). On the other hand, CRP has a significant correlation (p = 0.037), and the CRP category had a positive correlation with culture positivity. Procalcitonin has the highest association; its median was highest among neonates with positive culture results (10.73 vs. 0.5 ng/mL, p = 0.022). These findings highlighted that PCT and CRP have better prediction ability compared to MPV to distinguish confirmed neonatorum sepsis.

Table 2.
The Correlation of MPV, CRP, and PCT with Blood Culture Result

Markers	Positive Culture	Negative Culture	p-value
MPV (fL)[a]	10.25 (8.5–13.8)	9.9 (8–14.2)	0.104
CRP (mg/L)[b]			
< 0.7 mg/L	6 (10.7%)	50 (89.3%)	0.037
0.7 mg/L	1 (20%)	4 (80%)	
1.4 mg/L	3 (50%)	3 (50%)	
PCT (ng/mL)[a]	10.73 (0.05–320)	0.5 (0.04–56.2)	0.022

Note:
[a]Mann–Whitney test
[b]Kruskal–Wallis test
MPV = Mean Platelet Volume; CRP = C-reactive protein; PCT = Procalcitonin

The Diagnostic Value of Parameters

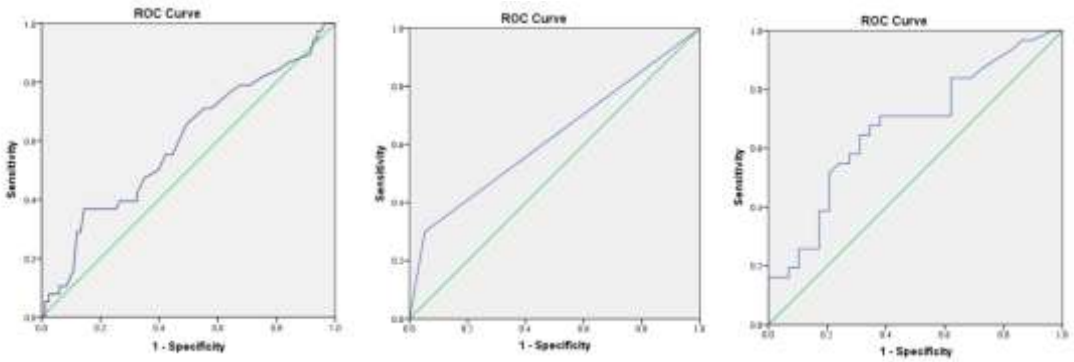
Based on the diagnostic accuracy analysis (Table 3), PCT has the best diagnostic performance with a cut-off value of ≥2.43 ng/ml. PCT has a sensitivity of 64.5%, specificity of 69.0%, accuracy of 66.7%, and LR+ of 2.08. C-reactive protein has the highest specificity (94.7%) with a cut-off value of ≥1 mg/L, but the sensitivity was low (30.0%), resulting in the accuracy of 85.1% and LR+ of 5.7, highlighting a strong rule-in ability. Furthermore, MPV ≥10 fL has a sensitivity of 65.8%, specificity of 50.6%, and accuracy of 55.4%. Overall, PCT offers the best sensitivity and specificity, while CRP is the strongest confirmatory marker.

Table 3.
The Diagnostic Performance of MPV, CRP, and PCT to Predict Sepsis

Markers (Cut-off)	Sensitivity (%)	Specificity (%)	PPV	NPV	LR+	LR-	Accuracy (%)
MPV ≥ 10 fL	65.8	50.6	37.9	76.4	1.33	0.68	55.4
CRP ≥ 1 mg/L	30.0	94.7	50.0	88.5	5.7	0.74	85.1
PCT ≥ 2.43 ng/ml	64.5	69.0	69.0	64.5	2.08	0.51	66.7

Abbreviations:
PPV = Positive Predictive Value; = Negative Predictive Value; LR+ = Positive Likelihood Ratio; LR– = Negative Likelihood Ratio; MPV = Mean Platelet Volume; CRP = C-reactive protein; PCT = Procalcitonin.

The value of Area Under the Curve (AUC) for MPV (Figure 1) was 0.692 (SE 0.057, 95% CI 0.481–0.704) with a p-value of 0.104 (p > 0.05), demonstrating that MPV did not have a statistically significant discriminative ability to distinguish positive- and negative-culture of neonatal sepsis. The AUC value of CRP (Figure 2) was 0.624 with a standard error of 0.107. The asymptotic significance of 0.215 means that these results did not differ statistically from a random prediction (AUC = 0.5). The AUC value for PCT was 0.672 with a standard error of 0.070 (Figure 3). The asymptotic significance of 0.022 is statistically significant (p < 0.05), indicating that PCT has a better discriminative ability than random prediction to distinguish between the two groups.



(**a**) (**b**) (**c**)

Figure 1. The ROC Curve. (a) MPC; (b) CRP; (c) PCT

DISCUSSION

Mean platelet volume has a limited diagnostic performance. The ROC analysis showed an AUC of 0.592, which did not differ significantly from random probability (p = 0,104). Although previous studies reported varied MPV cut-off values with moderate to high diagnostic accuracy (Suwarna et al., 2022), the diagnostic performance in our cohort was much lower. The inconsistency between studies reflects patient population, gestational age, and underlying inflammatory condition differences.

C-reactive protein has a significant association with culture results. Higher CRP category correlated with higher sepsis proportion. Low CRP (<0.7 mg/L) has a strong negative predictive value, demonstrating its value to exclude bacterial infection. This finding is consistent with previous studies, which showed increased CRP in sepsis, although the late increase of CRP can lower the sensitivity in initial infection (Anugu & Khan, 2021; Yu et al., 2022; Al-Atwi et al., 2023; Sagheb et al., 2022). C-reactive protein is still valuable if it is interpreted with clinical findings, but its application as a single initial marker is limited

Procalcitonin has the strongest diagnostic performance among other diagnostic markers in this study. The AUC for PCT was 0.672 (p = 0.022), showing a better dis-criminative ability than random prediction, surpassing MPV and CRP in this cohort study. It offers a balanced diagnostic profile with a sensitivity of 63.5% and specificity of 69% with a cut-off value of 2.43 ng/ml. Previous studies consistently showed that PCT is more accurate than CRP because it increases rapidly after bacterial endotoxin exposure, enabling the early detection of neonatal sepsis (Sodha et al., 2023; De Rose et al., 2024; Putra et al., 2024). The kinetic profile of PCT, including a rapid increase in hours and sustained elevation in systemic infection, supports its value for early diagnostic and disease monitoring.

Procalcitonin is the most reliable diagnostic marker, while CRP may give valuable supplementary information, particularly to exclude infection. Mean platelet volume has a limited diagnostic utility. These findings highlighted that a multimodal diagnostic approach that combines biomarkers with clinical assessment is required to increase early detection of neonatal sepsis.

This study has several limitations. First, the blood culture results may be confounded with various factors, including blood sampling time, blood volume, sampling technique, previous antibiotic exposure, and contamination. These factors were not evaluated in this research and may affect the culture positivity levels. Second, neonatal sepsis diagnosis was made based on maternal and neonatal risks, clinical characteristics, and laboratory examinations. However, the detailed infection risk factors, organ involvement, and disease severity were not analysed, which could limit the cohort's clinical characteristics. Third, procalcitonin was measured only on late-onset sepsis, while

CRP was measured only in early-onset sepsis; therefore, the biomarker data were not complete for all populations.

CONCLUSION

Most participants were term girl neonates with a median length of stay of 12 days, with a high caesarean rate, positivity, and mortality of blood culture was 31.4% and 26.4%, respectively. The laboratory parameters showed lower haemoglobin and haematocrit, higher leukocytes and thrombocytes, also increased NLR and PLR in positive-culture neonates with a median MPV of 10 fL, median PCT of 1,15 ng/ml, and most CRP values were lower than 0.7 mg/L. Mean platelet volume did not differ significantly between culture groups. Increased CRP had a positive association with sepsis risk, and PCT values between positive- and negative-culture differ significantly. The diagnostic accuracy of each marker in descending order was 85.1% for CRP, 66.7% for PCT, and 55.4% for MPV, indicating that although these biomarkers are clinically valuable, they are not reliable enough to be used as a screening tool for neonatal sepsis.

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