Editorial
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Eosinophil count and neutrophil-to-lymphocyte count ratio as biomarkers for predicting early-onset neonatal sepsis

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Despite advances in neonatal intensive care, sepsis remains a major cause of neonatal death and morbidity. Culture-confirmed early-onset neonatal sepsis (EONS), defined as that occurring within 48–72 hours after birth, was determined to have an incidence of 0.4–0.8 per 1,000 live-born term infants in a culture study of developed countries.[1] However, the use of systemic antibiotics in infants with culture-negative EONS is reportedly 6–16 times higher than in infants with culture-confirmed EONS.[2,3]

Many biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), and interleukins have been used to identify infants with sepsis and in clinical decision-making for their management. CRP, a widely used biomarker in the clinical setting, has been extensively studied in research for newborn infants, although it is highly nonspecific as it reportedly increases up to 40–50 mg/L in infants delivered vaginally.[4] PCT, a promising biomarker for sepsis in newborn infants, has the advantage of not being affected by maternal fever during labor because of its inability to cross the placenta.[5] However, few studies have reported the clinical usefulness of PCT for the early diagnosis of EONS.

Eosinopenia, a historical biomarker for infection, has been investigated to differentiate sepsis in non-infectious conditions. Shaaban et al.[6] reported that an eosinopenia count <50 cells/mm^3 showed a sensitivity of 81%, specificity of 65%, positive predictive value (PPV) of 66%, and negative predictive value (NPV) of 80% for predicting sepsis in adults and concluded that eosinopenia is a very sensitive but nonspecific marker of sepsis in the intensive care setting. Wibrow et al.[7] reported that eosinophil counts had very little overall predictive ability (area under the receiver operating characteristic curve [AUROC], 0.448; 95% confidence interval [CI], 0.363–0.533; P=0.237) for sepsis, while sensitivity (54%; 95% CI, 47%–61%) and specificity (56%; 95% CI, 49%–63%) of eosinopenia <10/mm^3 to predict bloodstream infection in pediatric patients were both low.

The neutrophil-to-lymphocyte count ratio (NLCR), a simple marker of inflammation, is useful for identifying many diseases including sepsis in adults. Dursun et al.[8] reported that NLCR had a sensitivity of 75.6%, specificity of 38.4%, PPV of 35.6%, and NPV of 77.8% to predict sepsis in children. Westerdijk et al.[9] reported that the NLCR in adults with sepsis was significantly higher than in those without sepsis (median [interquartile range]:15.3 [10.8–38.2] vs. 9.3 [6.2–14.5], P<0.001) but that the AUROC was significantly higher for CRP (0.89; 95% CI, 0.87–0.92) and PCT (0.88; 95% CI, 0.86–0.91) than NLCR (0.66; 95% CI, 0.62–0.71).

A recent study of the diagnostic value of eosinopenia and NLCR as biomarkers of EONS indicated that eosinopenia of <140 cells/mm^3 had a sensitivity of 60.0%, specificity of 90.0%, PPV of 94.7%, and NPV of 42.9%, while an NLCR with a 1.245 cutoff value had a sensitivity of 83.3%, specificity of 93.3%, PPV of 94.7%, and NPV of 65.2%.[10] However, this study should be interpreted with caution. First, bacteria were identified only in 20% (18 of 90) of patients in the EONS group, which differs from the diagnostic criteria for EONS, whereby EONS is defined

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exclusively by culture-positive cases in many developed countries. Second, this study did not compare basic patient characteristics including perinatal factors for the EONS and non-EONS groups. This study also excluded infants with neonatal respiratory diseases such as respiratory distress syndrome, transient tachypnea of the newborn, and congenital pneumonia and included only a small number of preterm infants in the study population.

In conclusion, further studies of the clinical utility of eosinopenia and NLCR as early biomarkers of EONS should focus on invasive bacterial infections leading to critical status and developing therapeutic decision-making strategies.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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