Advancing Diagnosis of Pediatric Sepsis Through Biomarker-Based Stratification: A Systematic Review and Meta-Analysis

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Abstract

Background: Pediatric sepsis remains a major cause of morbidity and mortality worldwide, particularly in low- and middle-income countries. Early diagnosis is critical, yet reliance on conventional biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) is limited by suboptimal specificity. Several emerging biomarkers have been proposed; however, their comparative diagnostic performance in pediatric populations has not been comprehensively synthesised.

Methods: A systematic review and meta-analysis were conducted in accordance with PRISMA guidelines. PubMed, Scopus, and Embase were searched for diagnostic accuracy studies published up to October 1, 2025, evaluating serum biomarkers for pediatric sepsis. Eligible studies included children aged >1 month to <18 years diagnosed with sepsis using clinical or microbiological reference standards. Pooled diagnostic performance was assessed using area under the receiver operating characteristic curve (AUC) with 95% confidence intervals (CIs) under a random-effects model.

Results: Forty-five studies met the inclusion criteria. Among the evaluated biomarkers, Endocan demonstrated the highest pooled diagnostic accuracy (AUC = 0.87; 95% CI: 0.82–0.93), followed by sTREM-1 (AUC = 0.86; 95% CI: 0.83–0.89). IL-6 and suPAR showed good diagnostic performance (AUC = 0.80 each), whereas presepsin and PTX-3 yielded a pooled AUC of 0.79. Conventional biomarkers showed moderate accuracy, with pooled AUCs of 0.75 for PCT and 0.74 for CRP, accompanied by substantial heterogeneity. Funnel plot analysis suggested possible small-study effects for several emerging biomarkers.

Conclusion: Emerging biomarkers, particularly Endocan and sTREM-1, demonstrate superior diagnostic performance compared with traditional markers in pediatric sepsis and may serve as valuable adjunctive tools. However, heterogeneity and limited pediatric evidence warrant further large-scale, multicenter prospective studies to validate these findings and establish standardized diagnostic thresholds.