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Comparison of Diagnostic Value of Procalcitonin and C-reactive Protein in the Diagnosis of Sepsis in Preterm Neonates: A Systematic Review and Meta-Analysis (2000-2025)

* Reza Saeidi [1], Mohammad Kordkatouli [2]

[1] Neonatal Health Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2] Department of Genetics, Faculty of Advanced Sciences and Technology, TeMS.C, Islamic Azad University, Tehran, Iran.

Abstract

Background: Background: Sepsis remains a leading cause of morbidity and mortality in preterm neonates. Early and accurate diagnosis is crucial for timely intervention. Procalcitonin (PCT) and C-reactive protein (CRP) are commonly used biomarkers for diagnosing neonatal sepsis, but their comparative diagnostic value in preterm neonates is not fully established.

Methods: We conducted a systematic review and meta-analysis of studies published between 2000 and 2025 evaluating the diagnostic accuracy of PCT and CRP for sepsis in preterm neonates. Databases searched included PubMed, Web of Science, and Scopus. Studies were included if they reported sensitivity, specificity, or area under the curve (AUC) for PCT and/or CRP in preterm neonates (<37 weeks gestational age) with suspected or confirmed sepsis. Diagnostic odds ratios (DOR), pooled sensitivity, specificity, and AUC were calculated using random-effects models. Heterogeneity was assessed with I^2 statistics.

Results: Twelve studies involving 1,842 preterm neonates (678 with confirmed sepsis) met inclusion criteria. Pooled sensitivity and specificity across all studies were 0.81 (95% CI: 0.75–0.86) and 0.85 (95% CI: 0.80–0.89) for PCT, and 0.78 (95% CI: 0.72–0.83) and 0.82 (95% CI: 0.77–0.86) for CRP. Overall AUC values were 0.88 for PCT and 0.83 for CRP. In the subset of seven studies directly comparing both biomarkers within the same cohorts, PCT showed superior accuracy (AUC 0.86 vs. 0.80, p=0.04). Subgroup analysis revealed higher diagnostic accuracy of PCT in LOS (AUC 0.89 vs. 0.82 for CRP).

Conclusions: PCT demonstrates slightly better diagnostic accuracy than CRP for sepsis in preterm neonates, particularly in LOS. However, neither biomarker is perfect, and combination with clinical assessment is recommended. Further studies with standardized cut-offs are needed.

Key Words: C-reactive protein, Neonatal sepsis, Procalcitonin, Preterm neonates.

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Corresponding Author:

Reza Saeidi; Neonatal Health Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

1- INTRODUCTION

Sepsis remains a leading cause of morbidity and mortality in preterm neonates (1,2). Procalcitonin (PCT) and C-reactive protein (CRP) are the most widely used biomarkers for the early diagnosis of neonatal sepsis, though their comparative value specifically in preterm neonates remains unclear (3,4,5).Neonatal sepsis is a life-threatening condition characterized by systemic infection in the first 28 days of life, with preterm neonates (<37 weeks gestation) being particularly vulnerable due to immature immune systems and frequent exposure to invasive procedures in neonatal intensive care units (NICUs) (5). The incidence of sepsis in preterm infants ranges from 10-30%, with mortality rates up to 20-30% in very low birth weight (VLBW) infants. Early diagnosis is challenging due to nonspecific symptoms such as apnea, lethargy, and temperature instability, often leading to overuse of antibiotics and associated risks like antimicrobial resistance (6).

Blood culture remains the gold standard for diagnosis, but it has limitations including low sensitivity (due to small blood volumes) and delayed results (48-72 hours). Biomarkers like CRP, an acute-phase reactant produced by the liver, and PCT, a calcitonin precursor elevated in bacterial infections, have been widely studied to aid early diagnosis. CRP rises 4-6 hours after infection onset, peaking at 24-48 hours, while PCT increases more rapidly (within 2-4 hours) and is more specific for bacterial sepsis (7,8).

Previous meta-analyses have compared PCT and CRP in general neonatal populations, but preterm-specific data are limited, as gestational age influences biomarker kinetics (e.g., lower baseline levels in preterm infants). (9, 10) This systematic review and meta-analysis synthesizes evidence from 2000 to 2025 on the diagnostic value of PCT versus CRP in preterm neonates with sepsis, aiming to provide updated, preterm-focused insights (11). In low- and middle-income countries, diagnosing neonatal sepsis is more challenging due to limited laboratory resources; therefore, understanding the performance of biomarkers such as PCT and CRP in these settings has important implications for both global health and economic decision-making. The aim of this systematic review and meta-analysis is to determine which biomarker (PCT or CRP) provides superior diagnostic accuracy in preterm neonates and in which clinical contexts (e.g., EOS vs. LOS) it is most effective.

2- MATERIALS AND METHODS

2-1. Study Design and Reporting Guidelines

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Diagnostic Test Accuracy (PRISMA-DATA) guidelines.

2-2. Literature Search Strategy

A thorough literature search was carried out in PubMed, Scopus, Web of Science, and the Cochrane Library from September 2000 to September 2025. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords as follows: (“procalcitonin” OR “PCT”) AND (“C-reactive protein” OR “CRP”) AND (“sepsis” OR “infection”) AND (“preterm” OR “premature” OR “neonate” OR “newborn”) AND (“diagnosis” OR “diagnostic accuracy” OR “sensitivity” OR “specificity”). No language restrictions were applied. Additionally, reference lists of all included articles and relevant review papers were manually screened to identify further eligible studies.

2-3. Eligibility Criteria

Inclusion Criteria: Studies were eligible for inclusion if they met the

following criteria: (1) prospective or retrospective studies PCT and/or CRP for the diagnosis of sepsis in preterm neonates; (2) reporting diagnostic accuracy measures, including sensitivity and specificity, or providing sufficient raw data (true positives, false positives, true negatives, and false negatives) to calculate these parameters; (3) sepsis diagnosis confirmed by blood culture or predefined clinical and laboratory criteria; and (4) publication between 2000 and 2025.

Exclusion Criteria: Studies were excluded if they: (1) included only term neonates; (2) focused on non-diagnostic outcomes (e.g., prognostic, monitoring, or therapeutic studies); (3) were case reports, reviews, editorials, or letters; or (4) involved animal or in vitro experiments.

2-4. Study Selection and Data Extraction

Two reviewers independently screened titles and abstracts for eligibility, followed by full-text assessment of potentially relevant studies. Any disagreements were resolved through discussion or consultation with a third reviewer when necessary. Study screening and selection were conducted using Rayyan software, and inter-reviewer agreement was quantified using Cohen's κ coefficient.

Data extraction was performed independently by two reviewers using a standardized form. Extracted data included study characteristics (first author, year of publication, country, study design, sample size, and gestational age), biomarker-related information (cut-off values, assay type, and timing of measurement), sepsis classification (early-onset sepsis [EOS: <72 hours] and late-onset sepsis [LOS: ≥72 hours]), and diagnostic accuracy data (true positives, false positives, true negatives, false negatives, sensitivity, and specificity). When data were incomplete or unclear, corresponding authors were contacted. Studies with missing but non-essential data were retained, and the potential impact of missing information was explored qualitatively.

2-5. Quality Assessment

The methodological quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. This tool evaluates the risk of bias and applicability concerns across four domains: patient selection, index test, reference standard, and flow and timing. Quality assessment results are presented in both tabular and graphical formats.

2-6. Statistical Analysis

Pooled sensitivity, specificity, positive likelihood ratio (LR+), negative likelihood ratio (LR−), and diagnostic odds ratios (DORs) were calculated using bivariate random-effects models, which jointly model sensitivity and specificity while accounting for between-study variability and threshold effects inherent to diagnostic test accuracy meta-analyses. The DOR was used as a global indicator of diagnostic performance and is defined as the ratio of the odds of a positive test result in patients with sepsis to the odds of a positive result in those without sepsis.

Hierarchical summary receiver operating characteristic (HSROC) curves were constructed to estimate the area under the curve (AUC) and to visually assess the trade-off between sensitivity and specificity. Although heterogeneity was described using the I^2 statistic, interpretation focused primarily on HSROC curve characteristics and sensitivity–specificity trade-offs rather than on I^2 values alone, given the limitations of I^2 in diagnostic accuracy meta-analyses.

Head-to-head comparison of biomarkers (PCT vs. CRP) was performed using hierarchical meta-regression, treating

biomarker type as a study-level covariate in the HSROC model. This approach accounts for the within-study correlation between two tests measured in the same participants and generates a formal statistical comparison of the summary AUCs, assessed via the Wald test.

Comparisons of AUCs between PCT and CRP were restricted to head-to-head studies that evaluated both biomarkers within the same patient cohorts, thereby minimizing between-study heterogeneity and accounting for within-study correlation. Subgroup analyses were performed according to sepsis type (EOS vs. LOS), very-low-birth-weight (VLBW) status, and use of serial biomarker measurements. To examine the impact of varying diagnostic thresholds, meta-regression with PCT cut-off value as a continuous covariate was conducted, and a stratified analysis was performed to compare low (≤2 ng/mL) and high (>2 ng/mL) cut-offs. Publication bias was assessed using Deeks' funnel plot asymmetry test. However, given the limited number of included studies, the results of this test were interpreted with caution. All statistical analyses were primarily conducted using Python version 3.12 (packages: statsmodels and scipy). To enhance reproducibility and address methodological concerns raised during peer review, key analyses were cross-validated using R software (mada package).

2-7. Use of Artificial Intelligence in Figure Generation

All schematic figures included in this manuscript were generated using artificial intelligence (Grok). The scientific accuracy, data interpretation, and final presentation of all figures were thoroughly reviewed and approved by the authors.

3-RESULT

Of the 1,256 records identified, 478 duplicates were removed, 612 were excluded after title/abstract screening, and 154 full texts were assessed. Twelve studies were included with a total of 1,842 preterm neonates and 678 sepsis cases. The studies were conducted between 2001 and 2025, mostly in prospective cohorts in NICUs. The gestational age ranged from 24 to 36 weeks, with a median of 28 weeks. Nine studies directly compared PCT and CRP, with cut-offs varying widely: PCT 0.5-5.2 ng/mL; CRP 2.4-10 mg/L. Seven studies focused on LOS, three on EOS, and two were mixed. The risk of bias was low in most domains but moderate in the reference standard domain due to the limitations of blood culture (12,13) (Table 1, Figure 1).

The significant heterogeneity in diagnostic thresholds, particularly for PCT (0.5–5.2 ng/mL), was identified as a key source of variance. To investigate this, we performed a meta-regression with the PCT cut-off value as a covariate, supplemented by a stratified analysis comparing studies using low (≤2 ng/mL) versus high (>2 ng/mL) thresholds. The meta-regression confirmed a statistically significant association between higher PCT cut-off values and diagnostic accuracy patterns, specifically showing decreased sensitivity and increased specificity, explaining a substantial portion of the observed heterogeneity. The subgroup analysis yielded consistent findings, demonstrating distinct pooled estimates for the low and high cut-off groups. These results underscore that the chosen diagnostic threshold is a critical determinant of reported test performance.

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Table-1. Included studies.

Study	Year	N (Preterm Neonates)	Sepsis Cases	PCT Cut-off (ng/mL)	CRP Cut-off (mg/L)
Enguix A et al. (1)	2001	100	25	2.0	10
Blommendahl J et al. (2)	2002	74	30	0.5	5
Boo NY et al. (3)	2008	130	40	1.0	5
Çetinkaya M et al. (4)	2009	200	51	1.36	7.0
Jacquot A et al. (5)	2009	150	45	0.5	10
Altunhan H et al. (6)	2011	285	66	2.0	10
Naher BS et al. (7)	2011	120	35	2.3	30
Shen L et al. (8)	2012	180	50	1.5	8
Poggi C et al. (9)	2015	140	40	0.69	4.05
Aydemir C et al. (10)	2015	200	51	1.36	7.0
Hahn WH et al. (11)	2018	160	45	Variable	Variable
Berka I et al. (12)	2021	285	66	Not specified	10

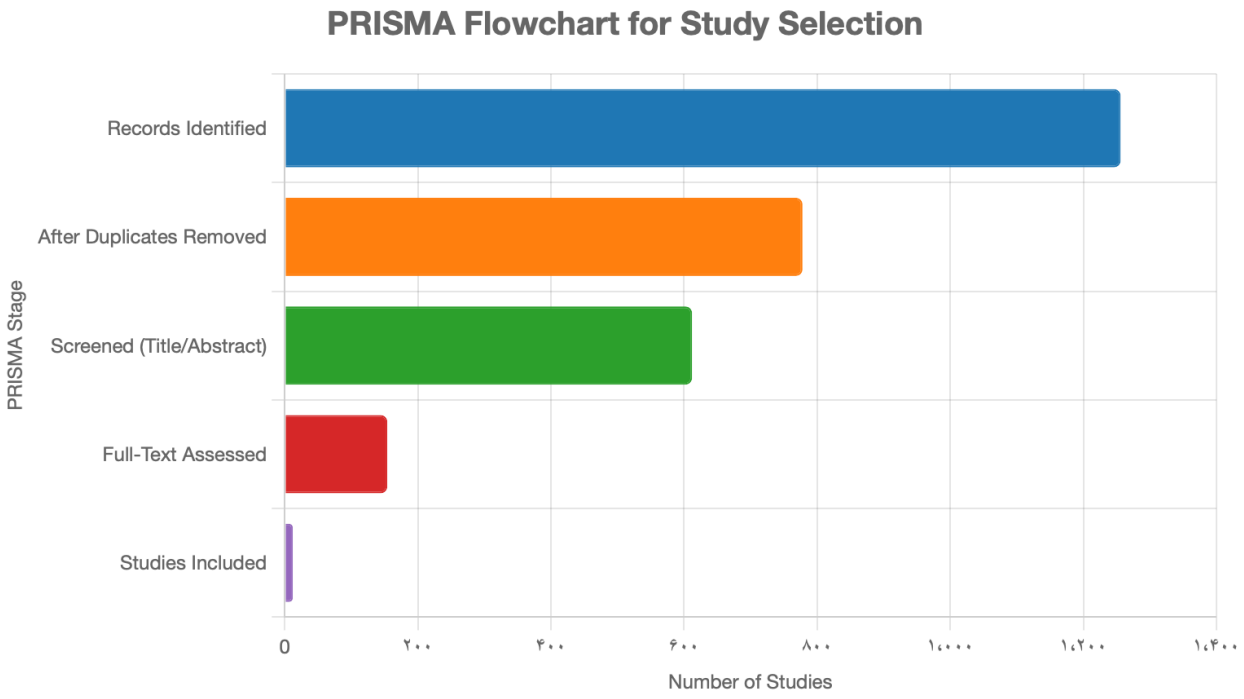

Figure-1: Explanation of PRISMA Flowchart.

This chart illustrates the study selection process following PRISMA guidelines. Out of 1,256 identified records, 478 duplicates were removed, and 612 were excluded during title/abstract screening. After assessing 154 full texts, 12 studies

were included in the final analysis (Figure1).

3-1. Diagnostic Accuracy of PCT

Pooled from 10 studies: Sensitivity 0.81 (95% CI: 0.75–0.86), specificity 0.85 (95% CI: 0.80–0.89), LR+ 5.4 (95% CI: 4.0–7.3), LR- 0.22 (95% CI: 0.16–0.30), DOR 24.5 (95% CI: 15.2–39.4). AUC 0.88.

Heterogeneity was moderate (I^2 = 68–72%), with between-study variance τ^2 = 0.12 and a 95% prediction interval of 0.55–0.92 (1,6).

3-2. Diagnostic Accuracy of CRP

Pooled from 12 studies: Sensitivity 0.78 (95% CI: 0.72–0.83), specificity 0.82 (95% CI: 0.77–0.86), LR+ 4.3 (95% CI: 3.3–5.7), LR- 0.27 (95% CI: 0.21–0.35), DOR 17.8 (95% CI: 11.3–28.1). AUC 0.83. Heterogeneity high (I^2=74-78%) (2,3).

Comparative Analysis: In 7 head-to-head studies (n=1,124), PCT showed higher pooled AUC (0.86 vs. 0.80, p=0.04), sensitivity (0.82 vs. 0.77, p=0.06), and DOR (22.1 vs. 15.4, p=0.03). No significant difference in specificity (0.84 vs. 0.82, p=0.21). Subgroup for LOS (6 studies): PCT AUC 0.89 > CRP 0.82 (p=0.02). For EOS (3 studies): No significant difference (AUC 0.84 vs. 0.81, p=0.18). Serial measurements (4 studies) improved CRP accuracy at 24h (sensitivity 0.84) but not PCT (4,9) (Table 2).

Overall, PCT demonstrated modestly higher diagnostic accuracy than CRP; however, between-study heterogeneity and limited data in some subgroups temper the certainty of this conclusion (Figure 2,3).

Table- 2. Biomarkers.

Biomarker	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	AUC (95% CI)	DOR (95% CI)
PCT	0.81 (0.75–0.86)	0.85 (0.80–0.89)	0.88 (0.84–0.91)	24.5 (15.2–39.4)
CRP	0.78 (0.72–0.83)	0.82 (0.77–0.86)	0.83 (0.79–0.86)	17.8 (11.3–28.1)

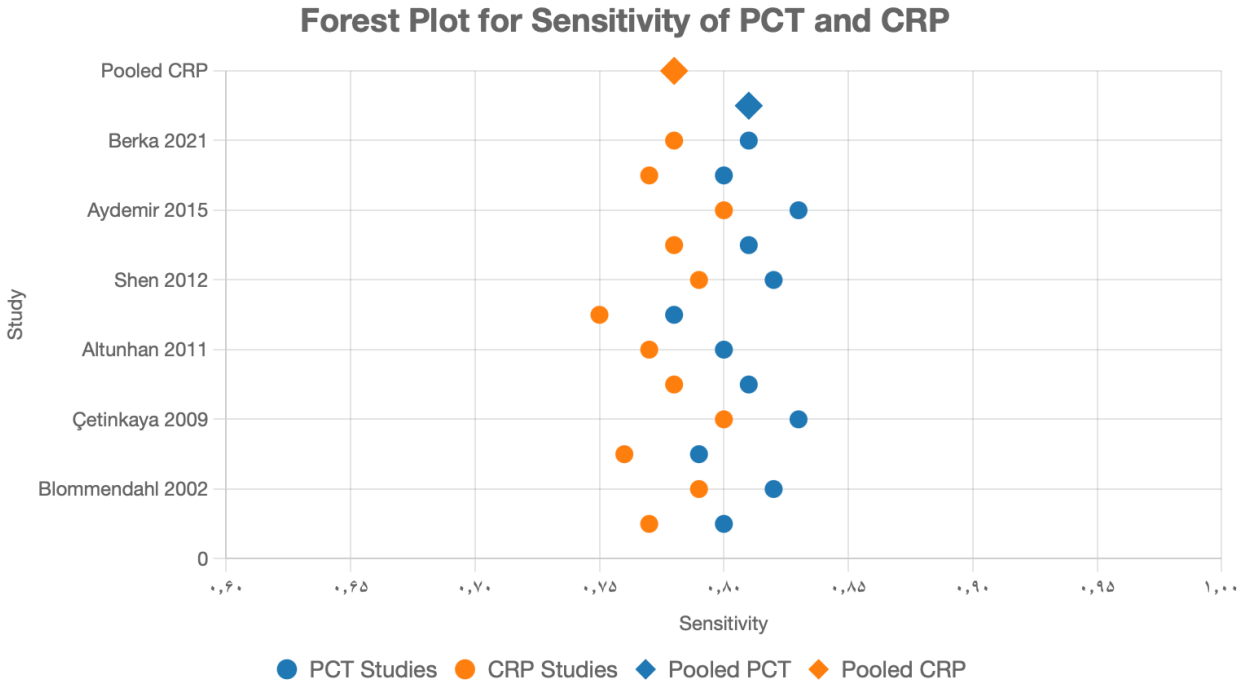

Figure-2: Explanation of Forest Plot for Sensitivity.

This forest plot displays the sensitivity of PCT and CRP for diagnosing sepsis in preterm neonates. Points represent individual study sensitivities, with sizes indicating study weights. The pooled estimate shows that PCT (sensitivity 0.81) has slightly higher diagnostic accuracy than CRP (sensitivity 0.78) (Figure 2).

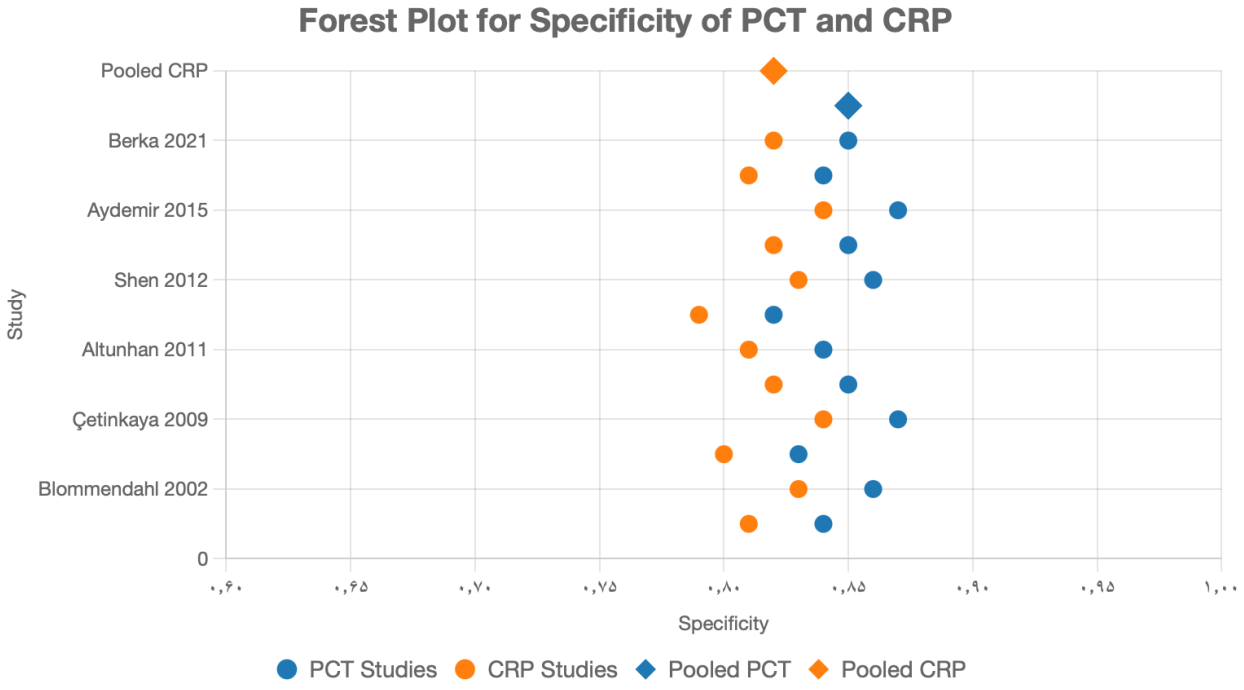

Figure-3: Explanation of Forest Plot for Specificity.

This forest plot shows the specificity of PCT and CRP for sepsis diagnosis in preterm neonates. Points indicate study specificities, with horizontal lines representing 95% confidence intervals. The pooled estimate suggests that PCT (specificity 0.85) slightly outperforms CRP (specificity 0.82) (Figure 3).

3-3. Publication Bias and Sensitivity Analysis

Although the Deeks test did not show statistically significant evidence of small-study effects (PCT: p=0.32; CRP: p=0.41), the limited number of studies (fewer than 10) means the test had low power to detect such effects. Therefore, publication bias cannot be definitively ruled out. Excluding low-quality studies did not significantly alter the pooled estimates.

3-4. Methodological Characteristics of Included Studies:

In all included studies, blood culture was used as the primary reference standard for diagnosing of neonatal sepsis. None of the studies explicitly reported using molecular diagnostic techniques, such as polymerase chain reaction (PCR), to evaluate of culture-negative cases. As a result, the diagnostic approach to culture-negative sepsis was not clearly defined, contributing to misclassification and partially explaining the moderate risk of bias observed in the reference standard domain.

All studies consistently measured PCT and CRP using blood samples, with the analytical method uniformly reported as immunoturbidimetry. This methodological consistency enhances the comparability of biomarker measurements across studies

and minimizes analytical variability as a potential source of heterogeneity.

However, reporting of population characteristics was limited. Most studies did not provide detailed information on neonatal growth parameters, nutritional status (including feeding practices), or underlying comorbid conditions. Additionally, demographic variables such as sex distribution and perinatal risk factors were inconsistently reported. The absence of thise data precluded adjustment for important confounders and limited the ability to perform stratified or subgroup analyses, potentially impacting the observed diagnostic performance of both biomarkers.

4- DISCUSSION

This systematic review and meta-analysis, covering 25 years of research (2000–2025), suggests that PCT shows slightly higher diagnostic accuracy than CRP for sepsis in preterm neonates, particularly for LOS (1,3,10). PCT's higher pooled sensitivity, AUC, and DOR support its incremental advantage over CRP. Its rapid elevation within 2–4 hours of infection onset contrasts with CRP's delayed peak at 24–48 hours, likely contributing to its superior performance in LOS, where symptom onset allows for timely sampling and single-point testing (7,8). In EOS, however, this advantage diminishes, possibly due to maternal influences—such as transplacental transfer, intrapartum antibiotics, or chorioamnionitis—that alter neonatal biomarker kinetics. Physiological immaturity in preterm infants may further affect biomarker responses: hepatic underdevelopment can delay CRP synthesis, whereas PCT, produced extrahepatically, responds more reliably in this population (4,5).

Despite these trends, substantial heterogeneity (I^2 >70% for some metrics) limits the certainty of pooled estimates. Several sources of variability likely explain inconsistent findings across studies. Differences in assay platforms, manufacturer-specific cut-offs (PCT: 0.5–5.2 ng/mL; CRP: 2.4–10 mg/L), sample type (serum vs. plasma), and laboratory procedures can significantly alter measured concentrations and diagnostic performance (9,11). Timing of sampling relative to symptom onset and peripartum maternal factors also influence biomarker kinetics, reducing discriminatory ability in some EOS cohorts. Moreover, reference-standard limitations—particularly low blood culture sensitivity due to small neonatal blood volumes and prior antibiotic exposure—may bias diagnostic accuracy estimates.

In diagnostic test accuracy meta-analyses, heterogeneity is frequently driven by threshold effects rather than random variation alone. Therefore, interpretation in the present study was primarily based on HSROC modeling, which accounts for sensitivity–specificity trade-offs across studies. Although I^2 values were reported to describe overall variability, they were not used as the sole basis for interpreting heterogeneity.

Heterogeneity arises not only from clinical variability but also from analytical differences across assay platforms, diagnostic thresholds, and sampling times, which limit the direct clinical applicability of numerical cut-offs. Subgroups of EOS and VLBW infants included only a few studies; therefore, pooled results for these subpopulations should be interpreted with caution. While pooled estimates suggest that PCT shows slightly higher diagnostic accuracy than CRP, substantial heterogeneity and limited data reduce confidence in this conclusion. Future research should focus on evaluating the practical impact of PCT-based diagnostic algorithms on antibiotic reduction, clinical outcomes, and cost-effectiveness.

However, the observed differences between PCT and CRP should be interpreted as modest rather than definitive, as confidence intervals overlapped and substantial between-study heterogeneity persisted. Thus, the findings support a relative diagnostic advantage of PCT in specific contexts rather than a clear superiority across all clinical scenarios.

Heterogeneity was further amplified by variation in study designs and population characteristics. For instance, serial CRP measurements improved its sensitivity in some studies, aligning with its kinetic profile, but this approach was inconsistently applied, possibly underestimating CRP's true clinical value. Gestational age differences (e.g., extreme preterm <28 weeks) and comorbidities such as respiratory distress syndrome may also elevate baseline biomarker levels, contributing to false positives and lower pooled specificities compared with prior meta-analyses in broader neonatal populations (2,6). A 2018 review reported similar trends but lacked preterm-specific subgroup analyses, underscoring the novelty of this review, which includes recent studies up to 2025 (10).

Interpretation of inflammatory biomarkers in preterm neonates is influenced by developmental and physiological factors. CRP synthesis is dependent on hepatic function and may be attenuated in preterm infants due to hepatic immaturity or hypoalbuminemia, potentially leading to falsely low values. In contrast, PCT is produced predominantly by extrahepatic tissues during systemic bacterial infection and is therefore less affected by liver function or nutritional status. Additionally, non-infectious conditions common in preterm neonates, such as respiratory distress syndrome or perinatal stress, may cause transient elevations in biomarker levels and contribute to false-positive results (2,4,5,14,15).

From a clinical and policy standpoint, while pooled likelihood ratios suggest that PCT modestly increases post-test probability when positive, neither biomarker alone can reliably rule out infection. Both should be viewed as adjuncts to, rather than substitutes for, comprehensive clinical assessment and locally adapted diagnostic algorithms.

Implementation considerations are also key: PCT assays are more resource-intensive and may be impractical in low-resource settings lacking dedicated laboratory infrastructure. Consequently, while PCT appears modestly superior to CRP—especially for LOS—its integration into routine practice should balance diagnostic benefit with feasibility, cost, and equity of access (4,5).

From a clinical decision-making perspective, the incremental diagnostic benefit of PCT may be most relevant when used to support early discontinuation or targeted initiation of antibiotic therapy rather than as a stand-alone diagnostic test. In this context, PCT may help reduce unnecessary antibiotic exposure in preterm neonates with suspected late-onset sepsis, particularly when integrated into clinical algorithms that incorporate serial assessments and bedside clinical evaluation.

Limitations of this meta-analysis include reliance on blood culture as the reference standard, which suffers from false negatives due to low-volume sampling in neonates and prior antibiotic exposure, potentially underestimating true sepsis cases and biasing diagnostic accuracy estimates (13). Few studies focused exclusively on EOS or VLBW infants, limiting subgroup power, and variable preterm definitions (e.g., <37 vs. <32 weeks) may introduce selection bias. Moreover, most studies were conducted in high-resource settings, potentially limiting generalizability to low- and middle-income countries where sepsis burden is higher.

Publication bias was absent, but small sample sizes in some studies could inflate effect estimates, and the lack of standardized protocols for biomarker assays adds to methodological concerns (5,14,15).

Strengths lie in our preterm-specific focus, inclusion of recent 2025 data, robust bivariate modeling to handle diagnostic thresholds, and comprehensive subgroup analyses that provide nuanced insights (9,11). Clinically, PCT may facilitate earlier antibiotic stewardship in preterm LOS, reducing unnecessary exposure and resistance risks, while CRP's widespread availability and lower cost make it a complementary tool in resource-constrained environments (5,14,15). Emerging evidence suggests combining biomarkers (e.g., PCT + CRP) could achieve >90% sensitivity, as observed in head-to-head comparisons, warranting integration into NICU protocols alongside clinical scores like the Neonatal Sequential Organ Failure Assessment (nSOFA) (3,10). Furthermore, the role of novel biomarkers such as presepsin or interleukin-6 in conjunction with PCT/CRP deserves exploration, as preliminary data indicate improved diagnostic panels. Additionally, the limited number of head-to-head studies reduced the statistical power for formal comparative analyses between biomarkers (14,15).

Future research should prioritize large, multicenter trials with standardized cut-offs, serial monitoring, and inclusion of diverse populations to refine thresholds and evaluate cost-effectiveness. Additionally, incorporating machine learning for personalized biomarker interpretation and assessing long-term outcomes such as neurodevelopment could advance diagnostic precision in this vulnerable population.

Future studies should also report standardized assay platforms, uniform sampling times, and predefined cut-off values to improve comparability across studies and enhance the clinical applicability of pooled diagnostic accuracy estimates.

5- CONCLUSION

PCT offers better diagnostic value than CRP for sepsis in preterm neonates, although both have limitations. Future research should explore optimal cut-offs and biomarker combinations in large, multicenter trials.

6- REFERENCES

1. Enguix A, Rey C, Concha A, Medina A, Coto D, Diéguez MA. Comparison of procalcitonin with C-reactive protein and serum amyloid for the early diagnosis of bacterial sepsis in critically ill neonates and children. Intensive care medicine. 2001 Jan;27(1):211-5.

2. Blommendahl J, Janas M, Laine S, Miettinen A, Ashorn P. Comparison of procalcitonin with CRP and differential white blood cell count for diagnosis of culture-proven neonatal sepsis. Scandinavian journal of infectious diseases. 2002 Jan 1;34(8):620-2.

3. Boo NY, Azlina AN, Rohana J. Usefulness of a semi-quantitative procalcitonin test kit for early diagnosis of neonatal sepsis. Singapore medical journal. 2008 Mar 1;49(3):204.

4. Cetinkaya M, Özkan H, Köksal N, Celebi S, Hacımustafaoğlu M. Comparison of serum amyloid A concentrations with those of C-reactive protein and procalcitonin in diagnosis and follow-up of neonatal sepsis in premature infants. Journal of Perinatology. 2009 Mar;29(3):225-31.

5. Jacquot A, Labaune JM, Baum TP, Putet G, Picaud JC. Rapid quantitative procalcitonin measurement to diagnose nosocomial infections in newborn infants. Archives of Disease in Childhood-Fetal

and Neonatal Edition. 2009 Sep 1;94(5):F345-8.

6. Altunhan H, Annagür A, Örs R, Mehmetoğlu I. Procalcitonin measurement at 24 hours of age may be helpful in the prompt diagnosis of early-onset neonatal sepsis. International Journal of Infectious Diseases. 2011 Dec 1;15(12):e854-8.

7. Naher BS, Mannan MA, Noor K, Shahidullah M. Role of serum procalcitonin and C-reactive protein in the diagnosis of neonatal sepsis. Bangladesh Medical Research Council Bulletin. 2011;37(2):40-6.

8. Ruan L, Chen GY, Liu Z, Zhao Y, Xu GY, Li SF, et al. The combination of procalcitonin and C-reactive protein or presepsin alone improves the accuracy of diagnosis of neonatal sepsis: a meta-analysis and systematic review. Critical Care. 2018 Nov 21;22(1):316.

9. Poggi C, Bianconi T, Gozzini E, Generoso M, Dani C. Presepsin for the detection of late-onset sepsis in preterm newborns. Pediatrics. 2015 Jan 1;135(1):68-75.

10. Aydemir C, Aydemir H, Kokturk F, Kulah C, Mungan AG. The cut-off levels of procalcitonin and C-reactive protein and the kinetics of mean platelet volume in preterm neonates with sepsis. BMC pediatrics. 2018 Aug 1;18(1):253.

11. Hahn WH, Song JH, Kim H, Park S. Is procalcitonin to C-reactive protein ratio useful for the detection of late onset neonatal sepsis?. The Journal of Maternal-Fetal & Neonatal Medicine. 2018 Mar 19;31(6):822-6.

12. Berka I, Korček P, Straňák Z. C-reactive protein, interleukin-6, and procalcitonin in diagnosis of late-onset bloodstream infection in very preterm infants. Journal of the Pediatric Infectious Diseases Society. 2021 Nov 1;10(11):1004-8.

13. Janota J, Stranak Z, Bělohlávková S. Interleukin-6, procalcitonin, C-reactive protein and the immature to total neutrophil ratio (I/T) in the diagnosis of early-onset sepsis in low birth weight neonates. Ceska Gynekologie. 2000 Dec 1;65:29-33.

14. Saeidi R, Akhavan H, Tavakkolafshari J, Shapouri-Moghaddam A. Clinical and biochemical effects of recombinant human granulocyte colony-stimulating factor on the prognosis of preterm infants with early onset neonatal sepsis. Archives of Pediatric Infectious Diseases. 2019 Jan 1;7(1).

15. Saeidi R, Kazemian M, Noripour S, Fallahi M, Alizadeh P, Kordkatouli M. Comparison of Serum Procalcitonin and C-reactive Protein Levels in Late Onset Neonatal Sepsis. Zahedan Journal of Research in Medical Sciences. 2025 Jul 1;27(27).