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Evaluating Sepsis Markers Versus Blood Culture for Diagnosing Neonatal Sepsis: A Prospective Study

Dr Samandeep Kaur[1], Dr. Priyanka Chaudhary [2], Dr Anil Mori[3], Dr Sakshi Patel[4*], Elby K Paul[5]

[1]Assistant Professor, Microbiology, CMCH, Bhopal
[2]Associate Professor, Pediatrics, CMCH, Bhopal
[3]Senior Resident, Pediatrics, NSCB Medical College, Jabalpur
[4*]Senior Resident, Microbiology, CMCH, Bhopal
[6]Associate Professor, Chirayu Nursing College, Bhopal

***Corresponding Author:** Dr. Sakshi Patel,
*Senior Resident, Microbiology, CMCH, Bhopal, email: sakshi.patel1801@gmail.com

Abstract

Background: Neonatal sepsis is a leading cause of morbidity and mortality in neonates, requiring early and accurate diagnosis for effective management. While blood culture is considered the gold standard for diagnosing sepsis, it has limitations such as long processing time and low sensitivity. This study aims to evaluate the efficacy of various sepsis markers, including C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6, in comparison to blood culture for diagnosing neonatal sepsis.

Methods: This prospective observational study was conducted in a tertiary care hospital in central India over six months. A total of 100 neonates with clinical signs of sepsis were enrolled. Blood samples were collected for blood culture and sepsis marker assays. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each sepsis marker were calculated against blood culture results.

Results: Out of 100 neonates, 35 had positive blood cultures. The pathogens identified included Escherichia coli (34%), Klebsiella pneumoniae (29%), and Staphylococcus aureus (23%). PCT demonstrated the highest sensitivity (90%) and NPV (95%), followed by CRP (sensitivity 85%, NPV 90%) and interleukin-6 (sensitivity 80%, NPV 90%). The chi-square test confirmed the statistical significance of the association between sepsis markers and blood culture results ($p < 0.05$).

Conclusion: Sepsis markers, particularly PCT, exhibit high diagnostic accuracy and can serve as valuable adjuncts to blood culture in diagnosing neonatal sepsis. Integrating sepsis markers with clinical assessment and blood culture results can enhance early detection and improve neonatal outcomes. Further research is needed to validate these findings in larger, multi-center studies and explore the cost-effectiveness of routine sepsis marker testing in neonatal care.

Introduction

Neonatal sepsis remains a major challenge in neonatal care, contributing to high mortality rates in developing countries. Traditional blood culture, the gold standard for diagnosing sepsis, often has limitations such as time consumption and low sensitivity. Sepsis markers like C-reactive protein (CRP), procalcitonin (PCT), and interleukins have been proposed as rapid diagnostic tools. This study aims to compare the diagnostic accuracy of these sepsis markers against blood culture in neonates suspected of sepsis.

Methodology

This prospective observational study was conducted over six months at a tertiary care hospital in central India. The study population comprised neonates admitted to the neonatal intensive care unit (NICU) with clinical signs of sepsis. A total of 100 neonates were enrolled in the study based on predefined inclusion and exclusion criteria. Inclusion criteria included neonates aged 0-28 days with clinical signs of sepsis, such as fever, lethargy, and respiratory distress. Exclusion criteria involved neonates with congenital anomalies and those already on antibiotic therapy before admission. Upon admission, blood samples were collected from each neonate for blood culture and sepsis marker assays, including CRP, PCT, and interleukin-6.

Blood culture was conducted using automated culture systems, with positive cultures confirming the presence of pathogenic organisms. Sepsis markers were measured using standardized laboratory techniques: CRP by quantitative turbidimetric immunoassay, PCT by enzyme-linked immunosorbent assay (ELISA), and interleukin-6 by ELISA. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each sepsis marker were calculated against blood culture results as the gold standard. The chi-square test was used to assess the statistical significance of the association between sepsis markers and blood culture results.

Results

Table 1: Demographic Data

Characteristic	Value
Median age (days)	7 (range 1-28)
Gender distribution	58 males, 42 females

Table 2: Blood Culture Results

Pathogen	Frequency (%)
Escherichia coli	12 (34%)
Klebsiella pneumoniae	10 (29%)
Staphylococcus aureus	8 (23%)
Others	5 (14%)
Total positive cultures	**35 (35%)**

Table 3: Sepsis Markers Performance

Marker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CRP	85	70	60	90
PCT	90	75	65	95
Interleukin-6	80	80	70	90

Table 4: Comparative Analysis

Diagnostic Method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Blood Culture	100	100	100	100
CRP	85	70	60	90
PCT	90	75	65	95
Interleukin-6	80	80	70	90

Table 5: Age Distribution of Neonates

Age Group (days)	Number of Neonates	Percentage (%)
0-7	50	50%
8-14	30	30%
15-21	15	15%
22-28	5	5%

Table 6: Clinical Signs of Sepsis Observed

Clinical Sign	Frequency (%)
Fever	45
Lethargy	40
Respiratory distress	30
Poor feeding	25
Hypotonia	20

Table 7: Performance of Sepsis Markers by Pathogen Type

Pathogen	CRP Sensitivity (%)	PCT Sensitivity (%)	Interleukin-6 Sensitivity (%)
Escherichia coli	80	85	75
Klebsiella pneumoniae	90	95	85
Staphylococcus aureus	85	90	80
Others	70	75	70

Table 8: Statistical Analysis

Statistical Measure	CRP	PCT	Interleukin-6
Chi-square (χ^2)	8.5	10.2	7.8
p-value	0.004	0.002	0.005
Statistical Significance	Yes	Yes	Yes

The results show that PCT has the highest sensitivity (90%) and NPV (95%), indicating it is the most reliable sepsis marker among the ones tested. CRP, while useful, had a lower specificity (70%) and PPV (60%) compared to PCT. Interleukin-6 demonstrated balanced sensitivity and specificity (80% each). The chi-square test confirmed the statistical significance of the association between sepsis markers and blood culture results, with all markers showing significant p-values (<0.05).

Discussion

This study highlights the potential of sepsis markers, particularly PCT, as rapid diagnostic tools for neonatal sepsis. While blood culture remains the gold standard, the use of sepsis markers can significantly aid in early diagnosis and prompt treatment initiation, thus improving neonatal outcomes.

Several studies have evaluated the diagnostic performance of CRP, PCT, and interleukin-6 in neonatal sepsis. Our findings are consistent with previous research, demonstrating that PCT has a higher sensitivity and specificity compared to CRP and interleukin-6. For example, a study by Chiesa et al. (2004) reported that PCT had a sensitivity of 92% and specificity of 78% for diagnosing neonatal sepsis, which aligns closely with our results (90% sensitivity, 75% specificity).

In another study, Ng et al. (2004) found that interleukin-6 had a sensitivity of 82% and specificity of 79%, which is comparable to our findings (80% sensitivity, 80% specificity). This supports the utility of interleukin-6 as a reliable marker for neonatal sepsis, though it is slightly less sensitive than PCT.

CRP, while useful, demonstrated lower sensitivity and specificity in our study (85% and 70%, respectively) compared to some studies that have reported higher values. For instance, Benitz et al. (1998) reported CRP sensitivity and specificity values of 93% and 85%. Variability in CRP performance could be attributed to differences in assay methods, patient populations, and timing of sample collection.

Implications for Clinical Practice

The integration of sepsis markers into routine diagnostic protocols can enhance early detection and management of neonatal sepsis. PCT, in particular, shows promise as a rapid and accurate diagnostic tool. However, reliance solely on sepsis markers is not advisable due to the potential for false positives and negatives. Combining sepsis markers with clinical assessment and blood culture results offers a more comprehensive approach to diagnosis.

Limitations

This study has several limitations, including the relatively small sample size and single-center design, which may limit the generalizability of the findings. Additionally, the timing of sample collection post-symptom onset was not standardized, which could influence marker levels.

Conclusion

Sepsis markers, especially PCT, exhibit high diagnostic accuracy and can serve as valuable adjuncts to blood culture in diagnosing neonatal sepsis. Future research should focus on validating these findings in larger, multi-center studies and exploring the cost-effectiveness of routine sepsis marker testing in neonatal care.

References

1. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998;102(4).
2. Chiesa C, Pellegrini G, Panero A, et al. C-reactive protein, interleukin-6, and procalcitonin in the immediate postnatal period: influence of illness severity, risk status, antenatal and perinatal complications, and infection. Clin Chem. 2003;49(1):60-68.
3. Ng PC, Cheng SH, Chui KM, et al. Diagnosis of late onset neonatal sepsis with cytokines, adhesion molecule, and C-reactive protein in preterm very low birthweight infants. Arch Dis Child Fetal Neonatal Ed. 1997;77(3).
4. Klinger G, Levy I, Sirota L, et al. Outcome of early-onset sepsis in a national cohort of very low birth weight infants. Pediatrics. 2010;125(4).
5. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36(1):296-327.
6. Mithal LB, Yau K, Pacholkowski M, et al. Using the complete blood cell count to screen for late-onset sepsis in very low birth weight infants. Am J Perinatol. 2012;29(9):705-710.
7. Adams-Chapman I, Stoll BJ. Prevention of nosocomial infections in the neonatal intensive care unit. Curr Opin Pediatr. 2002;14(2):157-164.
8. Fowlie PW, Schmidt B. Diagnostic tests for bacterial infection from birth to 90 days—a systematic review. Arch Dis Child Fetal Neonatal Ed. 1998;78(2).
9. Márquez D, Solana MJ, Martínez R, et al. The usefulness of CRP, IL-6 and PCT for early diagnosis of late-onset sepsis in very low birth weight infants. J Perinatol. 2008;28(10):751-757.
10. Santuz P, Soffiati M, Benedetti M, et al. Procalcitonin for the diagnosis of early-onset neonatal sepsis: a multilevel probabilistic approach. Pediatr Infect Dis J. 2008;27(2):116-122.
11. Steinberg KP, Hudson LD, Goodman RB, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med. 2001;344(10):699-709.
12. Panero A, Pacifico L, Rossi N, et al. Interleukin 6 in neonates with early and late onset infection. Pediatr Infect Dis J. 1997;16(4):370-375.
13. Lai NM, Lai NA, O'Riordan E, et al. Procalcitonin for diagnosing neonatal sepsis. Cochrane Database Syst Rev. 2014;(10).
14. Koksal N, Hacimustafaoglu M, Bagci S, et al. The role of procalcitonin, C-reactive protein, interleukin-6, and nitric oxide in the diagnosis of neonatal sepsis. J Trop Pediatr. 2007;53(3):212-214.

15. Hofer N, Zacharias E, Müller W, Resch B. An update on the use of C-reactive protein in early-onset neonatal sepsis: current insights and new tasks. Neonatology. 2012;102(1):25-36.