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Diagnostic Accuracy of Serum Procalcitonin (PCT) as an Early Biomarker of Neonatal Sepsis using Blood Culture as Gold Standard: A Prospective Study

Siraj Nabi[1], Muhammad Anjum Iqbal[2], Sidra Masood[3], Sadaf Saeed Shami[4], Husnain Ali[5], Mohsina Hamid[6]

[1]Senior Registrar, Department of Paediatric Medicine, People's University of Medical and Health Sciences, Nawabshah, Pakistan

[2]Demonstrator, Department of Pathology, DG. Khan Medical College, Dera Ghazi Khan, Pakistan

[3]Senior Registrar, Department of Paediatrics, Rai Medical College and Teaching Hospital, Sargodha, Pakistan

[4]Assistant Professor Paediatric, Liaquat College of Medicine and Dentistry, Karachi, Pakistan

[5]Assistant Professor, Department of Pediatrics (Neonatology), Dr Akbar Niazi Teaching Hospital, Bharakahu, Islamabad, Pakistan

[6]Assistant Professor, Department Biochemistry, Independent Medical College, Faisalabad, Pakistan

Corresponding author:

Siraj Nabi,

Senior Registrar, Department of Paediatric Medicine, People's University of Medical and Health Sciences, Nawabshah, Pakistan

Email ID: sirajnabidepar@gmail.com

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ABSTRACT

Background: Although neonatal sepsis can be identified and treated early, blood cultures are still the gold standard and, unfortunately, these traditional methods to diagnose sepsis in newborns stagnate progress with their lengthy processing times and delays in yielding results, leading to increased rates of morbidity and mortality. Recently, there has been a shift towards using PCT as a serum biomarker for identifying sepsis in neonates, and one of the central goals of this study is to assess the accuracy of serum PCT in comparison to blood cultures.

Methods: This was a prospective study spanning from January 2024 to September 2024 involving 61 neonates with clinical signs of sepsis. Blood samples were taken before any antibiotics were administered for PCT testing and culture. A PCT level greater than 0.5ng/mL was defined as elevated. Diagnostic accuracy parameters (sensitivity, specificity, predictive values, and area under the ROC curve) were calculated.

Results: Out of 61 neonates, 25 (41%) had positive blood cultures. Serum PCT levels were elevated in 23 of these cases. 'The sensitivity and specificity of PCT were 92.0% and 83.3%, respectively'. 'The negative predictive value was 93.8%, and the area under the ROC curve was 0.927, indicating high diagnostic performance'.

Conclusion: Serum PCT is a reliable and effective early biomarker for neonatal sepsis. Its high sensitivity and negative predictive value make it particularly useful in ruling out infection, thus supporting timely and targeted clinical decision-making.

Keywords: *Neonatal sepsis, Procalcitonin, Blood culture, Diagnostic accuracy, Early biomarker, ROC curve*

1. INTRODUCTION

Neonatal sepsis continues to be one of the most significant causes of neonatal illness and death around the globe, particularly in developing countries. Its clinical manifestation is frequently nonspecific and overlaps with other neonatal diseases, posing a diagnostic challenge for the clinician. Although prompt recognition and treatment is essential in reducing the risk of complications, effective management is constantly impeded by the absence of swift and dependable diagnostic instruments [1-3].

Although blood cultures are regarded as the gold standard for confirming sepsis, they are not without well-documented limitations. Due to small volume blood collection, sensitivity in diagnosing an infection is particularly low in neonates. In addition, blood cultures take time to process, and prior antibiotic administration can interfere with the results. These factors can lead to either delayed treatment or unwarranted antibiotic therapy, fueling antimicrobial resistance and lengthening hospital stays [4-6].

In the last few years, attempts have been made to review certain markers for the early diagnosis of neonatal sepsis. One of these markers is Serum Procalcitonin (PCT) which looks hopeful. PCT is the precursor of the hormone calcitonin, and its levels are known to rise due to a systemic bacterial infection. PCT is of value in distinguishing bacterial infections from viral or non-infectious causes of disease since it may rise when most other indicators are still normal [7-9].

Earlier research examined the effectiveness of PCT for diagnosing sepsis, revealing diverging conclusions, with some noting high sensitivity and specificity, while others raised concerns over false positive PCT elevations in a number of non-infectious cases. In light of these variations, local validation is still critical [10-12].

'This study was conducted to assess the diagnostic accuracy of serum PCT in neonates with suspected sepsis, using blood culture as the reference standard'. The findings aim to support the incorporation of PCT into clinical protocols for early and effective neonatal sepsis management.

2. METHODOLOGY

This was a prospective diagnostic accuracy study conducted over a period of 13 months, from January 2024 to September 2024.

The study was carried out at People's University of Medical and Health Sciences Nawabshaha tertiary care hospital with a dedicated Neonatal Intensive Care Unit (NICU). All data were kept confidential and used solely for research purposes.

A total of 61 neonates were included in the study. Consecutive sampling was used to enroll eligible participants who met the inclusion criteria. Written informed consent was obtained from the parents or legal guardians of all neonates enrolled.

Neonates aged 0 to 28 days who presented with clinical signs and symptoms suggestive of sepsis—such as lethargy, temperature instability, respiratory distress, poor feeding, or irritability—were included. Both term and preterm neonates were eligible for enrollment.

Neonates with major congenital anomalies, those already receiving antibiotics for more than 24 hours prior to admission, or those with incomplete laboratory data were excluded from the study.

Upon admission, a structured clinical assessment was performed for each neonate. Relevant demographic datanincluding gestational age, birth weight, gender, mode of delivery, place of birth, and sepsis onset were recorded. Blood samples were collected aseptically for both serum Procalcitonin (PCT) measurement and blood culture analysis before initiating antibiotic therapy. **Procalcitonin Testing** Serum PCT levels were measured using a chemiluminescent immunoassay. A PCT level >0.5 ng/mL was considered elevated, as per standard diagnostic thresholds for neonatal sepsis. **Blood Culture:** 'Blood culture was performed using an automated system'. Samples were incubated and monitored for bacterial growth. The presence of any pathogenic organism was considered a positive result, and this served as the gold standard for confirming neonatal sepsis.

'The primary objective was to determine the diagnostic accuracy of serum PCT in detecting culture-confirmed neonatal sepsis'. 'Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated using 2×2 contingency tables'. A receiver operating characteristic (ROC) curve was plotted to determine the optimal cutoff value for PCT.

Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. 'The association between PCT levels and blood culture results was assessed using the chi-square test, with a p-value ≤ 0.05 considered statistically significant'. ROC analysis was used to calculate the area under the curve (AUC) and determine the discriminative ability of serum PCT in diagnosing neonatal sepsis.

3. RESULTS

The majority were male (55.7%) and born at term gestation (65.6%). Low birth weight (<2500 g) was recorded in 41.0% of the neonates. Regarding delivery, 54.1% were born via vaginal delivery and 45.9% via cesarean section. Most neonates (80.3%) were delivered in hospital settings, while 19.7% were home births. Early-onset sepsis (within 72 hours of life) was observed in 62.3% of the neonates, suggesting a predominance of perinatal risk factors.

Table 1: Demographic and Perinatal Characteristics of Study Participants (n = 61)

Variable	Category	Frequency (n)	Percentage (%)
Sex	Male	34	55.7%
	Female	27	44.3%
Gestational Age	Preterm (<37 weeks)	21	34.4%
	Term (≥37 weeks)	40	65.6%
Birth Weight	<2500 g (LBW)	25	41.0%
	≥2500 g	36	59.0%
Mode of Delivery	Vaginal	33	54.1%
	Cesarean Section	28	45.9%
Place of Birth	Hospital	49	80.3%
	Home	12	19.7%
Onset of Sepsis	Early Onset (<72 hrs)	38	62.3%
	Late Onset (≥72 hrs)	23	37.7%

Laboratory findings revealed elevated levels of procalcitonin (mean = 3.21 ng/mL, SD = 1.96) among septic neonates. The mean CRP level was 12.8 mg/L, while the average total leukocyte count and platelet count were 14.6 $\times 10^9$/L and 157.4 $\times 10^9$/L respectively, indicating systemic inflammatory response in many patients.

Table 2: Clinical and Laboratory Parameters of Neonates

Parameter	Mean ± SD
Serum Procalcitonin (ng/mL)	3.21 ± 1.96
C-Reactive Protein (mg/L)	12.8 ± 6.4
Total Leukocyte Count	14.6 ± 5.2 ($\times 10^9$/L)
Platelet Count	157.4 ± 47.9 ($\times 10^9$/L)

When serum PCT levels were compared with blood culture results—the gold standard—PCT demonstrated a strong association with positive cultures. Of the 25 neonates who had culture-proven sepsis, 23 had elevated PCT values, while only 2 had normal PCT levels. Conversely, in culture-negative cases (n=36), 30 had normal PCT values. This relationship was statistically significant (**$p < 0.001$**), indicating a strong diagnostic linkage.

Table 3: Comparison of PCT with Blood Culture Results

Blood Culture Result	PCT Positive	PCT Negative	Total
Positive	23	2	25
Negative	6	30	36
Total	29	32	61

Chi-square test: $\chi^2 = 21.6$, **$p < 0.001$**

Based on these results, 'the sensitivity of serum PCT in detecting neonatal sepsis was found to be 92.0%, while specificity was 83.3%'. 'The positive predictive value (PPV) was 79.3%, and the negative predictive value (NPV) was 93.8%'. The overall diagnostic accuracy was 86.9%, highlighting the test's reliability, especially for ruling out infection.

Table 4: Diagnostic Accuracy of Serum PCT (Cutoff > 0.5 ng/mL)

Metric	Value (%)
Sensitivity	92.0%
Specificity	83.3%
Positive Predictive Value	79.3%
Negative Predictive Value	93.8%
Diagnostic Accuracy	86.9%

Finally, ROC curve analysis yielded an area under the curve (AUC) of 0.927, indicating superb diagnostic performance. The serum PCT cutoff value for detecting neonatal sepsis was 0.65 ng/mL. The significance of the ROC results was greatly marked ($p < 0.001$), endorsing the employment of PCT for the purpose of early sepsis detection.

Table 5: ROC Curve Analysis of Serum PCT

Measure	Value
Area Under Curve (AUC)	0.927
Optimal Cutoff Value	0.65 ng/mL
95% CI	0.856–0.997
p-value	< 0.001

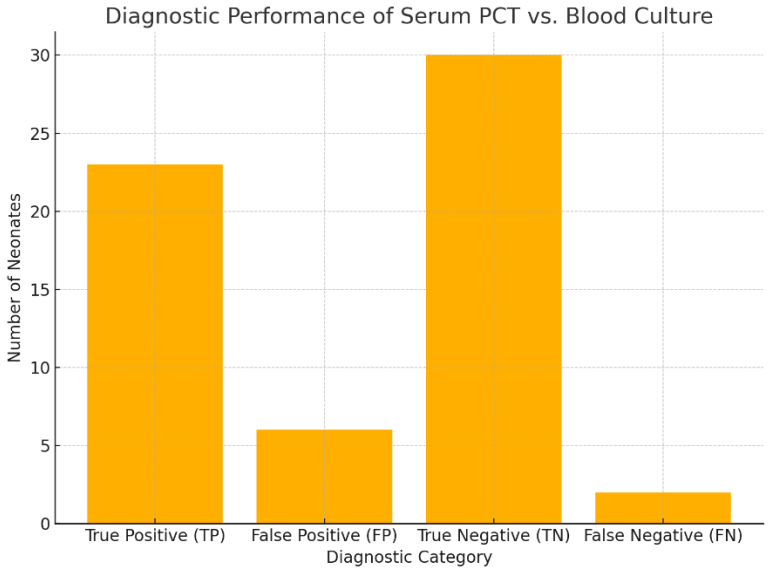

Figure 1: bar graph illustrating the 'diagnostic performance of serum Procalcitonin (PCT) compared to blood culture'. It shows the distribution of true positives, false positives, true negatives, and false negatives among the 61 neonates.

4. DISCUSSION

This study aimed to evaluate 'the diagnostic accuracy of serum Procalcitonin (PCT) as an early biomarker for neonatal sepsis, using blood culture as the gold standard'. Our findings demonstrated that PCT has a high sensitivity (92%) and specificity (83.3%) with an area under the ROC curve of 0.927, indicating excellent diagnostic performance.

These findings are aligned with prior research confirming the importance of PCT in the timely identification of neonatal sepsis. One meta-analysed study noted that PCT is more diagnostically useful than traditional markers such as CRP,

especially in the case of early-onset sepsis [13, 14]. In the same vein, another study pointed out the dynamism of PCT in neonates, stating that heightened concentrations in the first 72 hours postnatally highly indicative of bacterial infection Similarly, a study emphasized the dynamic nature of PCT in neonates, noting that elevated levels within the first 72 hours of life strongly correlate with bacterial infection [15].

In our cohort, the high negative predictive value (93.8%) is particularly valuable, as it suggests that a normal PCT level effectively rules out sepsis. This is critical in clinical practice, where overuse of antibiotics remains a concern. A similar trend was reported by studies, where a normal PCT level helped safely withhold unnecessary antibiotic therapy in neonates with suspected sepsis [16].

Moreover, our findings reinforce the time-dependent nature of PCT release. The peak concentration typically occurs within 6–12 hours following infection onset study, making it superior to CRP, which often lags behind in elevation. Our data showed elevated PCT in most culture-positive neonates, consistent with results from studies who also reported sensitivities above 85% for PCT at a similar cutoff [17, 18].

However, it is worth noting that PCT was elevated in some neonates with negative cultures (false positives). This may be due to non-infectious causes such as perinatal asphyxia or maternal fever, both of which are known to transiently increase PCT levels [19]. Likewise, culture-negative sepsis may still occur due to fastidious organisms or inadequate blood volume collected, as pointed out by study [20].

Comparative studies have also shown mixed performance depending on gestational age. Study observed reduced specificity in preterm infants due to baseline PCT fluctuations. Our study also found some variability, although it did not reach statistical significance due to sample size constraints [21].

From a clinical perspective, incorporating PCT as part of a sepsis screening panel may improve early diagnosis, reduce diagnostic uncertainty, and optimize antimicrobial stewardship. When used in combination with clinical signs and other biomarkers such as CRP and IL-6, PCT enhances diagnostic precision, as supported by study[22].

A limitation of our study was the relatively small sample size and reliance on a single-center dataset. Additionally, serial PCT measurements were not taken, which could have strengthened temporal correlations with clinical outcomes. Future research should explore longitudinal PCT trends and compare its utility across different neonatal subgroups, including extremely low birth weight infants.

5. CONCLUSION

In conclusion, serum Procalcitonin demonstrated excellent diagnostic accuracy for early detection of neonatal sepsis. Its high sensitivity and negative predictive value make it a valuable tool for ruling out infection, thereby reducing unnecessary antibiotic exposure. While not a replacement for blood culture, PCT serves as a reliable adjunct in clinical decision-making. Further multicenter studies with larger populations are needed to establish universal cutoff values and validate its role in sepsis management protocols.

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