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ORIGINAL RESEARCH

Role of Presepsin for the Early Identification of Neonatal Sepsis

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ABSTRACT

Introduction: Sepsis is a prevalent illness that requires quick diagnosis and treatment due to its high death and morbidity rates. Soluble CD14 subtype (sCD14-ST), Presepsin appears to be an accurate biomarker in diagnosing neonatal sepsis patients. **Material and Methods**: One aerobic BacT/ALERT bottle was inoculated with collected blood samples, and the bottle was then incubated at 35°C for five days, or until microbial growth was observed. The semi-quantitative latex agglutination test revealed the presence of CRP. For measuring procalcitonin, the PCT sandwich ELISA assay was utilised. A human ELISA kit was used to measure the amount of presepsin. **Results**: Out of the 356 newborns admitted, 102 neonates in total were included in our study.There were 34 female infants and 68 male neonates. 45 newborns were full term, whilst 57 were preterm. With 16.12% of cases each, *Staphylococcus aureus* and *Escherichia coli* were the most prevalent.The symptoms that patients reported, fever accounting for 50% of cases and being the most common symptom. Presepsin was 1682±765.3 pg/ml, procalcitonin was 10.98±4.67 ng/ml, and C-reactive protein (CRP) was 21.58±15.60 mg/ml. Neonates had considerably greater presepsin levels, ranging from 85% to 96%. **Conclusion**: Presepsin may prove helpful in the future for identifying neonatal sepsis when combined with other test indicators.

Keywords: Early onset sepsis (EOS), Neonatal sepsis (NS), Prespsin (P-SEP), Procalcitonin (PCT), C-Reactive protein (CRP)

INTRODUCTION

A condition known as sepsis occurs when the immune system overreacts to an infection, causing the peripheral circulation to fill with inflammatory mediators and resulting in widespread inflammation. Multiple organ dysfunctions (MODS) brought on by severe sepsis and septic shock may be avoided by early identification and prompt treatment of the aforementioned pathologic processes. In critically ill patients, sepsis is the primary cause of death and affects 1-2 percent of hospital admissions.[1,2]One of the most frequent causes of newborn morbidity and mortality is neonatal sepsis (NS). Early diagnosis and treatment of systemic bacterial infection is essential in neonates because delaying the treatment of major bacterial infections can have unintended consequences.[3]Because critically illnewborns can have systemic inflammatory response syndrome without infection, the diagnosis of non-susceptible syndrome (NS) is highly challenging and may be deceptive due to the non-specific clinical symptoms.[4]Neonatal sepsis is diagnosed by the complete blood count with differential (CBC); however, a single time-point sampling has a low predictive value. Due to the delayed hepatic synthesis of C-reactive protein (CRP) and the existence of additional infection-independent inductive factors, CRP has limited diagnostic use in the early stages of

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sepsis.[5]One of the most commonly used indicators of sepsis, procalcitonin (PCT), is less useful in newborns due to its reliance on gestational and postnatal age since levels of PCT can remain physiologically elevated for up to 48 hours following birth.[6,7] The soluble N terminal fragment of CD14, known as presepsin (P-SEP), is a new and promising biomarker that has a better predictive potential than PCT in the early stages of sepsis. It is naturally expressed on the surface of macrophages and monocytes and is excreted into the bloodstream in response to exogenous antigens originating from bacteria, like bacterial lipopolysaccharide. After induction, the blood concentration of P-SEP begins to rise two hours later, peaks at three hours, and continues to rise for up to five hours.[8] A more recent generation of inflammatory markers called presepsin has been identified, and it has superior sensitivity and specificity than other markers.[9]Presepsin's biological characteristics are quite distinctive because it doesn't increase in any inflammatory condition; rather, it does so solely upon bacterial phagocytosis. Both Gram-positive and Gram-negative bacteria can bind to complexes of bacterial lipopolysaccharides (LPS) through CD14. Soluble CD14 (sCD14) is released from the cell membrane and enters the blood. There, it is further broken down by proteases like cathepsins or sCD14 subtype (sCD14-ST) or presepsin during phagocytosis. With a peak around three hours after the infection started, presepsin levels were risen substantially earlier than procalcitonin (PCT) and even earlier than IL-6.[10] A growing body of research is demonstrating that presepsin (P-SEP) can be an effective marker for adult sepsis diagnosis also.[11,12]Additionally, recent research has shown that P-SEP is a valid biomarker for the identification of late-onset newborn sepsis and that it can be used to track how well septic children are responding to treatment.[12,13] So, the aim of this study was to evaluate the role of presepsin in EOS(Early onset Sepsis) and to compare it with other inflammatory markers that are currently used routinely.

MATERIAL AND METHODS

This study was carried out atAutonomous State Medical College, Lalitpur (Uttar Pradesh) for the duration of 6 months. Before starting antibiotic therapy for infants suspected of having sepsis, peripheral blood culture samples (in a paediatric bottle) were taken from every patient as part of their normal evaluation in the paediatric and nursery departments. One aerobic BacT/ALERT bottle was inoculated with collected blood samples, and it was then incubated in the BacT/ALERTdevice at 35°C for five days, or until microbial growth was noticed.The BACTEC blood culture system's positive bottles were taken out, the Gram's stain was performed, and the cells were then subcultured on nutrient agar, MacConkey, blood, and chocolate agar medium before being incubated at 35°C. By using Gram's staining, colony features, and biochemical characteristics, the isolates were identified. The entireties of the bacteria were identified using conventional biochemical and bacteriological techniques.

The semi-quantitative latex agglutination test was used to detect CRP; the CRP kits' cutoff value was 9 mg/ml, and the test's measurement range was 0.10 to 20.0 mg/l. For measuring procalcitonin, the PCT sandwich ELISA assay kit (Thermo Fisher, Scientific) was utilized. At 450 nm, absorbance was measured. The threshold value for the analysis was 5.6 ng/ml using a human ELISA kit, the level of presepsin (sCD14 ST) was determined. Sandwich enzyme-linked immune-sorbent assay technology (Human Presepsin ELISA kit from Nordic Biosite) served as the foundation for this kit. The threshold value for O.D. absorbance at 450 nm was 500 pg/mL.Version 22 of SPSS software was used to enter the data.

RESULTS

Of the 356 newborns admitted, 102 were included in our study.There were 34 female infants and 68 male neonates. 45 newborns were full term, whilst 57 were preterm. For newborns, the gestational mean age was 32±5 weeks. The average birth weight was 1980±150.5 g.

Table 1: Frequency of Causative Organisms of Neonatal Sepsis

Microorganism	Number	Percentage
E. coli	15	16.12
S. aureus	15	16.12
Klebsiella pneumonia	14	15.05
CONS	12	12.90
Pseudomonas aeruginosa	10	10.75
Acinetobacterbaumannii	09	9.67
Candida albicans	08	8.60
MRSA	06	6.45
Enterococcus	04	4.30
Total	93	100%

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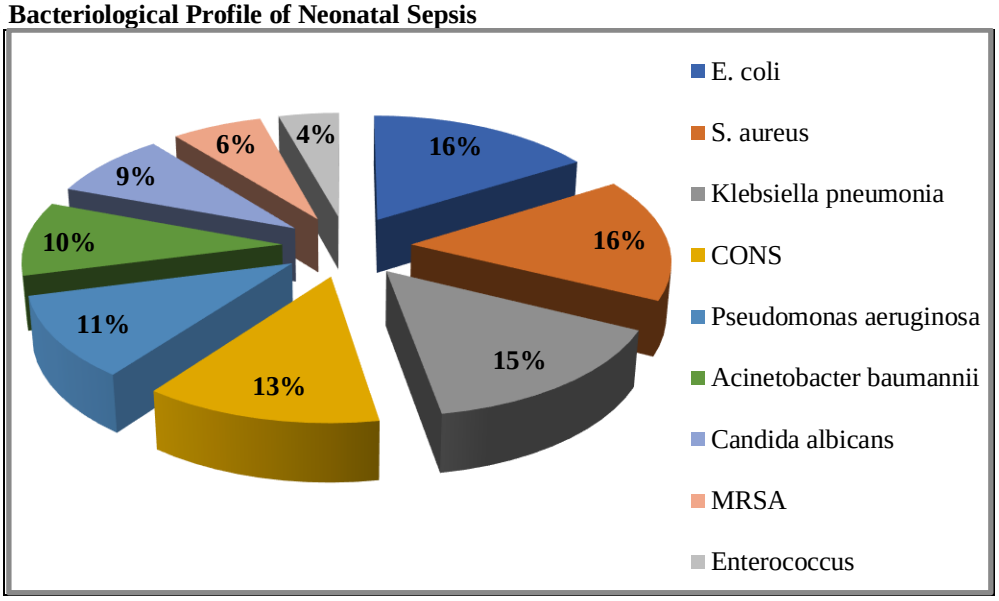
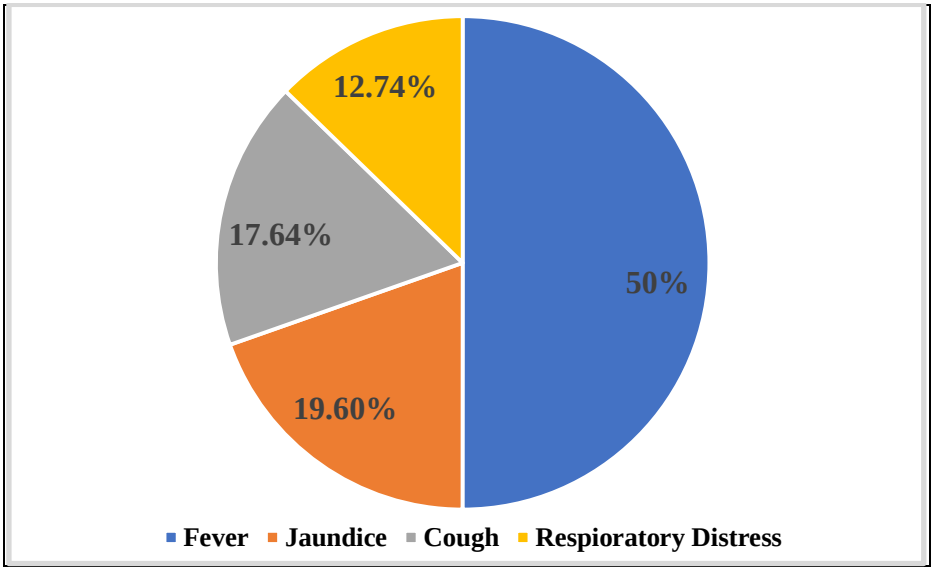
Graph 1: Bacteriological Profile of Neonatal Sepsis



With 16.12% of cases each, *Staphylococcus aureus* and *Escherichia coli* were the most prevalent. Fifteen percent of the cases had *Klebsiellapneumoniae*, and thirteenpercent had Coagulase-Negative Staphylococci (CONS). *Acinetobacterbaumannii* and *Pseudomonas aeruginosa* accounted for 9.67% and 10.75% of the total, respectively. 8.60% of cases had *Candida albicans*, while 6.45% had Methicillin-resistant Staphylococcus aureus (MRSA). At 4.30%, *Enterococcusspecies* had the lowest prevalence.

Graph 2: Clinical manifestation of newborns



The most prevalent symptom among patients, accounting for 50% of cases (51 patients), was fever. Of the cases, 19 out of 20 patients had jaundice, and 18 out of the cases had a cough. The least frequent symptom, occurring in 12.74% of cases (13 patients), was respiratory distress.

Table 2: Comparison among serum levels of CRP, Procalcitonin & Presepsin

Sepsis Biomarker	Mean±SD	*P* value
CRP (mg/ml)	21.58±15.60	<0.0001
Procalcitonin (ng/ml)	10.98±4.67	<0.001
Presepsin (pg/ml)	1682±765.3	<0.001

Presepsin was 1682±765.3 pg/ml, procalcitonin was 10.98±4.67 ng/ml, and C-reactive protein (CRP) was 21.58±15.60 mg/ml. Procalcitonin and presepsin both had P values of less than 0.001, while CRP had a P value

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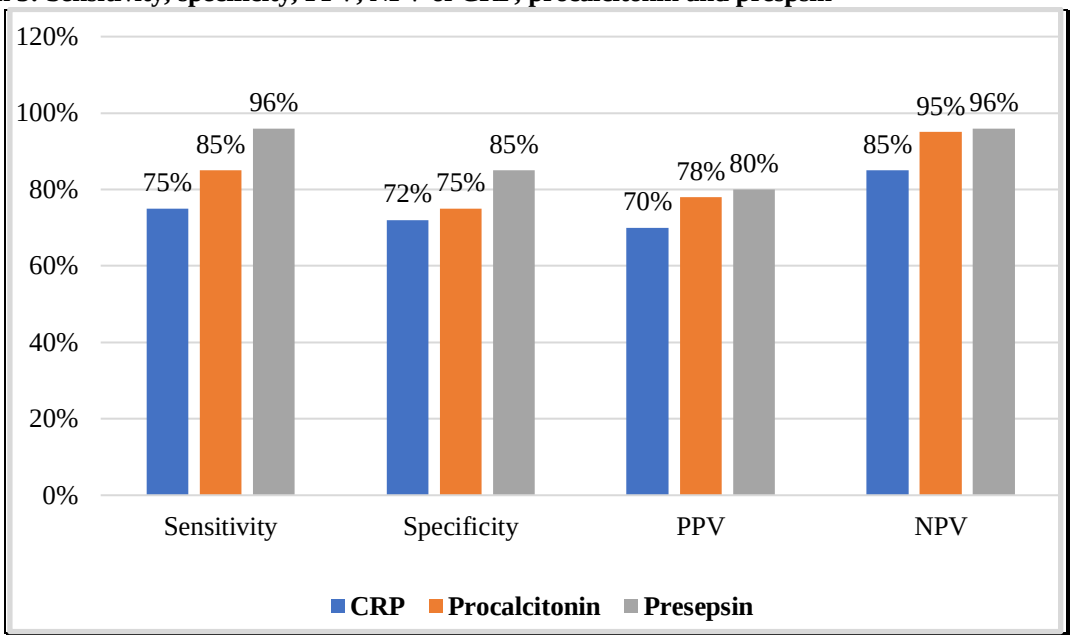
of less than 0.0001, demonstrating substantial statistical significance in the differences observed. All of the P values for these assays were highly significant.

Graph 3: Sensitivity, specificity, PPV, NPV of CRP, procalcitonin and prespsin



Procalcitonin, presepsin, and CRP were assessed for their diagnostic performance based on their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The results for CRP showed a 75% sensitivity, 72% specificity, 70% PPV, and 85% NPV. Procalcitonin demonstrated enhanced NPV of 95% and PPV of 78%, along with better sensitivity and specificity of 85% and 75%, respectively. Presepsinshowed the best diagnosis accuracy, with a 96% sensitivity, 85% specificity, 80% positive predictive value, and 96% negative predictive value.

DISCUSSION

One of the most frequent causes of mortality in the paediatric population, particularly in newborns, is sepsis. Timely diagnosis is crucial because it lowers mortality and morbidity when therapy is started early. However, the current consensus on paediatric sepsis definitions (sepsis-3)[14,15]is not suited for preterm newborns and has poor accuracy in term neonates. This is mostly due to the fact that neonatal literature rarely takes into account organ dysfunction, the crucial diagnostic criterion, and it is yet unknown how to screen neonates for organ failure in the most precise way.[16]The detection of a pathogenic organism from an otherwise sterile source (blood or cerebrospinal fluid) is the gold standard approach for confirming sepsis in neonates with risk factors, clinical suspicion, and abnormal test results.[17] However, because of the unique characteristics of the neonatal population, blood cultures are not sensitive enough.[18]Fever is the most prevalent in the current study, accounting for 50% of cases. In study Enas Sh. Khater[19]observed that 36 babies (40%) with neonatal sepsis showed signs of respiratory distress; 10 babies (11.1%) had jaundice; 8 babies (8.88%) had coughed; 28 babies (31.1%) had fever; and 8 babies (8.88%) had other symptoms. In a study by Al-Shamahy H. et al.[20](Yemen), the most common clinical picture was difficulty breathing (42.2%).With 16.12% of cases each, *Staphylococcus aureus* and *Escherichia coli* were the most prevalent.The bulk of the pathogenic organisms of newborn sepsis have been shown to be gram-negative bacteria in other studies from underdeveloped countries.[21-24] The microbiological aetiologies reported in other investigations similarly indicated that CONS is the primary causative pathogen.[25-26]One of the most widely researched, widely accessible, and widely used laboratory assays for the diagnosis of newborn sepsis is CRP.[27] The first noticeable changes in CRP occur 10–12 hours following infection start. Its sensitivity is increased by repeatedly measuring CRP 24–48 hours following the beginning of symptoms. In this study, CRP's specificity and positive predictive value fall between 70% and 80%. As a result, CRP may be regarded as a "specific" but "late" indicator of newborn infection. After exposure to bacterial endotoxin, serum concentrations of PCT start to rise four hours later, peak six to eight hours later, and stay elevated for at least twenty-four hours.[28-30] Procalcitonin demonstrated increased sensitivity and specificity at 85% and 75%, respectively, with a PPV of 78% and an NPV of 95%. In contrast, the PCT reaction is faster and has higher sensitivity and specificity. However, PCT has its own drawbacks because it may rise in healthy neonates. We discovered that neonates had much greater presepsin levels, ranging from 85% to 96%.

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CONCLUSION

Neonatal sepsis is a horriblesituation with a great effect in terms of morbidity and mortality. Obtaining a biological marker with maximum sensitivity and maximum negative predictive value would help to prevent the serious consequences of sepsis in many newborns. Although CRP and PCT are themost widely used biomarkers of neonatal sepsis, their accuracy is still controversial. Based on current study results, most factors affecting CRP and PCT levels seem not to affect presepsin levels. P-SEP has shown good accuracy in diagnosing neonatal EOS .When P-SEP was used in combination with CRP, the best negative predictive power was achieved. Consequently, presepsin can be utilized as a trustworthy biomarker for timely diagnosis of neonatal sepsis and also is a promising marker for recognition of improvement.

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