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Diagnostic Accuracy of C Reactive Protein (CRP) and White Blood Cell (WBC) Count in Diagnosing Cases with Clinical Suspicion of Neonatal Sepsis

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Abstract

Background: *Neonatal fatalities account for around 40% of all mortality among children under the age of five. In developing nations, 50 percent of all newborn deaths occur within the first 24 hours of life, and 75 percent occur within the first week of life*

Objective: *To determine the accuracy of C-reactive proteins (CRPs) and white blood count (WBC) in predicting sepsis in suspected neonates.*

Methods: *This validation study included 150 neonates who were admitted with suspicion of sepsis (on clinical examination as per WHO guidelines) in the NICU of Bolan Medical Complex Hospital Quetta from Nov-2021 to Feb-2022. Neonates with CRP >6 mg/dL were labelled as having sepsis. CRP measurements were obtained at 3 consecutive days and patients having any abnormal CRP levels were labelled as having sepsis. Patients with WBC levels ≥13 × 10^9/L were labelled as having sepsis. WBC measurement was performed only on first admission day.*

Results: *CRP levels were 64.2% sensitive, 74.2% specific, with PPV of 57.6% and NPV 79.1%. While WBC levels were 58.5% sensitive, 69.1% specific, with 50.8% PPV and 75.3% NPV. After combining CRP with WBC, the sensitivity increased to 86.8% and specificity 89.7%, with PPV of 82.1% and NPV 92.6%.*

Conclusion: *In the diagnosis of newborn sepsis, serial CRP qualitative assays paired with elevated WBC have a high sensitivity.*

Keywords: neonatal sepsis, C-reactive proteins, While blood cell count.

INTRODUCTION:

Neonatal fatalities account for around 40% of all mortality among children under the age of five. In developing nations, 50 percent of all newborn deaths occur within the first 24 hours of life, and 75 percent occur within the first week of life.[1] Among the most common serious bacterial infections that occur in newborn babies is neonatal sepsis, which has a very high fatality rate.[2, 3] It has been reported that neonatal sepsis is responsible for more than 520,000 infant fatalities per year. Because the early

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indications of neonatal sepsis are neither specific nor sensitive, so it often diagnosed after severity reaches.[4]

It is one of the most difficult difficulties that doctors face today to recognize sepsis in the neonate in its early stages.[5] The delayed identification and incorrect management of newborn sepsis have been linked to an increased risk of systemic complications, which are associated with a high fatality rate. The blood culture is the gold standard test for the diagnosis of newborn sepsis. However, the time-consuming nature of the procedure and the possibility of receiving false negative results limit its application.[6]Moreover, The full results of blood culture are not accessible for more than 3 days, and the method is not available in many settings in developing nations.[7] This has resulted in the diagnosis of neonatal sepsis being made solely on the basis of clinical assessment, and the management of the condition being based on empirical treatment protocols [4, 5]. This has resulted in unnecessary hospitalizations, increased irrational antibiotic use, and additional financial burden on the family.[8]

A number of potential biochemical indicators, including CRP, PCT, and TNF-, have been postulated as prospective markers for the identification of newborn infection.[9] However, the use of these biochemical markers is still in its initial trials. In many impoverished nations, the CRP assay can be used as a fast test to support the usage and duration of antibiotics treatment. In the first six hours following the commencement of the infectious process, the liver produces C-reactive protein, an acute-phase reactant protein. For each type of septicemia, CRP's ability to accurately diagnose it is affected by the cause and location.[10]When it comes to the work-up of sepsis, one of the most routinely conducted diagnostic procedures is the white blood cell count (WBC), and several components of the leukocyte count have been explored for their predictive value in determining the presence of the sepsis.[11]

In this study we determined the diagnostic accuracy of CRP and WBC count in determining neonatal sepsis.

METHODS:

This validation study included 150 neonates who were admitted with suspicion of sepsis (on clinical examination as per WHO guidelines) in the NICU of Bolan Medical Complex Hospital Quetta from Nov-2021 to Feb-2022.Neonates with history of antibiotics administration within 72 hours at the time of inclusion, and those with weight <1.5 Kg were excluded.

After inclusion, venous blood samples of all neonates were sent to the hematology laboratory for determination of CRP and WBC count. Neonates with CRP >6 mg/dL were labelled as having sepsis. CRP measurements were obtained at 3 consecutive days and patients having any abnormal CRP levels were labelled as having sepsis.Patients with WBC levels $\geq 13 \times 10^9$/L were labelled as having sepsis. WBC measurement was performed only on first admission day.

Final diagnosis of sepsis was made using blood cultures reports. Bacterial cultures were done using OxoidLtd's Brain Heart Infusion broth (BHI) in a 1:10 ratio of blood to BHI. Day 1, 3, and 7 were used for subsequent sub-cultures on 5% sheep blood agar, chocolate agar, and MacConkey agar. (Oxoid, UK). Conventional physiological and biochemical approaches were used to identify bacteria.[12] Whenever Coagulase negative staphylococcus (CNS) was found in the blood, a second blood culture was requested. A blood culture result was deemed positive if there was the re-isolation of the CNS.

STATA version 11 was used to evaluate the data. We used 2-by-2 contingency tables to estimate the CRP's sensitivity and specificity in the diagnosis of newborn septicemia.

RESULTS:

Out of 150 neonates with suspected sepsis, 78 (52.0%) were females. 97 (64.6%) presented after 72 hours of birth. There were 125 (83.3%) normal weight neonates. Out of 150, 118 (78.7%) were born full term (Table 1).

Diagnostic accuracy values of CRP and WBC levels are given in Table 2. CRP levels were 64.2% sensitive, 74.2% specific, with PPV of 57.6% and NPV 79.1%. While WBC levels were 58.5% sensitive, 69.1% specific, with 50.8% PPV and 75.3% NPV. After combining CRP with WBC, the sensitivity increased to 86.8% and specificity 89.7%, with PPV of 82.1% and NPV 92.6% (Table 2).

Table 1. Data of baseline Characteristics.

Neonate Characteristic	Value
Gender	
Male	78 (52.0%)
Female	72 (48.0%)
Age	
>72 hours	97 (64.6%)
≤72 hours	53 (35.3%)
Birth Weight	
Low Birth Weight	25 (16.6%)
Normal Weight	125 (83.3%)
Gestational Age at Birth	
Full Term	118 (78.7%)
Preterm	32 (21.3%)

Table 2. Diagnostic Accuracy of Serum CRP and WBC Count in Predicting Sepsis.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CRP	64.2%	74.2%	57.6%	79.1%
WBC	58.5%	69.1%	50.8%	75.3%
CRP+WBC	86.8%	89.7%	82.1%	92.6%

DISCUSSION:

Because of the ambiguous clinical presentation, delayed diagnosis, and associated high risk of mortality, diagnosing neonatal sepsis is one of the most difficult tasks faced by neonatologists or pediatricians in the NICU. CRP has been thoroughly investigated and is available at most sites as an acute phase reactant to identify and follow the course of newborn sepsis.[9, 13]

Among the various proposed biomarkers for predicting sepsis in neonates, in this study we determined the accuracy of CRP and WBC count. We found a sensitivity of 64.2%, and specificity 74.2% for CRP levels and a sensitivity of 58.5% and specificity 69.1% for WBC levels, and after combining WBC and CRP levels sensitivity increased to 86.8% and specificity 89.7%.

Chacha et al. in a study from Tanzania including 305 suspected neonates with sepsis, reported CRP sensitivity of 63% and specificity of 73%. For WBC levels the sensitivity was 64.9% and specificity was 66.7%. After combining WBC with CRP, the sensitivity increased to 90.3% but specificity decreased down to 50.2%.[14]

Another study by Sorsa A from Ethiopia including 303 neonates, reported CRP sensitivity of 78.5%, and specificity 66.0%, for WBC the sensitivity was 59.5% and specificity was 79.5%. After combining WBC with CRP levels, the authors reported sensitivity of 78.5% and specificity 83%.[15]

However, study by Caldas et al. reported higher sensitivity (78.6% to 85.7%) and specificity (87.5% to 91.7%) of CRP for determining sepsis. And for combination of CRP plus WBC, the sensitivity was 87.5% and specificity 90.9%.[16]

Still no normal reference values of CRP levels have been established in normal neonates and upper CRP values have only been reported in symptomatic septic neonates. After a traumatic delivery, intraventricular hemorrhage, fetal discomfort, perinatal hypoxia, or meconium aspiration, CRP may rise physiologically. CRP levels normally return to normal within 24–48 hours in these circumstances. These factors contribute to the CRP qualitative assay's low specificity in the diagnosis of newborn sepsis.[17, 18] In many cases, a single normal value is insufficient to diagnose newborn sepsis, hence serial testing are indicated to boost specificity. Neonates with elevated CRP levels over an extended period of time are more prone to develop neonatal sepsis. Positive rates of CRP among neonates increased from day 1 to day 3 in this study, with the majority of neonates who were positive on day 1 being positive on day 3. The majority of our newborns with elevated CRP had sepsis, also according to the previously published data.[19] The culture technique utilized in this investigation could explain the disparity between CRP and culture results. Manual blood culture was used in this study; nevertheless, when compared to automated procedures, this methodology has been proven to contribute to reduced CRP sensitivity. However, due to differing reference levels and test techniques, a wide range of CRP sensitivity has been observed, ranging from 47 to 100 percent.[20] CRP assays have been found to have higher sensitivity than qualitative approaches when using quantitative methodologies.

CONCLUSION:

In the diagnosis of newborn sepsis, serial CRP qualitative assays paired with elevated WBC have a high sensitivity. CRP and WBC counts can be used as affordable approaches to diagnose newborn sepsis in developing countries, especially in centers where blood culture facility is restricted.

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