

DAIGNOSTIC VALUE OF C-REACTIVE PROTEIN AND HAEMATOLOGICAL MARKERS IN NEONATAL SEPSIS

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ABSTRACT

Background: Early diagnosis of neonatal sepsis is often difficult because of the non-specific symptoms and signs. An attempt to set a screening test that can identify infected infants at the time of initial presentation, sparing others from invasive procedures, antimicrobial therapy and parent's anxiety especially by mother infant separation is a challenging task for a neonatologist. The objective of this study was to determine the diagnostic value of C-reactive protein and other hematological marker in predicting early neonatal sepsis.

Material & Methods: A retrospective study was conducted at the NICU of Rehman Medical Institute, Peshawar. A total of 700 neonates with age group of first 28 days of life were included in the study, all of which were suspected to have sepsis on clinical settings. All the neonates were investigated by sending blood to the laboratory for blood culture, CRP, and complete blood count and the final results were compared.

Results: Sepsis was confirmed in 54% of cases on the basis of positive blood culture. Among the hematological markers, CRP was the most sensitive and specific test with sensitivity and specificity of 88.36% and 89.13% respectively, followed by platelet counts with sensitivity of 87.04%. Absolute Neutrophil Count and WBC had the sensitivity of 84.39% and 84.13%.

Conclusion: There is no ideal test for the diagnosis of early or late-onset neonatal sepsis. Physical examination has an important role in identifying infants at low risk for sepsis. Sepsis markers like CRP and neutrophil indices are useful adjunct tests in identifying infants with a low probability of infection.

KEYWORDS: C-reactive protein; Absolute neutrophil count; White blood cells; Platelets; Neonatal sepsis.

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INTRODUCTION

The non-specific symptoms and signs of neonatal sepsis make it difficult to establish an early clinical diagnosis and antibiotic therapy is usually initiated on risk factor or neonatologist suspicion^{1,2} and it's one of the challenging condition for the neonatologist to prompt early treatment as even delay of few hours in initiating treatment can lead to serious morbidity or in some cases, mortality.³ Traditional methods, such as blood culture, though it's a gold standard but its accuracy is being questioned because of spurious positive results due to contamination, negative blood cultures even sometime in fatal cases and the time it takes to get a final result. Thus in addition to blood culture different laboratory tests are evaluated in the

diagnosis of early neonatal sepsis³ of which complete blood count with different neutrophil parameters and C-reactive protein (CRP) are most frequently used^{4,5}. In acute phase the concentration of many serum proteins rises in response to inflammation, infection, and trauma or tissue damage. Among these proteins, the important one is C-reactive protein which can be used as a non-specific indicator of bacterial culture⁶.

The hematological response to inflammation in neonates includes changes in total white cell count (WBC), total neutrophil count and platelet numbers. Though the predictive value of white cell count is non-specific and it can be normal in up to 30% of neonates with culture proven sepsis⁷ while a decrease count is more specific indicator of bacterial infection than leukocytosis.⁸ However the absolute neutrophil count (ANC) is more sensitive and specific indicator of bacterial sepsis than WBC count, particularly if below the normal range has the greatest specificity of neutrophil indices.⁹ The platelet count however has limited predictive value as prognostic

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indicator. Platelet count represents an insensitive and non-specific indicator of neonatal sepsis and can be commonly noted in variety of neonatal disorders other than sepsis and up to 50% of neonates with bacterial infection will develop low platelet count as a late event.¹⁰

A combination of hematological and biochemical tests may provide a more rapid diagnosis of sepsis than the conventional microbiological methods. The objective of this study was to determine the diagnostic value of C-reactive protein and other hematological marker in predicting early neonatal sepsis.

MATERIAL AND METHODS

This cross-sectional retrospective study was conducted in January 2013 at Neonatology Unit of Rehman Medical Institute (RMI), Peshawar, Pakistan. It is a tertiary care hospital with grade IIIA care NICU. The study included case records from January 2006 to December 2011. Ethical approval was obtained from the RMI Ethical Review Board regarding data collection and use for research purpose.

A total of 700 cases were included in the study with clinical symptoms and signs of sepsis like fever, lethargy, poor feeding, jaundice, hypothermia, poor perfusion, diarrhea, vomiting, abdominal distension, prolong capillary refill, weak or excessive cry, grunting, apnea, bulging anterior fontanel or any maternal risk factor like maternal pyrexia (within first week of prenatal and 48 hours of postnatal, foul smelling vaginal discharge, PROM > 18hours, maternal UTI in last month, or instrumental delivery. All the neonates were examined in detail by the pediatric trainees in NICU according to the screening criteria for sepsis. Neonates with birth asphyxia, meconium stained liquor, low birth weight (< 1500 grams), preterm babies (<32 weeks) or neonates who were already on antibiotics therapy were excluded from the study.

Blood for blood culture, complete blood count (CBC) and C-reactive protein had been taken under strict aseptic condition soon after the patient was admitted to the neonatology unit and was assessed clinically for any sign of sepsis. Samples were sent to pathology department in aseptic and controlled environment. A standard procedure was followed for CRP, CBC and Blood culture.

RESULTS

Blood culture was positive in 378 (54%) out of 700 cases confirming sepsis. The age of onset of sepsis in most of the patient was first week of life.

Looking at table 1, the C-reactive protein was significantly elevated in 334 (88.4%) cases with positive blood culture while it was also positive in 35 (10.9%) cases with negative blood culture (false positive), the test was negative in 44 (11.6%) of cases with positive blood culture and negative in 287 (89.1%) with negative blood culture.

The WBC count was abnormal in 319 (84.4%) with positive blood culture but it was also abnormal in 67 (20.8%) with negative blood culture. WBC were normal in 255 (79.2%) and 59 (15.6%) in culture negative and positive cases respectively. The absolute neutrophil count was abnormal in 318 (84.12%) cases with culture proven sepsis, it was normal in 287 (89.1%) cases with culture negative sepsis.

Figure 1 shows the sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) of tests. Looking at the figure we can see that C-reactive protein has highest sensitivity, specificity, PPV and NPV followed by platelets count, whose sensitivity and NPV are 87.04% and 85.11% respectively while the absolute neutrophil count has sensitivity and NPV less than platelets count but its specificity and PPV is higher than the platelet count.

Table 1: Results of Screening Tests in 700 cases of Neonatal Sepsis.

Screening test	Blood Culture positive n=378 (Percentage)	Blood Culture Negative n= 322 (Percentage)
CRP > 0.5mg/dl	334 (88.35)	35 (10.8)
CRP < 0.5mg/dl	44 (11.65)	287 (89.2)
WBC <5000/>23000	319 (84.4)	67 (20.8)
WBC Normal	59 (15.6)	255 (82.2)
Platelets Abnormal	329 (87.03)	42 (13.04)
Platelets Normal	49 (12.97)	280 (86.96)
ANC <2/>6	318 (84.12)	35 (10.86)
ANC 2-6	60 (15.88)	287 (89.13)
Hemoglobin Abnormal	234 (61.9)	48 (14.9)
Hemoglobin Normal	144 (38.1)	274 (85.1)

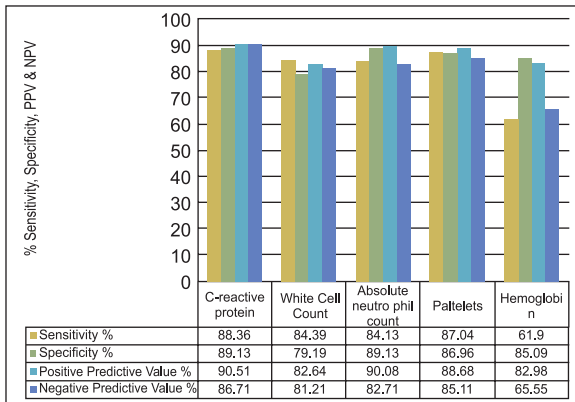


Figure 1: Comparative Analysis of Screening Tests in Neonatal Sepsis.

DISCUSSION

Neonatal sepsis is one of the major problems for neonatologists of a developing country like ours partly because of poor antenatal care and partly because of poverty. The objective of our study was to evaluate the usefulness of CRP and other hematological marker in predicting early neonatal sepsis. The reason to carry out this study was to set a screening test that can help us in time management of neonatal sepsis and to prevent complications resulting in serious morbidity or mortality, keeping in mind its simplicity, cost effectiveness and rapid availability of the results. No doubt blood culture is still the gold standard but due to the emergence and dissemination of antimicrobial resistance that has been well documented as a problem worldwide,¹¹ and also its non-availability in most of the secondary and even some tertiary neonatal care setups, high cost, more chances of contamination and much delayed results, we need a test that is more convenient, cost effective and whose results can be readily available.

The C-reactive protein has some practical advantage over other tests as it is not affected by the previous antimicrobial therapy¹² but despite all we still recommend to rely both on clinical correlation and laboratory findings to confirm diagnosis of sepsis.

In this study 54% of neonates were proved to have neonatal sepsis that was confirmed on positive blood culture, other national and international studies have reported frequency of sepsis ranging from 20-30%.¹³⁻¹⁵ Hussein et al reported the frequency of sepsis to be 34%.¹⁶

Zeeshan et al¹⁷ have reported 28%, Anwar et al⁶ 42% and Aurangzeb et al¹⁸ has reported 55.8% of neonatal sepsis to be blood culture positive. The variation of blood culture positivity may be due to the criteria of studied group, study sample and the standard of neonatal facilities.

In our study, the sensitivity, specificity, PPV

and NPV of CRP were: 88.36%, 89.13%, 90.51% and 86.71% respectively for proven sepsis, these results are almost in consistency with other previous studies.

Zeeshan et al¹⁷, in 2005 reported the sensitivity, specificity, PPV and NPV of CRP as: 85.5%, 95.0%, 82.7% and 95.9% respectively while Shabir et al¹⁹ has reported that CRP had 74% sensitivity and 76% specificity.

Our study has shown that sensitivity, specificity, PPV and NPV of ANC were: 84.13%, 89.13%, 90.08% and 82.71% respectively, being the most sensitive test in the detection of neonatal sepsis after CRP.

In contrast to our study Hussein et al¹⁶ has reported the sensitivity, specificity, PPV and NPV of ANC to be 48.5%, 86%, 69.6% and 71.7% respectively while Zeeshan et al¹⁷ reported the sensitivity of ANC to be 71.4%. Chauhan et al¹¹ has reported the ANC to be 64.10% sensitive and 54.34% specific.

CONCLUSSION

There is no ideal test for the diagnosis of early or late-onset neonatal sepsis. Physical examination has an important role in identifying infants at low risk for sepsis. Sepsis markers like CRP and neutrophil indices are useful adjunct tests in identifying infants with a low probability of infection.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.