# Role of Complete Blood Count and C – Reactive Protein as Diagnostic Markers in Sepsis In Neonatal Intensive Care Unit Patients

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**Abstracts:** Background: Neonatal Intensive care unit is complex components of health care. Severe sepsis mortality ranges from 28% to 50%. Markers of inflammation, as C- reactive protein, erythrocyte sedimentation rate and complete blood counts are still useful investigations for sepsis in NICU. Research Objective: To access and analyse correlation between CBC and CRP concentration among NICU patients and to NICU outcome and its relationship with the diagnosis. Methodology: This cross-sectional study was carried on 327 patients admitted in NICU at C. U. Shah medical college and hospital. From time of admission to discharge day, signs and symptoms, clinical and laboratory data regarding CBC and CRP levels collected with other relevant tests according to the patient's clinical status. Results: In 92.92 % of all NICU patients with sepsis, CRP was >30 mg/L. Of all NICU patients with sepsis, leucocytosis, thrombocytopenia and raised absolute neutrophil count was observed in 66.13%, 13.53% and 56.8% respectively. Conclusion: Leukocytosis and neutrophilia are predictive of sepsis. CRP value greater than 30.0 mg/L is 90 percent sensitive and sequential assessment of CRP values is specific for diagnosis of sepsis. If the CRP level remains persistently normal, bacterial sepsis is unlikely.[Shivani TNJIRM 2017; 8(2):1-4]

**Key words**: CBC, HS CRP, NICU

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**Introduction:** Neonatal sepsis has been defined as a clinical syndrome manifested by systemic signs of infection and/or isolation of a bacterial pathogen from the blood stream in an infant 28 days of life or younger[1]. It is classified by the infant's age into early-onset sepsis (≤3 to 7 days) and late-onset sepsis (>3 or 7 to 28 days)[2,3]. Because the clinical manifestations of sepsis are nonspecific, including temperature instability (primarily fever), as well as respiratory, gastrointestinal, and neurologic abnormalities[4], early recognition and timely institution of antimicrobials is of utmost importance to prevent serious consequences. Despite impressive advances in neonatal intensive care units (NICU), sepsis continues to be a major source of morbidity and mortality in NICU patients. After thorough prenatal history and complete physical examination, the definitive diagnosis of neonatal sepsis is established by a positive blood culture. However, awaiting results of blood culture test may increase morbidity and mortality in this vulnerable population. Therefore a more expedient, sensitive, and specific diagnostic tool for bloodstream infections is needed. A complete blood count (CBC) obtained 6 to 12 hours after delivery and C-reactive protein (CRP), an acute phase reactant, may be helpful in the evaluation of early-onset sepsis. For detection of neonatal sepsis, a CRP value that is greater than 10.0 mg/L is 90 percent sensitive but highly nonspecific. Hence, sequential assessment of CRP values is important for supporting a diagnosis of sepsis and for guiding the duration of antibiotic therapy[5, 6]. We conducted this study to assess CBC profile and CRP concentrations among patients admitted in NICU, to assess their relation with diagnosis of sepsis and to assess their sensitivity and specificity as diagnostic markers.

**Methods:** This study was conducted in the neonatal intensive care unit at C U Shah Medical College and Hospital, Surendranagar with permission of ethical committee of our institute. Patients admitted in NICU with symptoms and signs of sepsis and whose parents or legal guardian gave informed consent were enrolled in this observational study. Total of 327 patients were enrolled. Evaluation of sepsis included CBC and CRP on day 1 of sepsis presentation prior to antimicrobial administration. Blood sample was collected for estimation of CBC and CRP in EDTA and Plain bulb. CBC was obtained from automated hematologyanalyzer (Beckman Coulter LH750) and CRP was obtained from fully automated biochemistry analyzer (SIMENS- Dimension Xpand Plus) by immunonephelometric method. Appropriate samples were collected for microbiological cultures depending on the clinical symptoms.

**Result:** A total of 327 patients, 61% of them being males, admitted in NICU were evaluated for suspected clinical presentation of sepsis. The median length of stay in NICU prior to presentation of sepsis was 2

days. The median age of neonates at presentation of sepsis was 3 days.

Among CBC parameters, haemoglobin, total leukocyte count, absolute neutrophil count and platelet count were evaluated. Out of the total of 327 patients, 92.7% of them had haemoglobin levels above 10 gm/dl. The results for total leukocyte counts and absolute neutrophil count are given in Tables 2 and 3 respectively.

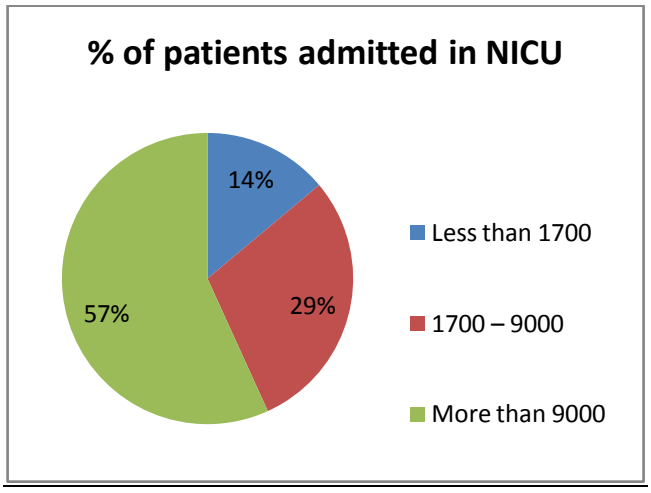
During assessment of platelet counts, the normal range taken for the study was 1.5 to 4.5 lacks/$mm^3$. Approximately three quarters of patients had platelet counts within normal range while 22.9% and 1.6% of patients had values lower and above the normal range.

**Table: 1**

| Total leukocyte counts in per mm3 | % of patients admitted in NICU |
|---|---|
| Less than 4000 | 3.7 |
| 4000 – 11000 | 34.2 |
| More than 11000 | 62.1 |

**Table: 2**

| Absolute neutrophil count in per mm3 | % of patients admitted in NICU |
|---|---|
| Less than 1700 | 13.9 |
| 1700 – 9000 | 29.3 |
| More than 9000 | 56.8 |




In our study, the peak cut off value for CRP was taken as 3 mg/L, with 89.6% of neonates with sepsis having values above 30 mg/L.

**Discussion:** Neonatal sepsis remains a significant diagnostic and therapeutic challenge for neonatal care providers in developing country like ours, with mortality rate reaching almost 50%. Hence rapid diagnosis of neonatal sepsis is vital for prevention of adverse consequences. The most definitive method for confirming the diagnosis is by isolation of pathogen via blood culture. However, due to the fact that cultures take time, the current practice is to start empirical antibiotics in all neonates whose clinical evaluation reveal infection – like symptoms. This practice, however, results in exposure of neonates to adverse drug effects, nosocomial complications and emergence of resistant strains[7]. Numerous markers, like inflammatory cytokines (IL-2, IL-6 and tumour necrosis factor alpha) have been evaluated to improve laboratory sepsis diagnosis. These cytokines are not routinely measured due to high cost of testing and because no single biomarker or panel is sufficiently sensitive to reliably detect neonatal sepsis. Hence we conducted this study to see whether CBC and CRP still remain the preferred tests for rapid diagnosis of possible sepsis.

A CBC obtained 6 to 12 hours after delivery may be more likely to be abnormal and clinically useful than those obtained immediately after birth in the evaluation of early-onset sepsis. In a multicentre study reported by Newman TB et al[8], low white blood cell count (WBC) (<5000/microL) and absolute neutropenia (<1000 neutrophils/microL), were associated with blood culture-proven, early-onset disease. The authors concluded that CBC was more sensitive as a predictor for sepsis if obtained after four hours of age because the WBC and absolute neutrophil count (ANC) normally increase during the first six hours of life. Similar results were obtained in another study reported by Hornik CP et al[9]. Hornik CP et al[10], in another analysis of same cohort of patients, demonstrated that both low and high WBC (<1000 and >50,000/microL), high absolute neutrophil count (>17,670/microL) and low platelet count (<50,000/microL) were associated with late-onset sepsis (defined as a positive culture between day of life 4 and 120). Although both elevated WBC and high neutrophil counts can be predictive of sepsis, neutrophilia may be a marker because it has greater specificity as seen in our study. Platelet count is not typically helpful in evaluating a neonate of sepsis as it may fall hours to days before the onset of clinical

sepsis. In our study thrombocytopenia was observed in only 22.9% of patients with sepsis.

CRP is a non-specific acute phase reactant produced in liver, with reported median CRP values for men and women being 1.5 and 1.52 mg/dl. Its elevation in neonate represents endogenous synthesis as it crosses placenta in very low concentration[11]. The sensitivity and specificity of CRP reported in various studies range from 29-100% and 6-100%, respectively. These extreme variations are due to different reference-values, test methodologies, patient characteristics and inclusion criteria, number of samples taken, and sampling time. CRP is nonspecific as it elevated in various non-infectious inflammatory conditions like maternal fever, stressful delivery, prolonged rupture of membranes and/or prolonged labour, asphyxia, meconium aspiration syndrome and intraventricular haemorrhage[12], but value greater than 1.0 mg/dl is 90 percent sensitive in detecting neonatal sepsis. Serial quantitative CRP measurements 24 to 48 hours after the onset of symptoms of sepsis is recommended, as it clearly improves diagnostic accuracy. The role of CRP in ruling out an infection, for monitoring the response to treatment and guiding the duration of the antibiotic therapy is determined by two consecutive values <10.0 mg/L determined more than 24 hours apart. We used a higher value of CRP as a cut-off to improve the specificity of the test. In our cohort 89.6% of neonates with sepsis had CRP value greater than 30 mg/L. However, due to nonspecific rise of CRP during first few days after birth due to stress of delivery and the influence of gestational age on its response to infection, it is recommended that dynamic reference values should be used to reflect its physiologic kinetics.

**Conclusion:** CBC and CRP are both most widely available, most used laboratory tests and among the cheapest markers for neonatal bacterial infection. Our study clearly highlights that they still play vital role in diagnosis of sepsis and monitoring the response to antimicrobials. Further research is needed in field of high sensitivity CRP (hsCRP), influence of gestational age on CRP kinetics and confounding effect of various non-infectious inflammatory disorders on CBC and CRP estimations.

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