Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i17.2532

C-REACTIVE PROTEIN (CRP) ACCURACY IN INFANTS PRESENTING WITH NEONATAL SEPSIS

Zulfiqar Ali Dahri[1*], Naseer Ahmed Memon[2], Mushtaque Ali Shah[3], Amanullah Lail[4], Khairjan Habib[5], Adnan Bashir[6]

[1*]Consultant Pediatrition, Shahdadpur Institute of Medical Sciences (SIMS) Shahdadpur Pakistan. Email: Zulfiqar_dahri@yahoo.com
[2]Associate Professor Pediatric Medicine, People's University of Medical and Health sciences Nawabshah Pakistan. Email: naseer.ahmed199@yahoo.com
[3]Assistant Professor of Pediatrics, Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad Pakistan. Email: drmushtaqueali@gmail.com
[4]Assistant Professor Pediatrics, DMC/DUHS Civil Hospital Karachi Pakistan., Email: aman_lail@yahoo.com
[5]Registrar Pediatrics Surgery section, Murshid Hospital and Health Care center Karachi Pakistan. Email: kj.habibi@gmail.com
[6]Assistant Professor Pediatrics, Hamdard College of Medicine and Dentistry Karachi Pakistan. Email: dr_adnan678@hotmail.com

***Corresponding Author:** Zulfiqar Ali Dahri
*Consultant Pediatrition, Shahdadpur Institute of Medical Sciences (SIMS) Shahdadpur Pakistan. Email: Zulfiqar_dahri@yahoo.com

Abstract

Background: Neonatal sepsis is a medical illness in which babies exhibit a constellation of systemic symptoms indicating circulation problems. Reduced peripheral perfusion, pallor, decreased muscular tone, and diminished responsiveness are among the symptoms. Prematurity, invasive medical procedures, low birth weight, and prolonged hospitalization are the key risk factors for neonatal sepsis.

Objective: The purpose of the study was to determine the accuracy of CRP as a diagnostic tool for neonatal sepsis.

Study design: A cross-sectional study

Place and Duration: This study was conducted in Shahdadpur Institute of Medical Sciences (SIMS) Shahdadpur from January 2022 to January 2023

Methodology: The WHO sample size calculator was used to calculate the sample size. There were a total of 60 neonates involved in this research who had clinical features or risk factors for neonatal sepsis. The blood sample for CRP and culture was taken at the time of admission. A serum CRP level greater than 6 mg/L was regarded as elevated C-reactive protein (CRP). Blood culture results were used as the gold standard to assess the diagnostic accuracy of CRP. The accuracy was tested using True Positive (TP) cases to calculate sensitivity and specificity.

Results: The percentage of males was a little higher than that of females. There were 32 males and 28 females enrolled in this research. This elaborates on the fact that neonatal sepsis has a male predisposition. The average age calculated was 15.47 days. The average weight calculated was 2.94 kg. Blood cultures were positive in 18 cases, of which 9 were early-onset sepsis and 9 were late-onset sepsis.

Conclusion: C-reactive protein has equivalent sensitivity and specificity to blood culture, which results in appropriately detecting newborn sepsis. Furthermore, the advantage of receiving test results quickly makes C-reactive protein testing highly recommended for examining neonates with any indications of sepsis.

Keywords: C-reactive protein, neonates, sepsis, blood culture.

INTRODUCTION

Neonatal sepsis is a medical illness in which babies exhibit a constellation of systemic symptoms indicating circulation problems [1, 2]. Reduced peripheral perfusion, pallor, decreased muscular tone, and diminished responsiveness are among the symptoms [3]. It happens as a result of bacteria entering the baby's circulation during the first month of life [4]. The incidence of neonatal sepsis is minimal, with 5 occurrences per 1,000 live births and a 39% frequency [5]. Its fatality rate, however, ranges from 5% to 20%. The incidence in developing countries can be substantially greater, with 22 instances per 1,000 live births, while the perinatal mortality rate in Pakistan has been estimated to be 60 per 1,000 live births.

Prematurity, invasive medical procedures, low birth weight, and prolonged hospitalization are the key risk factors for neonatal sepsis [6]. Fever, abdominal distention, feeding difficulties, rapid breathing, diarrhoea, decreased urine output, low blood pressure, rapid or slow heart rate, irritability, bulging fontanelle, convulsions, or bleeding are all symptoms of neonatal sepsis [7]. Cultures of blood or other ordinarily sterile body fluids are required to definitively identify neonatal sepsis. In 25% to 54% of instances, newborn blood cultures are positive [7].

Several studies have been done to find out how well tumour necrosis factor-alpha, procalcitonin, and interleukins work as ways to diagnose sepsis [8, 9]. Nevertheless, in practical clinical scenarios, C-reactive protein (CRP) is the most readily available and commonly employed indicator for detecting infections [10]. The liver produces CRP, an abnormal blood glycoprotein. It plays a role as an acute phase reactant in the innate immune system, and its levels significantly increase within 1 to 2 days of severe bacterial infections.

In confirmed cases of sepsis, CRP has a high sensitivity of 97.2% and a specificity of 95% [11]. While blood culture is still the gold standard for identifying neonatal sepsis and facilitating targeted antimicrobial treatment, its results can be up to 48 hours delayed and can have negative effects in many cases of septic shock. Furthermore, the difficulty of getting a sterile sample from newborns leads to higher rates of contamination.

Because of the potentially severe effects and mortality associated with sepsis, it is critical to begin antibiotic medication as soon as possible, even before culture results are available [12]. This method, however, raises concerns about the overuse of antibiotics, which can increase the risk of drug side effects and contribute to the development of drug resistance.

CRP testing allows for the rapid identification of infected persons while avoiding the need for a sterile sample, and a normal CRP value can aid in quickly ruling out infection [13]. Monitoring CRP levels over time is also useful for prognosis and serves as an indicator of the efficacy of antibiotic

treatment. The purpose of the study was to determine the accuracy of CRP as a diagnostic tool for neonatal sepsis.

METHODOLOGY

The WHO sample size calculator was used to calculate the sample size. There were a total of 60 neonates involved in this research who had clinical features or risk factors for neonatal sepsis. Neonatal sepsis is a condition that is diagnosed by the presence of two or more of the following clinical features: tachypnea, poor skin perfusion, oliguria, and temperature instability. The consent of all parents was obtained.

Based on blood culture results obtained upon admission, neonatal sepsis was either confirmed in positive cases or rejected in negative cases. A serum CRP level greater than 6 mg/L was regarded as elevated C-reactive protein (CRP). Blood culture results were used as the gold standard to assess the diagnostic accuracy of CRP. The accuracy was tested using True Positive (TP) cases to calculate sensitivity and specificity.

Exclusion criteria: Newborns who had a major systematic malformation, newborns who had received antibiotics before admitting to the hospital, weight <1000 grams, underlying surgical conditions, and multiple congenital anomalies were excluded from this research.

A detailed history was obtained, which included gender, age, gestational age, history of antibiotic administration, place of delivery, and duration of symptoms. A comprehensive physical examination was also conducted on the neonates. The blood sample for CRP and culture was taken at the time of admission.

Aseptic measures were conducted before collecting 2 ml of blood and inoculating it into a blood culture vial containing brain-heart infusion (BHI). A 3-mL syringe was used to draw 1 mL of blood for CRP determination. The laboratory assessed CRP using a latex agglutination assay, with a value of more than 6 mg/L indicating an increased CRP level. The results of the blood culture and CRP tests were entered into the Performa.

SPSS version 22 was used to analyse the data. The quantitative variables were expressed in terms of mean and SD. The qualitative variables were expressed in terms of percentages and frequencies. The chi-square test was used to analyze the outcomes. A significant p-value was expressed as <0.05.

RESULTS

Overall, there were 60 neonates involved in this research. The percentage of males was a little higher than that of females. There were 32 males and 28 females enrolled in this research. This elaborates on the fact that neonatal sepsis has a male predisposition. The average age calculated was 15.47 days. The average weight calculated was 2.94 kg.

Table No. 1: Biodata of the study participants

Quantitative variables	Mean±SD
Age (days)	15.47 ±7.26
Weight (kg)	2.94 ±0.63

Table No. 2: the clinical representation of the neonates involved.

Symptoms	%
Decreased urine output	45
Temperature instability	78
Tachypnea	75
Delayed Capillary refill	55
Tachycardia	66

Blood culture was positive in 18 cases of which 9 were early-onset sepsis and 9 were late-onset sepsis.

Table No. 3: the types of organisms isolated in the blood culture

Organisms	Early-onset sepsis	Late-onset sepsis
E. coli	2	4
K. pneumoniae	4	1
S. aureus	3	4

DISCUSSION

The deterioration of a neonate's state might be linked to a variety of causes, making it difficult to identify a single reason [14]. However, bacterial infection is frequently seen as the most serious threat. Although blood culture is the gold standard for detecting bacterial infections, it does not always produce conclusive results [15]. As a result, pediatricians advocate the use of surrogate testing to diagnose neonatal sepsis. The purpose of this study was to determine the efficacy of CRP as a potential indication of newborn sepsis.

Because sepsis is a medical emergency, failing to diagnose it quickly can have life-threatening effects. On the other hand, starting antibiotics for a non-septic newborn prematurely can place a financial strain on the family [16]. As a result, it is critical to use a high-sensitivity screening test to precisely detect all infected neonates while also ensuring that negative results have a strong negative predictive value to successfully rule out the disease.

Non-infectious diseases that produce positive results can reduce a test's specificity and positive predictive value [17, 18]. However, when the cost of treatment for non-infected individuals is much lower than the potential repercussions of missing an infected case with a life-threatening infection, this fall in specificity and positive predictive value is considered acceptable.

The most prevalent symptom found in individuals suspected of having neonatal sepsis was temperature instability, either pyrexia (fever) or hypothermia (low body temperature), which was present in around 78% of the cases. Tachypnea (rapid breathing) was the second most common symptom, observed in 75% of patients, followed by tachycardia (elevated heart rate) in 66% of cases. Delayed capillary refill was found in 55% of the patients, whereas reduced urine production was seen in 45% of the patients. In 18 (30%) of the patients, positive blood culture findings and raised CRP levels were discovered.

When the impact of weight on various features was examined, it was discovered that in weight groups under 3 kg, there were more female patients (n=33) than male patients (n=27). In weight groups exceeding 3 kg, male patients (n=36) outnumbered female patients (n=24). These data imply that females are more susceptible to developing neonatal sepsis in neonates with low birth weight, but the male gender becomes a risk factor in those with normal birth weight. Similar patterns were seen in infants with low birth weights.

When raised CRP levels were evaluated, it was found that 19 patients had raised CRP levels, out of which 18 had positive blood cultures. According to the data, CRP's sensitivity is slightly greater than its specificity. Prior research has found CRP to have good sensitivity, specificity, positive predictive value, and negative predictive value when compared to blood culture results. In a separate trial involving 76 neonates suspected of having neonatal sepsis, the test demonstrated 100% sensitivity, 94% specificity, 91.6% positive predictive value, and 100% negative predictive value [19, 20].

CONCLUSION

C-reactive protein has equivalent sensitivity and specificity to blood culture, which results in appropriately detecting newborn sepsis. Furthermore, the advantage of receiving test results quickly makes C-reactive protein testing highly recommended for examining neonates with any indications of sepsis. This method ensures that neonatal sepsis is included or excluded as part of the diagnostic procedure in a reliable and timely manner.

REFERENCES

1. Younis S, Sheikh MA, Raza AA. Diagnostic accuracy of C-reactive protein in neonatal sepsis. Journal of Bioresource Management. 2014;1(1):1.
2. Sundarapandian S, Chinnakkannan S, Shafath Ahmed M, Das RR. Serial serum C-reactive protein in the diagnosis of neonatal sepsis: A cross-sectional study. Indian Journal of Neonatal Medicine and Research. 2017;5(2).
3. West BA, Peterside O, Ugwu RO, Eneh AU. Prospective evaluation of the usefulness of C-reactive protein in the diagnosis of neonatal sepsis in a sub-Saharan African region. Antimicrobial Resistance and Infection Control. 2012 Dec;1(1):1-5.
4. Lamichhane A, Mishra A. Correlation between C-reactive protein and blood culture in neonatal sepsis at a tertiary care centre in Western Nepal. Journal of Lumbini Medical College. 2019 Nov 17;7(2):88-92.
5. Mohamed AF, Alaskar SA, Alkhamis RI, Fatmah O, Karar T. The association between neonatal sepsis and C-reactive protein: a cross-sectional study at tertiary care hospital. International Journal of Medical Research & Health Sciences. 2019;8(4):54-60.
6. Gandhi TN, Patel MG, Jain MR, Saxena RB, Bhuva PJ. Utility of C reactive protein as inflammatory marker in early diagnosis of neonatal septicaemia: A cross sectional study. National Journal of Medical Research. 2012 Dec 31;2(04):481-3.
7. Mannan MA, Shahidullah M, Noor MK, Islam F, Alo D, Begum NA. Utility of C-reactive protein and hematological parameters in the detection of neonatal sepsis. Mymensingh medical journal: MMJ. 2010 Apr 1;19(2):259-63.
8. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. Pakistan journal of medical sciences. 2015 May;31(3):527.
9. Jan AZ, Zahid SB, Ahmad S. ROLE OF C-REACTIVE PROTEIN IN DIAGNOSING NEONATAL SEPSIS. Khyber Medical University Journal. 2012 Oct 1;4(4).
10. Kayange N, Kamugisha E, Mwizamholya DL, Jeremiah S and Mshana SE (2010). Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza-Tanzania. BMC Pediatr, 10, 39.
11. Payne NR, Burke BA and Day DL (1998). Correlation of clinical and pathologic findings in early onset neonatal group B streptococcal infection with disease severity and prediction of outcome. Pediatr Infect Dis, 7,836
12. Ferreira RC, Rosane R, Melloa, Kátia S and Silva (2014). Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. J Pediatr (Rio J).
13. Maniaci V, Dauber A and Weiss S (2008). Procalcitonin in young febrile infants for the detection of serious bacterial infections. Pediatrics, 122, 701.
14. Arnon S, Litmanovitz I (2008). Diagnostic tests in neonatal sepsis. Curr Opin Infect Dis, 21, 223-37.
15. Stoll BJ (2008). Infections of the neonatal infant. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF editors. Nelson text book of paediatrics. Philadelphia:WB Saunders Company, 794-811.
16. Ahmed AS, Chowdhury MA, Hoque M, Darmstadt GL. Clinical and bacteriological profile of neonatal septicemia in a tertiary level pediatric hospital in Bangladesh. Indian Pediatr. 2002;39:1034- 39.
17. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998;102(4):E41.

18. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998;102(4):E41.
19. Lahariya C, Sudfeld CR, Lahariya D, Tomar SS. Causes of child deaths in India,1985-2008: a systematic review of literature. Indian J Pediatr. 2010;77:1303-11.
20. Jaswal RS, Kaushal RK, Goel A, Pathania K. Role of C-reactive protein in deciding duration of antibiotic therapy in neonatal septicaemia. Indian Pediatr. 2003;40: 800-03.