ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

CORRELATION OF C-REACTIVE PROTEIN AND BLOOD CULTURE IN NEONATAL SEPSIS-A RETROSPECTIVE STUDY

DR. PADALA TRISALI [1], DR. KARTHIK S [2], DR. NARENDRA RR [3]

1. Junior Resident, Department of Paediatrics, Sri Devaraj Urs Academy of Higher Education & Research, Tamaka, Kolar, India. **Mail ID**: trisali.padala@gmail.com
2. Assistant Professsor, Department of Paediatrics, Sri Devaraj Urs Academy of Higher Education & Research, Tamaka, Kolar, India. **Mail ID:** sk.karthik.1508@gmail.com
3. Assistant Professor, Department of Paediatrics, Sri Devaraj Urs Academy of Higher Education & Research, Tamaka, Kolar, India. **Mail ID**: rrnarendra1@gmail.com

Corresponding author:

Dr.Narendra RR

Assistant Professor

Department of Paediatrics

Sri Devaraj Urs Academy of Higher Education & Research, Tamaka, Kolar, India.

Mail ID: rrnarendra1@gmail.com

Abstract

Purpose: Septicaemia is recognized as foremost causes of mortality in neonates. Hence, premature diagnosis is vital to avoid fatal outcome.

Aim: The aim of the study is to correlate C-reactive protein and blood culture in neonatal sepsis.

Materials and Methods: A total of 132 neonates who were diagnosed with neonatal sepsis were included in the present study for a period of one year. All the subjects were subjected to blood culture test and CRP.

Results: CRP was reported to have Sensitivity of 84.85%, Specificity of 75.76%, Positive Predictive Value of 53.85%, Negative Predictive Value of 93.75% and diagnostic accuracy of 78.03% against blood culture.

Conclusion: CRP was originated to have a high diagnostic value in standings of sensitivity and sky crafting specificity. Hence, this early marker for sepsis can assist as central tool in diminishing the mortality rates in neonates.

Keywords: biomarkers, neonates, specificity, sensitivity.

Introduction

Neonatal sepsis is well-defined as infection in blood that will arise in neonates at first four weeks after birth. The symptoms of neonatal septicaemia are non-specific that include abdominal distension, bulging fontanel, bleeding problems, feeding difficulties, fever, respiratory distress and unexplained jaundice. [1] Apart from prematurity and intrapartum complications, neonatal sepsis stands as 3rd leading cause of mortality in neonates.[2] Worldwide, the neonatal sepsis kills around one million neonates. In India over 1,00,000 live births and 17,000 neonates are diagnosed with sepsis.[3]

Diagnosing neonatal sepsis remains a challenging task due to its non-specific signs and symptoms. Though gold standard method to diagnose neonatal sepsis is blood culture method, it requires well equipped laboratory along with trained laboratory personnel and is

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

time consuming. It can also be false negative due to little amount of drawn blood from neonates, antibiotic use or less level of bacteraemia.[4]

Postponement in culture reports mains to inappropriate use of antibiotics and hence early diagnosis is the need of the hour for better clinical outcome to avoid emergence of antibiotic resistance.[5]

In 1930, Tillet and Francis demonstrated about CRP at Rockefeller University. In response to inflammatory cytokines, it is synthesised in liver and plays a character in innate immunity. It mediates cytotoxicity that activates neutrophils and promote degranulation of platelets. [6] The half-life of CRP is 19 hours and it reaches thousand-fold in acute response and falls rapidly to 5-7 hours after treatment. In placenta, it crosses in low quantities and hence elevation in neonates represents endogenous synthesis.[7]

The levels of CRP can be evaluated easily by qualitative and quantitative tests. The benefits of qualitative methods are simple, rapid and requires less skill. Qualitative method is more feasible in countries where there are limited resources. The quality measures of quantitative methods are highly sensitive, fast and precise result but is more costly and need technical assistance and hence it is used widely in developed countries with well equipped laboratories. [8]

The present study is planned to estimate the correlation of CRP and blood culture in neonatal sepsis as an early predictor.

Materials and Methods

The retrospective study was performed in the department of Paediatrics, during the period of May 2021 to May 2022. This study was approved by the Institutional Ethical Committee. A total of 132 individuals suspected with sepsis or those who are having signs and symptoms were included in the present study. Babies who have congenital anomalies and infections, extreme preterm neonates, low birth neonates and those who are receiving antibiotics were excluded from the study.

After obtaining informed consent from neonates' parents, history, clinical examination and other findings were noted. In 5ml of Brain Heat Infusion Broth having blood culture, 1-2 ml of blood was collected and incubated overnight and examined for gas production, haemolysis or for the presence of colonies on the surface off sedimented red blood cells. If any of these is not present, the bottles were continued for 7-day incubation. The colonies grown were identified by standard laboratory methods followed by Gram staining and other biochemical reactions.

Estimation of CRP was performed by Latex Agglutination Card test and CRP was found positive if agglutination was detected and negative with no agglutination. Neonates with recorded diagnosis of septicaemia with positive and negative blood cultures were taken and were compared with the CRP levels.

Results

In the present study, a total of 132 neonates with clinical suspicion of sepsis were included. Out of 132 neonates 49.2% were female and 50.8% Male. Male to female ratio was 1:1. 19.7% of the neonates had prematurity. 19.7% of the neonates were having Low birth weight and 80.3% of neonates had normal birth weight. 98.5% of the neonates were alive and 1.5% of the neonates were dead. (Table 1, Figure 1& 2)

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

Table 1: Neonatal Factors

	N	%
Gender		
Female	65	49.2%
Male	67	50.8%
Prematurity		
NO	106	80.3%
YES	26	19.7%
Birth weight		
Low birth weight	26	19.7%
Normal	106	80.3%
Outcome		
Alive	130	98.5%
Dead	2	1.5%

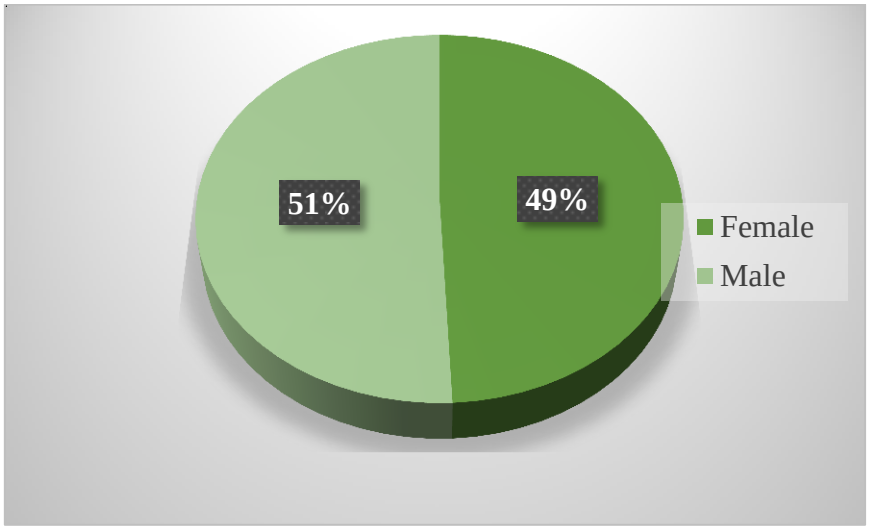

Fig 1. Graph showing distribution of subjects according to gender

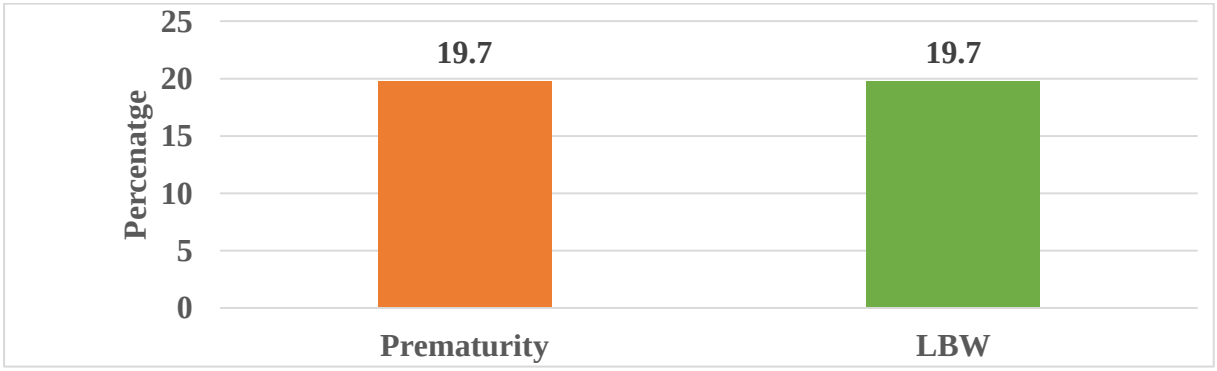

Fig 2. Graph showing neonatal factors

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

Table 2: Maternal factors

	N	%
Gestational age		
<37weeks	28	21.2%
>37weeks	104	78.8%
Mode of delivery		
LSCS	36	27.3%
NVD	96	72.7%
PROM		
NO	118	89.4%
YES	14	10.6%
MSAF		
NO	114	86.4%
YES	18	13.6%
Prolong labour		
NO	110	83.3%
YES	22	16.7%
Vaginal examinations		
≤3 times	111	84.1%
>3times	21	15.9%
Foul smelling		
NO	120	90.9%
YES	12	9.1%

21.2 % of the neonate's mother's gestational age was less than 37weeks and 78.8% of the neonate's mother's gestational age was more than 37 weeks.

72.7% of the neonate's mother had Normal vaginal delivery and 27.3% of the neonate's mother had LSCS.

Maternal factors like PROM were present in 10.6% of the neonates' mothers, MSAF was present in 13.6% of the neonate's mothers, 16.7% had prolong labour, 15.9% of the mothers had vaginal examinations more than 3times. (Table 2 & Figure 3)

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

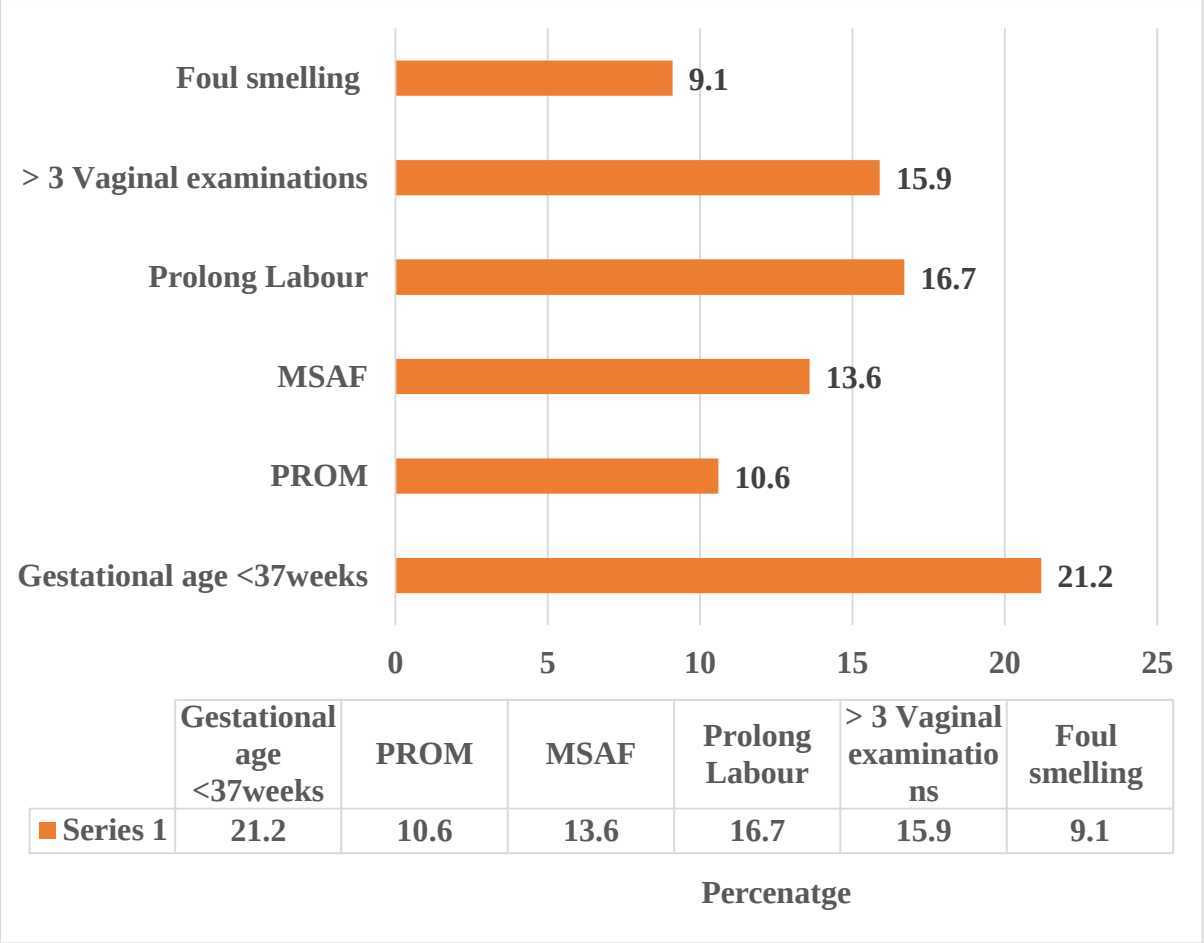

Fig 3. Graph showing maternal factors

Table 3: CRP vs Blood culture

	Blood culture Positive	Blood culture negative	Total
CRP Positive	28	24	52
CRP negative	05	75	80
Total	33	99	132

25 % of the study subjects were positive for blood culture. 33 subjects were Blood culture Positive among which 28 were also positive for CRP and 5 were negative for CRP.99 subjects were Blood culture negative among which 24 were positive for CRP and 75 were negative for CRP. (table 3 & 4)

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

Table 4: Predictive values of CRP

Statistic	Value	95% CI
Sensitivity	84.85%	68.10% to 94.89%
Specificity	75.76%	66.11% to 83.81%
Positive Predictive Value	53.85%	44.45% to 62.97%
Negative Predictive Value	93.75%	86.91% to 97.13%
Accuracy (*)	78.03%	70.00% to 84.77%

CRP reported to have Sensitivity of 84.85%, Specificity of 75.76%, Positive Predictive Value of 53.85%, Negative Predictive Value of 93.75% and diagnostic accuracy of 78.03% against blood culture.

Discussion

Neonatal sepsis is systemic disorder that is corelated with hemodynamic changes that are caused due to bacterial or fungal agents. The diagnosis of sepsis makes it challenging as it contains highly non-specific symptoms. Early onset of sepsis is from 24 hours which is due to vertical acquisition of microorganisms and late onset of sepsis is from 7-90 days which is due to horizontal transmission from individuals accountable for neonatal care or environmental sources. [9]

Abdominal distention, bulging fontanelle, body temperature problems, cyanosis, hypoactivity and difficulty sucking are the common symptoms of neonatal sepsis. And *Streptococcus, E. faecalis*, *H. influenzae* type B are most common causes of sepsis. [10] Hence, early finding of sepsis is essential to prevent mortality and morbidity rates in neonates. In this scenario, management of neonatal sepsis influence the use of antimicrobial agents. The gold standard method for diagnosing neonatal sepsis is the blood culture method. All over the world, it is projected that isolation rates on blood culture ranges from 6.7 % to 55.4%. [11]

In our study 25 % of the study subjects were positive for blood culture which are comparable with many other studies conducted in India. [12,13] Low blood culture positivity in our study might be due to the low amount of blood drawn or possibility of infection with anaerobes or presence of fastidious organisms. The total percentage of male population in the present study are 50.08% and the female population accounted for 49.2% which were similar to findings of studies reported from India. [14-16]

Maternal risk factors like Premature Rupture of Membranes (PROM) and Meconium-Stained Amniotic Fluid (MSAF) were present in 10.6% and 13.6% of neonate mothers; prolonged labour was noted in 16.7% mothers and vaginal examinations were made more than 3 times in 15.9% of mothers in the present study. These finding were similar to the study reports of Bodkhe A et al., who reported PROM as the most common risk factor (30%) followed by MSAF (28.3%) and prolonged labour (15%). [17]

Though blood culture positions as benchmark for septicaemia, it takes 48-72 hours for reporting and hence infection rate will be increased if left untreated without antibiotic. In this

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

scenario, a screening test that can diagnose septic neonates rapidly and prevent antibiotic therapy in non-septic neonates is essential.

C reactive protein is an acute-phase protein made in the liver which is used to assess neonatal sepsis due to its easy availability, cost effectiveness and readily available results. In the present study CRP has shown sensitivity of 84.85%, specificity of 75.76%, positive predictive value of 53.85%, negative predictive value of 93.75% and diagnostic accuracy of 78.03% against blood culture. These results were in coordination with the results of Younis S et al. who stated that CRP sensitivity was found out to be 97.3%; specificity of 95.2 %; positive predictive value of 97.3% and negative predictive value of 95.2%.[18]

Another study by Niza Monga et al., stated that the sensitivity and specificity of CRP against blood culture was found to be 85.11% and 43.40% respectively. The positive and negative predictive value was 57.14% and 76.67% respectively. The diagnostic accuracy of CRP against blood culture in detecting neonatal septicaemia was 63%. [19] Abha Gupta and his co-investigators reported in their study that, CRP reports showed sensitivity of 86.7%, specificity of 42%, positive predictive value of 45.5%, negative predictive value of 85% with diagnostic accuracy of 69% against blood culture. [20] Similar study reports of Anshu Singha et al [11] showed sensitivity, specificity, positive predictive value, negative predictive values of CRP as 90.6%, 86.5%, 42% and 99% respectively. [21]

Reported literature suggests that, C-reactive protein has shown significant recital in early diagnosis of neonatal sepsis. Specificity, sensitivity, positive predictive value and negative predictive values demonstrated that CRP can be used as predictive biomarker for sepsis.

Conclusion

Diagnosis of sepsis by CRP aid in minimising the mortality and morbidity in neonates. The specificity and sensitivity of CRP against blood culture reinforce the practice of it in day-to-day life. To conclude, CRP can be used as inflammatory marker for neonatal sepsis.

Acknowledgements: I would like to acknowledge Department of Paediatrics, Sri Devaraj Urs Academy for providing all the requirements for carrying out the study.

Funding Agency: None

References

1. Shah BA, Padbury JF. Neonatal sepsis- An old problem with new insights. Virulence. 2014;5(1):170-78.
2. Odabasi IO, Bulbul A. Neonatal Sepsis. Sisli Etfal Hastan Tip Bul. 2020;54(2):142-158. doi: 10.14744/SEMB.2020.00236
3. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. Lancet Respir Med. 2018;6(3):223-230. doi: 10.1016/S2213-2600(18)30063-8
4. Zea-Vera A, Ochoa TJ. Challenges in the diagnosis and management of neonatal sepsis. J Trop Pediatr. 2015;61(1):1-13. doi: 10.1093/tropej/fmu079.
5. Fair RJ, Tor Y. Antibiotics and bacterial resistance in the 21st century. Perspect Medicin Chem. 2014; 6:25-64. doi: 10.4137/PMC.S14459.
6. Kral JB, Schrottmaier WC, Salzmann M, Assinger A. Platelet Interaction with Innate Immune Cells. Transfus Med Hemother. 2016;43(2):78-88. doi: 10.1159/000444807.

ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 03, 2023

7. Woollett LA, Heubi JE. Fetal and Neonatal Cholesterol Metabolism. [Updated 2020 Jan 4]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK395580/
8. Whitehead RD Jr, Mei Z, Mapango C, Jefferds MED. Methods and analysers for haemoglobin measurement in clinical laboratories and field settings. Ann N Y Acad Sci. 2019;1450(1):147-171. doi: 10.1111/nyas.14124.
9. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. Clin Microbiol Rev. 2014 Jan;27(1):21-47. doi: 10.1128/CMR.00031-13.
10. Minasyan H. Sepsis: mechanisms of bacterial injury to the patient. Scand J Trauma Resusc Emerg Med. 2019 Feb 14;27(1):19. doi: 10.1186/s13049-019-0596-4.
11. Venkatesh M, Flores A, Luna RA, Versalovic J. Molecular microbiological methods in the diagnosis of neonatal sepsis. Expert Rev Anti Infect Ther. 2010 Sep;8(9):1037-48. doi: 10.1586/eri.10.89.
12. Goswami Y, Jadav P, Rathod B. Study on significance of CRP estimation in early diagnosis of neonatal septicemia. IJSR. 2014;3(8):388-90.
13. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. Pak J Med Sci. 2015;31(3):527-31.
14. Patel BM, Basavaraj KN, Antony B. Bacterial spectrum of neonatal septicemia with their antibiogram with reference to various predisposing factors in a tertiary care hospital in Southern India. Ann Trop Med Public Health. 2013; 6:96-99.
15. Garg D, Agrawal N. Aetiology and presentation of neonatal septicaemia at tertiary care hospital of Southern Rajasthan. Int J Med Sci Edu. 2014;1(1):12-20.
16. Sharma A, Kutty CV, Sabharwal U, Rathi S, Mohan H. Diagnostic and prognostic role of CRP and ESR in neonatal septicemia. Indian Pediatr. 1993;30(3):347-50.
17. Bodkhe A, Sarkate P, Tardeja P. Bacterial profile of neonatal sepsis and the role of biomarkers. Int J Recent Trends in Sci Technol. 2014;12(1):141-46.
18. Younis S, Sheikh A, Raza Diagnostic Accuracy of C-Reactive Protein in Neonatal Sepsis A J. Bioresource Manage. 2014;1(1): 33-42.
19. Niza Monga, Nitya Vyas, Babita Sharma. Correlation of C-Reactive Protein and Blood Culture in Neonatal Sepsis. Indian J Neonatal Med Res. 2018; 6(3): PD05-PD08.
20. Gupta A, Rajput D, Sodani S, Mutha A. Comparison of CRP with blood culture in the diagnosis of neonatal septicaemia. Indian J Microbiol Res 2020;7(4):327-329.
21. Singhal A, Rati R, Jaggi N. C-reactive protein as a diagnostic marker of neonatal sepsis in association with blood culture a retrospective study at a tertiary care hospital. Indian J Microbiol Res 2021;8(4):291-296