Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-7, Issue-6 | November-December 2021
Page no- 20-25 | Section- Research Article (Paediatrics)

A Study of Neonatal Septicaemia Based on CRP and Blood Culture and Sensitivity in NICU of Tertiary Care Centre

Shruti Dhale[2], Mohammed Kashif Ali[1]*, , Fouziya Sultana S[3], Kuldip Shimpi[4]

[1]Associate Professor, Department of Paediatrics, Grant Govt Medical College, Mumbai, India.
Email: shruti.millenium@gmail.com,
Orcid ID: 0000-0003-2097-7583
[2]Junior Resident 3, Department Of Paediatrics, Affiliation-Grant Govt Medical College, Mumbai India.
Email: mdkashif8867@gmail.com,
Orcid ID: 0000-0003-0344-8241.
[3]Assistant Professor, Department of Paediatrics, Grant Govt Medical College, Mumbai, India. Email: drfouziyailan@gmail.com, Orcid ID:0000-0002-8655-2302
[4]Junior Resident 3, Department of Paediatrics, Grant Govt Medical College, Mumbai, India.
Email: kuldeepbagul@gmail.com,
Orcid ID:0000-0001-5303-8238

*Corresponding author

Received: 04 June 2021
Revised: 02 August 2021
Accepted: 11 August 2021
Published: 22 October 2021

Abstract

Background: In neonates, septicaemia is one of leading cause of morbidity and mortality. Therefore, timely diagnosis is important to prevent fatal outcome. C-reactive protein is an important biomarker that aids in the timely diagnosis of neonatal septicaemia. **Aim:** The present study was carried out to compare the accuracy of CRP in the diagnosis of neonatal septicaemia with blood culture. **Methods**: Two hundred and one neonates with clinical suspicion of sepsis were prospectively studied over a 6 month period. Blood was obtained from each subject recruited for the qualitative estimation of CRP. Blood culture was used as gold standard for diagnosis of NNS. **Results:** Of the 201 neonates studied, 54 were blood culture positive while 71 were CRP positive. The sensitivity, specificity, positive and negative predictive values of CRP were 92.5%, 97.2%, 92.5%, 97.2% respectively. **Conclusions:** The specificity and sensitivity of CRP against blood culture strengthen the use of this acute phase protein in the diagnosis of neonatal sepsis.

Keywords:- CRP and Blood culture and sensitivity.

INTRODUCTION

Neonatal sepsis (NNS) and neonatal septicaemia are terms that have been used to describe the systemic response to infection and/or isolation of bacteria from the blood stream in the first 28 days of life.[1] Globally, sepsis accounts for 26% of all neonatal deaths with 98% of these deaths occurring in developing countries.[2,3] Adequate and timely diagnosis of NNS remains an important challenge to the clinician. Blood culture is the gold standard for definitive diagnosis but it takes at least 48 hours by which time the infection may have progressed with important consequences on the morbidity and mortality of the neonate,[4] especially if antibiotic treatment is not initiated immediately.[5] Initiation of antibiotic therapy before diagnostic results are available is recommended for neonates with clinical signs or risk factors of sepsis,[6] but because the clinical signs of NNS are often non-specific, empiric antibiotic therapy may result in the

Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-7, Issue-6 | November-December 2021
Page no- 20-25 | Section- Research Article (Paediatrics)

treatment of as many as 30 uninfected neonates for every one who is eventually diagnosed to be infected.[7,8,9] Hence there is need for rapid screening test that can identify infected neonates at the time of initial assessment thus sparing the uninfected ones from unnecessary antibiotic therapy.

C-reactive protein is an acute phase protein which may be useful in the early diagnosis of NNS as it rises as much as a thousand fold within 4 to 6 hours of an inflammatory process.[10,11] As infection is the most likely cause of inflammation in the neonate, CRP has been shown to be useful in the diagnosis of neonatal sepsis. Upon resolution of the inflammation, CRP levels rapidly decline with an elimination half life of 19 hours.[11,12] Thus CRP level is also a useful marker in determining the duration of antibiotic therapy. Unlike blood culture, CRP level is not affected by prior antibiotic therapy,[13] so may be particularly useful in Sub-Saharan Africa where a significant number of neonates may have been given antibiotics before presentation at the hospital.

CRP can be assayed quantitatively or qualitatively. The quantitative method is more widely used in developed countries.[12] It provides rapid, highly sensitive and specific results but requires more time (about 15 to 30 minutes) and is more complex and expensive to perform.[12,14] The test kits may also not be readily available in some health centres in developing countries. The qualitative method provides rapid results within 15 minutes. However, it is less specific but has the advantage of being simple and easier to perform and interpret and as such can be performed at the patients bed side or side laboratory.[14,15] It is also less expensive and requires less skill. The qualitative method may therefore, be more feasible in resource poor centres, where poverty plays a prominent role in disease morbidity and mortality and where there may be no laboratory services or trained man-power for the investigation of neonates with suspected sepsis.

Aims & Objective

Aim of the study was to compare CRP against blood culture in diagnosis of neonatal Sepsis.

MATERIAL AND METHODS

A prospective Study design was used to study on combining use of CRP and blood culture in early diagnosis of neonatal sepsis. This is a hospital based study conducted in tertiary care hospital Mumbai

A prospective study was carried out in the neonatal intensive care unit (NICU) of tertiary care center within a 6 month period from November, 2020 to May 2021. All newborns with clinical suspicion or risk factors for sepsis were consecutively recruited into the study. Sepsis was suspected in the presence of clinical features like fever, respiratory distress, poor feeding, jaundice, hypothermia, convulsion, vomiting, irritability, lethargy and abdominal distension. Risk factors for sepsis included outborn delivery, perinatal asphyxia, preterm delivery, prolonged rupture of membranes, maternal peripartum pyrexia and foul smelling amniotic fluid.

Infants of mothers who had intrapartum antibiotics within 1 week of delivery as well as babies with prior antibiotic therapy for present illness before admission into the SCBU were excluded from the study.

Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-7, Issue-6 | November-December 2021
Page no- 20-25 | Section- Research Article (Paediatrics)

To detect serum CRP levels at or above 6 mg/l, which is considered the lowest concentration of clinical significance.

The results of laboratory investigations and other relevant data such as age, sex, birth weight and gestational age as well as symptoms present and risk factors for sepsis of recruited babies were recorded in a proforma. The results were analysed

- **Inclusion Criteria**
  All newborns who were admitted in NICU where investigation for CRP and Blood culture sensitivity was done to confirm the diagnosis

- **Exclusion Criteria**
  Neonates who had received antibiotics before collection of blood samples having surgical problems, chromosomal or congenital anomalies were excluded from the study.

RESULTS

Of the 201 neonates admitted into the NICU during the period of study. There were 121 (60.1%) males and 80 (39.8%) females with mean gestational age (±SD) of 36.8 weeks (± 3.6) and mean birth weight (±SD) of 2.5 kg (±0.9). 155(77.1%) of the study population had clinical features of sepsis. One hundred and fifty five (77.1%) of the study population had clinical features of sepsis.

Of 201 neonates screened for sepsis, 54 (26.8%) had positive blood culture.

Prevalence of positive C-reactive protein in neonates with suspected sepsis of the 155 neonates with suspected sepsis, 71 (45.8%) had positive CRP.

Proportion of neonates with true positive and negative C-reactive protein using blood culture as gold standard of the 201 neonates studied, 54 (26.8%) had positive blood culture while 147 (73.1%) had negative blood culture. Of the 54 neonates with positive blood culture, 50 (92.5%) had positive CRP (True positive) while 4 (7.4%) had negative CRP (False negative). Of 147 neonates with negative blood culture, 143 (97.2%) had negative CRP (True negative) and 4 (2.7%) had positive CRP (False positive) Sensitivity, specificity, positive and negative predictive values of C-reactive protein.

As shown in [Table 1], the sensitivity, specificity, positive and negative predictive values were 92.5%, 97.2%, 92.5% and 97.2%, respectively.

[Table 2] shows the clinical features suggestive of sepsis. Of the 155 neonates with clinical features of sepsis, the most common was respiratory distress in 51 (32.9%) of them, followed by fever in 25 (16.1%). The CRP correctly identified all (100%) of the neonates with positive blood culture who presented with apnoea, vomiting and lethargy.

As shown in [Table 3], of the 201 neonates with predisposing factors for sepsis, the most common was PROM in 37 (39.3%) of them followed by prematurity (28.7%).

As shown in [Table 4], of the 54 neonates with positive blood culture, the most common organism isolated was Group B streptococcus in 11 (20.3%), followed by Escherichia coli(18.5%). The CRP was able to correctly identify all cases (100.0%) of neonatal sepsis caused by Listeria, klebsiella, Enterococcus spp, Staphylococcus epidermidis and Streptococcus spp.

Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-7, Issue-6 | November-December 2021
Page no- 20-25 | Section- Research Article (Paediatrics)

Table 1: Sensitivity, Specificity, Positive and Negative Predictive Values of C-reactive protein using blood culture as gold standard.

Parameter	Formulae Used	Result (%)
Sensitivity	50	92.5%
	50 + 4	
Specificity	143	97.2%
	143 + 4	
Positive predictive value	50	92.5%
	50+ 4	
Negative predictive value	143	97.2%
	143 + 4	

Table 2: Evalution of CRP according to clinical features of sepsis

Clinical features	Total n = 155		Positive blood culture within clinical feature		Positive CRP within positive blood culture	
	No	%	No	%	No	%
Fever	25	16.1	13	52	18	100
Respiratory distress	51	32.9	27	52.9	25	92.5
Jaundice	24	15.4	8	33.3	8	100
Poor suck	7	4.5	5	71.4	5	100
Apnoea	5	3.2	2	40	3	100.0
Hypothermia	6	3.8	4	66.6	4	100
Convulsion	9	5.8	5	55.5	6	100
Vomiting	4	2.5	2	50	3	100.0
Irritability			6	60.0	5	83.3
Lethargy	24	15.4	16	66.6	16	100.0

Table 3: Evaluation of CRP according to predisposing factors for sepsis

Predisposing factors	Total n = 94		Positive blood culture within predisposing factor		Positive CRP within positive blood culture	
	No	%	No	%	No	%
Perinatal Asphyxia	11	11.7	3	27.2	3	100
Prolonged Rupture of membranes	37	36.9	32	32.0	24	75.0
Prematurity	27	28.7				
Foul smelling amniotic fluid	11	11.7	7	63.6		

Table 4: Evaluation of CRP in the neonates with proven sepsis

Organisms isolated	Total n = 54		Positive CRP within positive blood culture	
	No	%	No	%
GROUP B streptococcus	11	20.3	11	100
Staphylococcus aureus	3	5.5	3	100
Escherichia coli	10	18.5	10	100
Gram negative bacilli	3	5.5	3	100
Pseudomonas aerugenosa	2	3.7	2	100

Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-7, Issue-6 | November-December 2021
Page no- 20-25 | Section- Research Article (Paediatrics)

Candida	1	1.8	1	100
Enterococcus spp	5	9.2	5	100
Staphylococcus epidermidis	4	7.4	4	100
Streptococcus spp	9	16.6	9	100
Listeria	3	5.5	3	100
Acinetobacter	1	1.8	1	100
Klebsiella	2	3.7	2	100

DISCUSSION

The commonest organism isolated was klebsiella pneumonia followed by staphylococcus areus.

Among the clinical features of neonatal sepsis in the present study, CRP performance was highest in neonates with Respiratory distress, fever, apnoea, vomiting, hypothermia and lethargy among the risk factors for neonatal sepsis, CRP performance was highest in neonates born to mothers with PROM in 37 (39.3%) of them followed by prematurity (28.7%).

In the present study, CRP identified 54 out of 54 neonates who had culture-proven sepsis, with sensitivity of 92.5% and a negative predictive value of 97.2%, implying that neonates with suspected sepsis will be correctly diagnosed using CRP. This is much too high to base the decision to start empirical antibiotics for a neonate with suspected sepsis. Particularly as CRP was only tested to predict positive blood culture which may represent only a proportion of neonates with sepsis, especially if the patient had been on antibiotic therapy before presentation. A negative CRP, however can be useful in aiding the decision to discontinue antibiotics especially if the neonate has no clinical feature of sepsis. CRP can be a useful guide in making a decision to discontinue antibiotic therapy, thus facilitating early discharge with significantly reduced cost, complications of treatment and family anxiety.

Several authors in different settings have reported different performances for usefulness of CRP in the diagnosis and management of neonatal sepsis. This is probably due to the quantitative and qualitative sampling methods and qualitative method is used in the present study.

CONCLUSIONS

The qualitative method of CRP estimation, which is a rapid, inexpensive and simple test to perform, was found to have sensitivity, specificity and NPV of 92.5%, 97.2% and 97.2%, respectively. This implies that CRP would correctly identify neonates with sepsis.

The C-reactive protein may therefore, help in the early detection of neonatal sepsis while awaiting blood culture results. CRP may also be invaluable in the management of neonatal sepsis in resource poor centres where facilities for blood culture may not be readily available.

REFERENCES

1. Ershad M, Mostafa A, Dela Cruz M, Vearrier D. Neonatal Sepsis. Curr Emerg Hosp Med Rep. 2019;7(3):83-90. doi:10.1007/s40138-019-00188-z
2. Lawn JE, Cousens S, Zupan J; Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: when? Where? Why? Lancet. 2005;365(9462):891-900. doi: 10.1016/S0140-6736(05)71048-5.

3. Omene JA. Neonatal septicaemia in Benin City, Nigeria. A review of 74 cases. Trop Geogr Med. 1979;31(1):35-9.
4. Buttery JP. Blood cultures in newborns and children: optimising an everyday test. Arch Dis Child Fetal Neonatal Ed. 2002;87(1):F25-8. doi: 10.1136/fn.87.1.f25.
5. Høgåsen AK. Nye muligheter for diagnostikk og behandling ved neonatal sepsis [New diagnostic and therapeutic possibilities in neonatal sepsis]. Tidsskr Nor Laegeforen. 1997 10;117(27):3957-60.
6. Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010;59(RR-10):1-36.
7. Hammerschlag MR, Klein JO, Herschel M, Chen FC, Fermin R. Patterns of use of antibiotics in two newborn nurseries. N Engl J Med. 1977;296(22):1268-9. doi: 10.1056/NEJM197706022962206. PMID: 859516.
8. Philip AG, Hewitt JR. Early diagnosis of neonatal sepsis. Pediatrics. 1980;65(5):1036-41.
9. Gerdes JS, Polin RA. Sepsis screen in neonates with evaluation of plasma fibronectin. Pediatr Infect Dis J. 1987;6: 443-446. 10.1097/00006454-198705000-00005.
10. Vigushin DM, Pepys MB, Hawkins PN. Metabolic and scintigraphic studies of radioiodinated human C-reactive protein in health and disease. J Clin Invest. 1993;91(4):1351-7. doi: 10.1172/JCI116336.
11. Sproston NR, Ashworth JJ. Role of C-Reactive Protein at Sites of Inflammation and Infection. Front Immunol. 2018;9:754.
12. Clyne B, Olshaker JS. The C-reactive protein. J Emerg Med. 1999;17(6):1019-25. doi: 10.1016/s0736-4679(99)00135-3.
13. Bomela HN, Ballot DE, Cory BJ, Cooper PA. Use of C-reactive protein to guide duration of empiric antibiotic therapy in suspected early neonatal sepsis. Pediatr Infect Dis J. 2000;19(6):531-5. doi: 10.1097/00006454-200006000-00008.
14. Dinnes J, Deeks J, Kunst H, Gibson A, Cummins E, Waugh N, et al. A systematic review of rapid diagnostic tests for the detection of tuberculosis infection. Health Technol Assess. 2007;11(3):1-196. doi: 10.3310/hta11030. PMID: 17266837.
15. Mustafa S, Farooqui S, Waheed S, Mahmook K. Evaluation of c-reactive protein as early indicator of blood culture positivity in neonates. Pak J Med Sci. 2005, 21: 69-73.

Source of Support: Nil, Conflict of Interest: None declared