

Original article

Correlation of CRP and Blood Culture in evaluation of Neonatal Sepsis

Sumit Bhatia^{1*}, Chaman R. Verma², Balvir S. Tomar², Bhagwan S. Natani³, Pardeep Goyal³, Ankit Agarwal¹

¹Resident, Department of Pediatrics, National Institute of Medical Sciences and Research, Shobha Nagar, Jaipur, Rajasthan, India

²Professor, Department of Pediatrics, National Institute of Medical Sciences and Research, Shobha Nagar, Jaipur, Rajasthan, India

³Asst. Professor, Department of Pediatrics, National Institute of Medical Sciences and Research, Shobha Nagar, Jaipur, Rajasthan, India

*Corresponding author: Dr. Sumit Bhatia

ABSTRACT

Background: Optimal diagnosis and treatment strategies are difficult to define for Neonatal Septicemia. Clinical diagnosis is difficult because of subtle and non-specific features. Mortality and morbidity due to sepsis can be prevented with early diagnosis, rational antimicrobial therapy and aggressive supportive care. Blood culture which is considered as gold standard for diagnosis is costly and time consuming. Therefore, present study was intended to compare and evaluate the CRP results with the blood culture reports and to provide a feasible, rapid and a relative economic method to diagnose neonatal septicemia.

Methods : This Prospective Observational study was done in the Neonatal Intensive Care Unit of National Institute of Medical Sciences and Research, Shobha Nagar, Jaipur from 1st January 2015 to 30th June 2016. 90 cases who were admitted with clinical suspicion of neonatal sepsis were included in this study. Neonates who received antibiotics before admission and/or with congenital malformations were excluded from the study. Blood culture was sent for all neonates. CRP was done qualitatively by rapid slide latex agglutination method. Data analysis was carried out using computer software IBM SPSS and a p value of <0.05 taken as statistically significant. **Results :** We observed that 53.33% cases of neonatal sepsis were culture positive. CRP came out as a good predictor of sepsis with sensitivity, specificity, PPV, NPV and diagnostic accuracy of 81.25%, 42.86%, 61.90%, 66.67% and 63.33% respectively.

Conclusion: Serum CRP can therefore be employed as a rapid screening test for neonatal sepsis.

Keywords : Neonatal Sepsis, CRP, Blood Culture

INTRODUCTION

Neonatal Septicemia is defined as a clinical syndrome which occurs in the first 28 days of life is characterized by symptomatic systemic illness due to infectious agents.¹ It arises from various types of infections including those of the skin, lungs, abdomen and urinary tract.² It comprises systemic infection in newborn including Septicemia,

pneumonia, meningitis, osteomyelitis, arthritis, and urinary tract infection of the newborn. Sepsis in neonates is the worldwide major direct cause of neonatal deaths constituting 36% of neonatal deaths. Neonatal Septicemia with its high incidence and its grave prognosis, in spite of adequate treatment with modern antibiotics, has been a challenge for all times. Optimal diagnosis and treatment strategies are

difficult to define. Clinically diagnosing neonatal sepsis is a challenge because of subtle and non-specific signs and symptoms. Mortality and morbidity due to sepsis can be prevented with early diagnosis, rational antimicrobial therapy and aggressive supportive care.

Blood culture which is considered as gold standard for diagnosis is costly and time consuming (preliminary results are delayed for at least 48 hours). Moreover, the yield of blood culture is between 30%-70%, hence some neonates with sepsis go undetected. Various studies have shown that raised CRP had high sensitivity, specificity, positive and negative predictive value for neonatal sepsis. Detection of raised CRP in blood can be done rapidly by cheap and easily available kits. Since India is a developing country with high neonatal morbidity and mortality, there is requirement of rapid and economic diagnostic method to raise our medical health care levels to a next step. Therefore, present study was intended to compare and evaluate the CRP results with the blood culture reports and to provide a feasible, rapid and a relative economic method to diagnose neonatal Septicemia even at basic health care level.

AIMS & OBJECTIVES

1. To determine the sensitivity and specificity of CRP in neonates with sepsis in comparison with blood culture.
2. To determine the predictive value of CRP as an indicator of neonatal sepsis in comparison with blood culture.
3. To establish a correlation of CRP versus blood culture in the evaluation of neonatal sepsis.

MATERIALS & METHODS

This observational study was conducted in the Neonatal Intensive Care Unit of National Institute of Medical Sciences and Research, Jaipur. With

prevalence of 6% and margin of error of 5% and confidence level of 95%, a sample size of 90 is calculated.

The blood sample collected from 90 cases having clinical suspicion of neonatal sepsis admitted in Neonatal intensive care unit were analyzed after obtaining written informed consent from the parents of the neonates.

Neonates who received antibiotics before admission and neonates with congenital malformations were excluded from the study.

Thorough history along with clinical findings were recorded in the Performa.

All neonates who were clinically symptomatic were screened using CRP done by the qualitative method by rapid slide latex agglutination method using diagnostic kits supplied by Span Diagnostics Limited. At the same time blood culture were done by conventional methods. Relevant to clinical situation CSF, Urine analysis and swabs infective focus were taken.

C-Reactive protein (CRP) > 6ug/ml was considered as a positive test. Empirical antibiotic therapy was started according to antibiotic guidelines in the NICU, if CRP was positive, awaiting the culture reports.

The duration of treatment and duration of hospital stay was noted in all neonates.

Data analysis was carried out using computer software IBM SPSS v 17. Proportions were compared using Chi-square test of significance. p value of less than 0.05 was accepted to be statistically significant in the above given test.

RESULTS

This observational study was conducted in Department of Paediatrics, National Institute of Medical Sciences & Research, Jaipur from 1st January 2015 to 30th June

2016. Blood samples of 90 neonates who were clinically suspected to have neonatal sepsis and were admitted in NIMS Hospital, Jaipur were analyzed. 42 (46.67%) of these neonates were culture negative and

the rest 48 (53.33%) were culture positive. Demographic characteristics of the neonates are presented in Table 1.

Table 1: Demographic characteristics of neonates enrolled in the study

	N	%
Place of Delivery		
Inborn	43	47.78
Outborn	47	52.22
Mode of Delivery		
Normal	72	80.00
Instrumentation	8	8.89
LSCS	10	11.11
Sex		
Male	60	66.67
Female	30	33.33
Birth Weight		
Normal	24	26.67
LBW	48	53.33
VLBW	18	20.00
Risk Factors of sepsis		
H/o Birth Asphyxia	43	47.78
H/o PROM>18hrs	25	27.78
H/o Maternal Fever	13	14.44
H/o Foul smelling liquor	18	20.00

48 (53.33%) neonates had early onset sepsis whereas 42 (46.67%) had late onset sepsis. Statistically insignificant higher proportion of early onset sepsis (54.27%) was culture positive compared to late onset sepsis (52.38%). Clinical diagnoses of neonates are presented in Table 2.

Table 2: Clinical diagnosis of neonates enrolled in the study

Diagnosis	N	%
Infective diarrhea	5	5.56
Meningitis	14	15.56
NEC	1	1.11
Pneumonia	32	35.56
Septicemia	35	38.89
Umbilical sepsis	2	2.22
UTI	1	1.11
Total	90	100.00

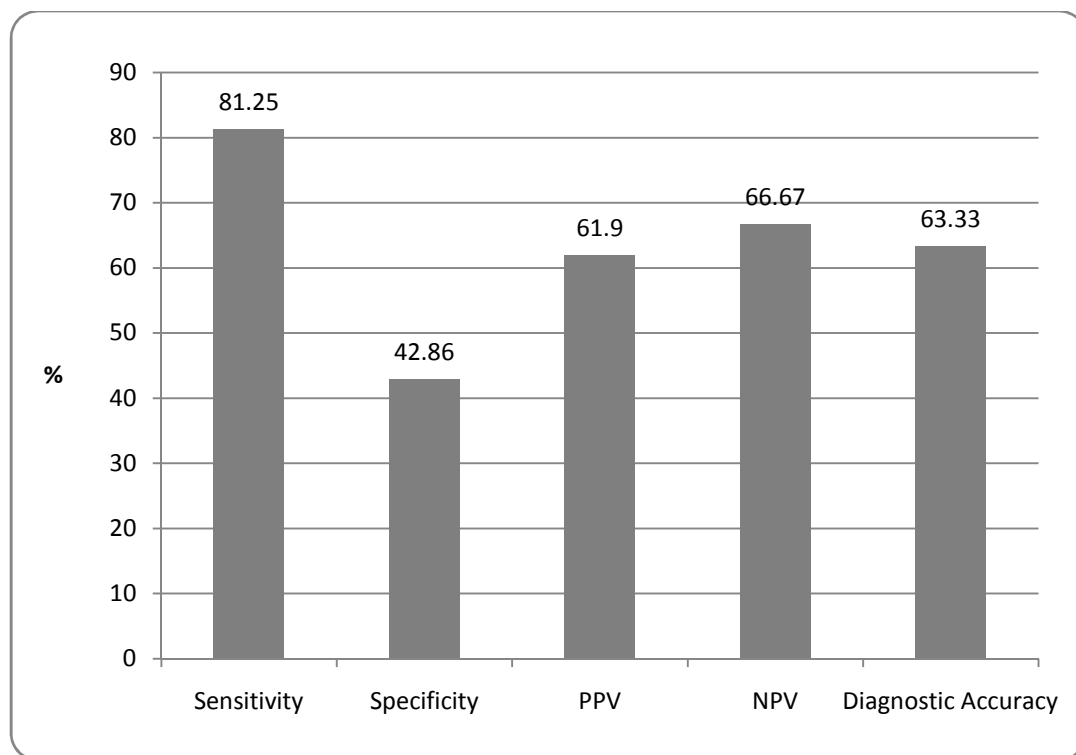
Pneumonia was the most common presentation in early onset sepsis (64.58%), followed by septicemia (33.33%). Septicemia (45.23%) followed by pneumonia (26.19%) were the commonest presentation in late onset sepsis. Correlation of CRP with blood culture status is tabulated in Table 3. Out of 48 culture positive cases, 39 cases (81.25%) were CRP positive and shows a significant relation with culture positivity (Fisher Exact Test, P = 0.020).

Table III: Correlation of CRP with blood culture status

CRP	Blood Culture				Total	
	Negative		Positive			
	No.	%	No.	%	No.	%
Negative	18	42.86	9	18.75	27	30.00
Positive	24	57.14	39	81.25	63	70.00
Total	42	100.00	48	100.00	90	100.00

CRP showed 81.25% sensitivity, 42.86% specificity, PPV of 61.90, NPV of 66.67 and diagnostic accuracy of 63.33 as shown in Figure 1.

Figure I: Sensitivity, specificity, positive predictive value and negative predictive values of CRP



Out of 48 culture positive cases, a significant (Fisher Exact Test, P = 0.033) 36 cases (75.00%) were discharged, 10 cases (20.83%) died and rest 2 left LAMA. Final outcome of all the neonates with respect to their culture status have been tabulated in Table 4.

Table IV: Outcome of the neonates with respect to their culture status

Outcome	Blood Culture				Total	
	Negative		Positive		No.	%
	No.	%	No.	%		
Died	2	4.76	10	20.83	12	13.33
Discharged	37	88.10	36	75.00	73	81.11
LAMA	3	7.14	2	4.17	5	5.56
Total	42	100.00	48	100.00	90	100.00

DISCUSSION

Neonatal septicemia with its high incidence and its grave prognosis has been a challenge for all times. Clinical diagnosis is non-specific. Blood culture, the gold standard for diagnosis, is costly and preliminary results are delayed. Studies have indicated that raised CRP could be used a marker for sepsis due to its high sensitivity, specificity, positive predictive value and negative predictive value. This study was done with the intention to compare and evaluate the CRP results with the blood culture reports and to provide a feasible, rapid and a relative economic method to diagnose neonatal septicemia even at basic health care level.

In the present study 53.33% of the neonates with clinical suspicion of sepsis were found to be culture positive. Joshi et al (2000) reported that 25% of sepsis suspected neonates were culture positive in their study on 1326 patients.³ Gandhi et al (2012) found culture positivity in 45% of their studied 286 neonates with clinical sepsis.⁴ Shaw et al (2012) in their study in 265 Nepalese neonates reported culture positivity in 37.76% of the clinically septic neonates.⁵ Raha et al (2014) reported culture positivity in only 8.9% of the 720 Bangladeshi neonates studied by them.⁶ In the South African study by West et al (2012) on 420 septic neonates, culture positivity was found in 43.1% of the subjects.⁷ This wide range in incidence of culture positive neonatal sepsis reported worldwide could be as a result of lack of standard definition of clinical sepsis across different centers, lack of proper information about antibiotics received prior to blood culture and difference in culture technique.

This study reported that a significant 81.25% of culture positive septic neonates were CRP positive, hence having the same sensitivity of 81.25%. Berger

et al (1995) in their study reported 75% sensitivity.⁸ Ayazi et al (2007) found the sensitivity of CRP to be 67%,⁹ Gandhi et al (2012) reported it to be 100%.⁴ West et al (2012) found CRP positive in 74% neonates with culture positivity, hence the same sensitivity.⁷ Goswami et al (2014) similarly reported that 91% of their culture positive neonates also had CRP positivity hence a sensitivity of 91%.¹⁰ Younis et al (2014),¹¹ Hisamuddin et al (2015)¹² and Marwa et al (2016)¹³ reported a sensitivity of 97.3%, 76.92% and 91% respectively of CRP for diagnosis of neonatal sepsis.

This study we found that 42.86% neonates with culture negative was also CRP negative has a sensitivity of 42.86%. Similar studies done throughout the world have given a wide range of specificities. Berger et al (1995) reported the Specificity of CRP to be 86%.⁸ Nuntnarumit et al (2002) reported it to be 94%.¹⁴ Ayazi et al (2007),⁹ Gandhi et al (2012),⁴ West et al (2012),⁷ Shaw et al (2012),⁵ Goswami et al (2014),¹⁰ Younis et al (2014),¹¹ Hisamuddin et al (2015)¹² and Marwa et al (2016)¹³ in their studies reported the specificity of CRP for diagnosis of neonatal sepsis to be 80%, 75%, 74.1%, 49.7%, 94%, 95.2%, 53.49% and 100% respectively.

In this study we reported that 61.90% of neonates with CRP positive also had blood culture positive hence giving a positive predictable value for CRP of 61.90%. Berger et al (1995) reported the positive predictive value for CRP to be 32%.⁸ Nuntnarumit et al (2002) reported it to be 91.6% in their study.¹⁴ Ayazi et al (2007),⁹ West et al (2012),⁷ Younis et al (2014)¹¹ and Hisamuddin et al (2015)¹² reported positive predictable value for CRP to be 24%, 68.4%, 97.3% and 80% respectively.

The present study reported that 66.67% of neonates with CRP negative also had blood culture negative hence giving a negative predictable value for CRP of 66.67%. Nuntnarumit et al (2002) reported negative predictable value to be 100% in their study.¹⁴ Ayazi et al (2007) in their study reported it to be 96%.⁹ West et al (2012),⁷ Goswami et al (2014),¹⁰ Younis et al (2014)¹¹ and Hisamuddin et al (2015)¹² reported negative predictable value for CRP to be 79%, 91.2%, 95.2% and 48.94% respectively.

In 63.33% of the cases with CRP correctly coincided with the culture results hence giving a diagnostic accuracy of 63.33%. Studies mentioning the same are scarce. Hisamuddin et al (2015) reported diagnostic accuracy to be 70.07%.¹²

Different studies have used different methods and different cut off value to denote CRP positivity. We

used rapid slide latex agglutination qualitative method for determination of CRP and used a cut off value of 6µg/ml for CRP positivity. This difference in method of CRP estimation and cut off value have resulted in such varied result in Sensitivity, specificity, PPV and NPV. Hence, it is difficult to compare these results.

The main limitation of this study is that we did not consider other cultures such as urine, CSF and surface culture to determine sepsis. Further this study was also limited by its small sample size.

CONCLUSION

With sensitivity, specificity, PPV, NPV and diagnostic accuracy of 81.25%, 42.86%, 61.90%, 66.67% and 63.33% respectively CRP correlates well with Blood culture results and can be used as an alternative to blood culture for diagnosis of neonatal sepsis.

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