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Correlation between CRP and Blood Culture in Evaluation of Neonatal Sepsis.

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ABSTRACT

Background: Ideal diagnosis and treatment strategies are difficult to define for Neonatal Septicemia and vary across the institutions. Clinical diagnosis is difficult because of early non-specific features. Mortality and morbidity due to sepsis can be prevented with early diagnosis and rational timely management. Non specific markers include CRP, leucopenia, Absolute Neutrophil Count, micro ESR (μ-ESR) , Procalcitonin etc. Amongst these CRP is easily available at many labs and is cost effective. Blood culture is considered as gold standard for diagnosis but it is costly and time consuming. Therefore, present study was done 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 Pediatrics and Microbiology Departments of Government Medical College, Amritsar from 1st January 2017 to 31st December 2017. 270 neonates admitted with clinical suspicion of neonatal sepsis were included in this study. Neonates who received antibiotics prior to admission, with alternative diagnosis and/or with congenital malformations were excluded from the study. Blood culture was sent before starting antibiotics. 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 50.74% 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 83.9%, 34.5%, 56.93%, 67.64% and 66.78% respectively. **Conclusion:** Serum CRP can therefore be employed as a rapid screening test for neonatal sepsis.

Keywords: Neonatal Sepsis, CRP, Blood Culture.

INTRODUCTION

Sepsis in neonates is the worldwide major direct and indirect cause of neonatal deaths .Neonatal Septicemia is defined as a clinical syndrome which occurs in the first 28 days of life and is defined by systemic inflammatory response syndrome (SIRS) due to infectious agents mostly bacterial.[1] It can be divided into early onset neonatal sepsis which occurs within 7 days of life and late onset neonatal sepsis which occurs from day 8 to 28. It can arise from focus of infections which can be present in any part of body including skin, lungs, abdomen and urinary tract.[2] It can comprise systemic infection in newborn including septicemia, pneumonia, meningitis, osteomyelitis, arthritis, and urinary tract infection of the newborn. Optimal diagnosis and treatment strategies for neonatal septicemia are difficult to define. Clinically diagnosing neonatal sepsis is a challenge because of subtle and nonspecific signs and symptoms. Mortality and morbidity due to sepsis can be prevented with early diagnosis and rational management.

Blood culture is considered as gold standard investigation for diagnosis but it is costly and time consuming as 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. Non specific markers for sepsis include CRP, leucopenia, absolute neutrophil count, micro ESR and Procalcitonin amongst others. There is no reliable method to distinguish babies that are actually infected from those with suspected sepsis the gold standard method is by blood culture results after 48 to 72 hours of incubation,[3] by which time 98% of cultures ultimately yielding an organism will be positive.[3] CRP in blood can be done rapidly by cheap and easily available kits. Various studies have shown that raised CRP had high sensitivity, specificity, positive and negative

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predictive value for neonatal sepsis. In a developing country such as India with high neonatal morbidity and mortality, there is requirement of rapid and economic diagnostic method so that management can be started at the earliest. 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 secondary health care level where facilities for blood culture are not available.

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 AND METHODS

This observational study was conducted in the Departments of Pediatrics and Microbiology of Government Medical College, Amritsar. The blood samples collected from 270 cases having clinical suspicion of neonatal sepsis admitted in neonatal ward were analyzed for CRP and blood culture in the Microbiology laboratory after obtaining written informed consent from the parents of the neonates. Neonates who received antibiotics before admission, neonates with alternative diagnosis and neonates with congenital malformations were excluded from the study. Thorough history along with clinical findings were recorded in the Performa. CRP was done by the qualitative method by rapid slide latex agglutination method. At the same time blood culture was collected by conventional methods in BHI agar medium and sent to the microbiology lab for culture and sensitivity analysis. CSF, urine analysis and swabs from infective focus were taken as per clinical case. C-Reactive protein (CRP) > 6ug/ml was considered as significantly positive. Empirical antibiotic therapy was started according to hospital protocol after collecting the blood culture. The duration of treatment and hospital stay were 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, Government Medical College, Amritsar, from 1st January 2017 to 31st December 2017. Blood samples of 270 neonates who were clinically suspected to have neonatal sepsis and were admitted in Pediatric unit of Government Medical College, Amritsar, were analyzed. 133(49.25%) of these neonates were culture negative and the rest 137 (50.74%) were culture positive.

Demographic characteristics of the neonates are presented in [Table 1].

Table 1: Demographic characteristics of neonates enrolled in the study

	Number	Percentage
Place of Delivery		
Inborn	122	45.19
Outborn	148	54.81
Mode of delivery		
Normal	212	78.51
Instrumentation	12	4.4
LSCS	46	17
Sex of Baby		
Male	148	54.81
Female	122	45.18
Birth weight		
Normal	85	31.48
LBW	130	48.14
VLBW	55	20.3
Risk factors for sepsis		
Prematurity	48	17.77
Birth asphyxia	66	24.44
PROM>18 hours	98	36.29
Maternal fever	33	12.22
Foul smelling liquor	25	9.2

168 (62.22%) neonates had early onset sepsis whereas 102 (37.78%) had late onset sepsis.

Clinical diagnosis of neonates are presented in [Table 2].

Table 2: Clinical diagnosis of neonates enrolled in the study

Diagnosis	N	%
Infective diarrhea	12	4.44
Meningitis	40	14.81
NEC	3	1.11
Pneumonia	87	32.22
Septicemia	118	43.7
Umbilical sepsis	7	2.5
UTI	3	1.11
Total	270	100

As shown in above table, septicemia (43.7%) followed by pneumonia (32.22%) were the commonest presentation in sepsis. Majority of neonates were having early onset sepsis (54.27%) as compared to late onset sepsis (45.73%).

Correlation of CRP with blood culture status is tabulated in [Table 3].

Table 3: Correlation of CRP with blood culture status.

CRP	Blood Culture				Total	
	Negative		Positive			
	No.	%	No.	%	No.	%
Negative	46	34.5	22	16	68	25.18
Positive	87	65.41	115	83.9	202	74.81
Total	133	100	137	100	270	100

Out of 137 culture positive cases, 115 cases (83.90%) were CRP positive and showed significant relation with culture positivity (Fisher Exact Test, P = 0.020).

As shown in [Table 3], CRP showed 83.9% sensitivity, 34.5% specificity, PPV of 56.93, NPV of 67.64 and diagnostic accuracy of 66.78%.

Final outcome of all the neonates have been tabulated in [Table 4].

Table 4: Outcome of the neonates with respect to their culture status

Outcome	Blood culture				Total	
	Negative		Positive			
	No.	%	No.	%	No.	%
Died	12	9	28	20	40	14.81
Discharged	115	86.46	103	75.18	218	80.74
Lama	6	4.5	6	4.3	12	4.44
Total	133	100	137	100	270	100

Out of 137 culture positive cases, 103 cases (75.18%) were discharged, 28 cases (20.00%) died and rest 6 cases left against medical advice (LAMA).

DISCUSSION

Neonatal septicemia has high incidence and due to its grave prognosis is a great challenge for all clinicians. Clinical diagnosis is non-specific. Blood culture which is considered the gold standard for diagnosis, is costly and results are often delayed. Studies have indicated that raised CRP could be used an early marker for sepsis due to its high sensitivity, specificity, positive predictive value and negative predictive value.

This study was done with the aim to compare the CRP results with the blood culture and to provide a feasible, rapid and a relative economic method to diagnose neonatal septicemia. In the present study 50.74% of the neonates with clinical suspicion of sepsis were found to be culture positive. In the study done by Joshi et al,[4] it was found that 25% of sepsis suspected neonates were culture positive. Gandhi et al,[5] found culture positivity in 45% of their studied 286 neonates with clinical sepsis while Shaw et al,[6] reported culture positivity in 37.76% of the clinically septic neonates .Chan DK and colleagues gave a cutoff CRP level of 7 mg/L. The sensitivity, specificity, negative and positive predictive values were 56%, 72%, 71% and 57% respectively.[7] In a study done in South Africa by West et al,[8] on 420 septic neonates, culture positivity was found in 43.1% of the subjects . In the study done by Bhatia et al,[16] 53.33 percent of neonates who were clinically suspected to be septic were found to be blood culture positive. This wide range in incidence of culture positive neonatal sepsis reported from different centres can due to lack of standard definition of clinical sepsis, lack of proper information about antibiotics received prior to collection of blood culture and difference in collection of specimens and culture techniques.

This study reported that a significant 83.9% of culture positive neonates were CRP positive, also meaning sensitivity of 83.9%. Berger et al9 (1995) in their study reported 75% sensitivity. Ayazi et al,[10] (2007) found the sensitivity to be 67%. Gandhi et al,[5] (2012) reported it to be 100%. West et al,[8] (2012) found sensitivity to be 74%. Bhatia S et al.[16] reported the sensitivity of CRP with blood culture to be 81.25%. Oswami et al,[11] (2014) similarly reported that 91% of their culture positive neonates also had CRP positivity hence a sensitivity of 91%. Younis et al,[12] Hisamuddin et al,[13] and Marwa et al14 reported a sensitivity of 97.3%, 76.92 % and 91% respectively of CRP for diagnosis of neonatal sepsis.

In this study we found that 42.86% neonates with culture negative was also CRP negative hence a specificity of 34.5%. Similar studies done throughout the world have given a wide range of specificities. Berger et al,[9] reported the Specificity of CRP to be 86%. Bhatia S,[16] in their study found specificity to be 42.86%. Nuntnarumit et al,[15] reported it to be 94%. Ayazi et al,[10] Gandhi et al,[5] West et al,[8] Shaw et al,[6] Goswami et al,[11] Younis et al,[12] Hisamuddin et al.[13] and Marwa et al.[14] 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 56.93% of neonates with CRP positive also had blood culture positive hence giving a positive predictable value for CRP of 56.93%. Berger et al,[9] reported the positive predictive value for CRP to be 32%. Nuntnarumit et al,[15] reported it to be 91.6% in their study. Ayazi et al,[10] West et al,[8] Younis et al,[12] and Hisamuddin et al,[13] reported positive predictable value for CRP to be 24%, 68.4%, 97.3% and 80% respectively. Bhatia S et al,[16] in their study found positive predictive value to be 61.90% .

The present study reported that 67.64% of neonates with CRP negative also had blood culture negative hence giving a negative predictable value for CRP of 66.67%. Nuntnarumit et al,[15] reported negative predictable value to be 100% in their study. Ayazi et al,[10] in their study reported it to be 96%. West et al,[8] Goswami et al,[11] Younis et al,[12] and Hisamuddin et al,[13] reported negative predictable value for CRP to be 79%, 91.2%, 95.2% and 48.94% respectively. In the study done by Bhatia S et al,[16] it was found that negative predictive value was 66.667%. In 66.78% of the cases with CRP correctly coincided with the culture results hence giving a diagnostic accuracy of 66.78%. Hisamuddin et al,[13] reported diagnostic accuracy to be 70.07%. In the study done by Bhatia S,[16] diagnostic accuracy was found out to be 63.33%.

CONCLUSION

The present study showed that CRP showed 83.9% sensitivity, 34.5% specificity, PPV of 56.93, NPV of

67.64 and diagnostic accuracy of 66.78% respectively with blood culture results and therefore can be used as an alternative to blood culture for diagnosis of neonatal sepsis in resource limited settings.

LIMITATIONS.

Different studies have used different methods and different cut off value to denote CRP positivity. The 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 other limitation of this study is that we did not consider other cultures such as urine, CSF and surface culture to determine sepsis.

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