ORIGINAL ARTICLE

UTILITY OF C REACTIVE PROTEIN AS INFLAMMATORY MARKER IN EARLY DIAGNOSIS OF NEONATAL SEPTICAEMIA: A CROSS SECTIONAL STUDY

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ABSTRACT

Introduction: Evaluation of tests used in diagnosis of neonatal sepsis is important. Infection can present very serious threat to the baby. In such cases, it will be urgent need to know whether the baby has sepsis so as to institute treatment as quickly as possible. C-reactive protein (CRP) is a very good inflammatory marker. CRP is helpful in early diagnosis of neonatal septicaemia, particularly in remote health care centres where there is no availability of well equipped laboratory setup for blood culture.

Methods: This study was conducted between 1st Jan. 2011 to 30th June 2011 at SMIMER Medical College Surat, Gujarat, INDIA. In this study, we selected 286 clinically suspected cases of neonatal septicaemia for screening by CRP.

Result: Out of 286 cases, 168 showed positive CRP and 130 cases showed positive blood culture. The predominant organisms were *Klebsiella* species followed by *Pseudomonas* species. CRP test showed 100.0% sensitivity and 75% specificity, considering Blood culture as gold standard method.

Conclusion: Blood culture reports are available only after 48-72 hours and this facility is available only in well-equipped centres, CRP can be use as inflammatory marker in early diagnosis of neonatal septicaemia.

Key Words: CRP, C reactive protein, Neonatal septicaemia, Blood culture.

INTRODUCTION

C-reactive protein (CRP) is a long-established marker of sepsis. In 1930, Tillet and Francis identified, in the sera of patients with pneumonia, the capacity to precipitate polysaccharide fractions, designated as fraction C, from *Streptococcus pneumoniae*[1]. This property quickly disappeared as patients recovered and was not identified in healthy volunteers. When the cause of this reaction was identified as a protein, it was named CRP. The "acute phase" designation was introduced to classify acutely ill patients with infection whose sera were CRP positive. Since then, several other acute phase proteins have been described. C-reactive protein binds to several polysaccharides and peptido-polysaccharides present in bacteria, fungi and parasites in the presence of calcium. These complexes activate the classical complement pathway, acting as opsonins and promoting phagocytosis. Together with complement components, CRP is the only acute phase protein directly involved in the clearance of micro-organisms.[2]

Neonatal septicaemia even today constitutes a significant cause of neonatal mortality in our country. Neonates are particularly vulnerable to infections because of weak immune barrier. Moreover, several risk factors have been identified both in the neonates and in the mothers making them susceptible to infections. Blood stream infections have been quoted as the most common infections in this neonatal age group. A very wide spectrum of organisms has been described for cases of neonatal septicaemia and this spectrum is subject to geographical alterations.[3] In many cases, clinical diagnosis of neonatal septicaemia is very difficult. Definite diagnosis of septicaemia depends on positive blood culture, which takes around 48-72 hrs. CRP level is a very good marker for inflammatory processes. CRP is synthesised within six to eight hours of exposure to an infective process or tissue damage. It has a half-life of 19 hours and may increase more than 1000-fold during an acute phase response.[4] Although, numerous screening tests are available for the early diagnosis of neonatal sepsis; C-reactive protein is a sensitive & rapidly reacting index

for inflammatory process. In a neonate, this could be invariably meaning an infection.[5]

Thus, present study was undertaken to evaluate the efficacy of CRP in the early diagnosis of neonatal septicaemia.

MATERIAL & METHODS

Total 286 neonates up to the age of 28 days, who were admitted in NICU, SMIMER from Jan-2011 to June-2011, with clinical diagnosis of neonatal sepsis, were included in the study.

Patients with neonatal sepsis were enrolled based on signs and symptoms as follows. Lethargy, refusal to suck, poor cry, not arousable, comatose, distension of abdomen, diarrhoea, vomiting, hypothermia, poor perfusion, sclerema, poor weight gain, excessive jaundice, poor neonatal reflaxes, shock, bleeding, renal failure, cyanosis, tachypnea, chest retraction, grunt, gasping, fever, seizures, blank look, high pitched cry, irritability, neck retraction or bulging frontanel.[6]

Blood was collected for CRP test and blood culture examination. CRP test was carried out from the patient's serum by using latex agglutination test, Span Diagnostic Pvt. Ltd. (Surat), which detects serum levels greater than 6 µg/ml of CRP. Another one ml blood was inoculated aseptically into blood culture bottle having 10 ml Brain Heart Infusion Broth containing 0.05% Sodium Polyanethole Sulfonate (SPS), so that blood is diluted to 1:10 fold. Blood culture bottles were incubated aerobically at 37°C for 7 days. Sub-cultures were done on 2nd, 4th & 7th day on blood agar & MacConkey agar plates. In cases where no growth was obtained after 7 days of incubation, then it was considered as a negative blood culture. In culture positive cases colonies were identified by standard microbiological techniques. All the laboratory procedures were done as per standard protocol & under all aseptic precautions.[7, 8]

RESULTS

Out of 286 clinically suspected cases of neonatal sepsis, 130 had positive blood cultures, which indicate prevalence of 45.45%. Remaining 156 (54.54%) blood cultures obtained no growth results. CRP was reactive in 168 (58.74%) cases out of which 38 (13.28%) were false positive and CRP was non-reactive in 118 (41.25%) cases.

Table 1: Correlation of CRP test and Blood Culture

CRP	Blood Culture		Total (%)
	Positive (%)	Negative (%)	
Positive	130 (45.45)	38 (13.28)	168 (58.74)
Negative	00 (0.00)	118 (41.25)	118 (41.25)
Total	130 (45.45)	156 (54.54)	286 (100)

The main isolates in blood culture were gram negative organisms like *Klebsiella pneumoniae 41* (31.53%), *Pseudomonas spp. 21* (16.15%), *E.coli 19* (14.61%), Acinetobacter *spp.* 10 (7.69%), *Enterobacter spp.* 3 (2.30%), C*itrobacter spp.* 2 (1.53%) and Gram positive organisms like *S.aureus 15* (11.53%), Coagulase Negative Staphylococcus spp (*CONS) 9* (6.92%), *Streptococcal spp. 2 (*1.53%), *Candida spp. 8* (6.15%).

Table 2: Different organisms isolated from blood culture

Organisms Isolated	Blood Culture Positive (%)	CRP test Positive
Gram -ve Organisms- 96 (73.81%)		
Klebsiella species	41(31.53)	41
Pseudomonas species	21(16.15)	21
E.coli	19(14.61)	19
Acinetobacter species	10(7.69)	10
Enterobacter species	3(2.3)	3
Citrobacter species	2(1.53)	2
Gram +ve Organisms- 34 (26.13%)		
Staphylococcus aureus	15(11.53)	15
CONS	9(6.92)	9
Streptococcal species	2(1.53)	2
Candida species	8(6.15)	8
Total	130 (100)	130

Table 3: Statistical Analysis of CRP test

Validity of CRP level Values	In present study (%)
Sensitivity	100%
Specificity	75%
Positive predictive Value	77 %
Negative Predictive value	100%

DISCUSSION

The varying microbiological pattern of neonatal septicaemia warrants the need for an ongoing review of the causative organisms responsible for the clinical situation.[3] Some reports from home and abroad show the incidence of neonatal septicaemia to vary between 36% to 55%.[1, 3, 9] in our study, incidence of neonatal septicaemia confirmed by culture was 45.45%. Gram negative organisms formed the majority of the isolates as compared to Gram positive organisms (73.81% vs 26.13% respectively) in the present study.[10]

Amongst the gram negative organisms, maximum number of isolates were *Klebsiella spp* 31.53% (41/130) which correlates with the study of *Anuratha et al* with 33.32% isolates. We isolated *E.coli* 14.61% (19/130) and *Citrobacter spp* 1.53% (2/130) which correlates with the study of *I Roy et al* who isolated 14 % and 1.7% strains respectively.[3]

Amongst the gram positive organisms, we isolated 11.53% (15/130) Staphylococcus aureus which corresponds to 14% S.aureus in the study by *I Roy et al.*[3] An incidence of 6.92 % (9/130) for CONS observed in our study found to be a matter of concern because this bacterium is often regarded as a contaminant, possibly

from the skin, but *I Roy et al* [3] opined that the presence of this bacterium in the blood can no longer be taken as contamination especially in patients in critical care units. We have also isolated 6.15% (8/130) of Candida species in co-relation with 16.4% in a study by S Bhattacharya (In a study of Roy, 1993 Calcutta 16.4% Neonatal candidaemia).[11]

The present study was undertaken to assess the utility of CRP test as marker for diagnosis of neonatal septicaemia. In our study, we found sensitivity of CRP 100%, specificity 75%, positive predictive value (PPV) 77 % & negative predictive value (NPV) 100% considering blood culture as gold standard method. Our study has good co-relation with study of *Anuratha et al* and *B K Jha et al. Anuratha et al* found CRP sensitivity 100%, specificity 87.3%, PPV 88.3% and NPV 100% [7] *B K Jha et al* found CRP sensitivity 100%, specificity 65.67%, PPV 87.3% and NPV 100% [9].

CONCLUSION

Estimation of serum CRP is simple for diagnosis of childhood septicaemia. CRP is a very good inflammatory marker and also highly sensitive in case of neonatal septicaemia. Instead of waiting for 48-72 hrs for a blood culture report, result of CRP test is available within an hour not only in tertiary care centres but also in remote area like primary health care centers.[7] Empiric Antibiotic therapy can be started immediately as soon as CRP report is available, so as it can reduce the morbidity and mortality in those children. CRP highly correlates with infection positivity, and can be used as a diagnostic as well as prognostic marker.[5]

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