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Diagnostic and Prognostic Significance of Crp in Paediatric Sepsis

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ABSTRACT *Children aged above neonatal age group with clinically suspected sepsis as per the definition given by International Pediatrics sepsis consensus conference were enrolled in this prospective observational study. The CRP, white blood cell count and bands% were measured at the same time. One twenty- nine patients were enrolled in the study. Forty (31%) were culture proven sepsis and eighty nine (69%) were non culture proven sepsis. Respiratory tract infection was the most common source of sepsis (35%) followed by central nervous system infection (13%) and urinary tract infection (10%). CRP was better predictor of culture positive sepsis {Beta- 2.180 and P-0.005 (Exp B-8.8) 95% CI 1.94, 40.21}.A CRP cutoff point of 40mg/l was determined to maximize both sensitivity and specificity (sensitivity 90%, specificity 46.06%, and likelihood ratio 1.67, 95% CI: 1.34, 2.08)*

INTRODUCTION

Sepsis is a complex syndrome caused by an uncontrolled systemic inflammatory response to

Infection, which can result in dysfunction or failure of one or more organs and even death. Sepsis word originated from Greek meaning "putrefaction". Sepsis caused by infection remains a major cause of mortality and morbidity among children[1, 2.] Delay in recognition and treatment significantly increases the risk of morbidity and mortality.

Clinical experience and various studies have shown that the most important measure in reducing mortality from sepsis is early identification of the condition and prompt initiation of therapy[3-6]. Clinical data alone may be unreliable in distinguishing between patients with sepsis and non-infectious systemic inflammatory response syndrome (SIRS) [7]. According to an epidemiological study in the USA, the incidence of sepsis increased from 82.7 to 240.4/100 thousand inhabitants, however the mortality rate among the patients with sepsis was reduced over the period of past 20years[8].

Diagnosis of sepsis in children is difficult in everyday practice for many reasons. The clinical signs in children are variable at the start of the infection; microbiological culture results are expected only after 48-72 hours; and false negatives are common. The turning – point in clinical recognition of sepsis is considered to have been the International Sepsis Consensus Conference in the USA in 2002, in which specific clinical definitions of systemic inflammatory response syndrome (SIRS) and sepsis in children were adopted. The diagnosis of pediatric SIRS requires temperature or leukocyte abnormalities which is the major difference between adult and pediatric SIRS definition[3].

In the literature reviewed, several inflammatory markers have failed to meet the requirements for early and reliable diagnosis of sepsis. Combination of biochemical markers offers the best prospect for research on early diagnosis of sepsis. Taking into account the new definition of sepsis in children and evaluating the need for effective and rapid laboratory (quantitative) indicators, the study was planned.

AIMS & OBJECTIVES

To evaluate diagnostic and prognostic significance of Serum CRP in Sepsis in children (beyond 1month age group).

MATERIALS AND METHODS

This prospective observational study was carried out in the Department of Paediatrics, Kasturba Hospital, Manipal, from September 2012 to March 2014. All children aged from 1month to 18 years admitted in Paediatrics Department of Kasturba Hospital in whom Sepsis was diagnosed as per definition of International Pediatric sepsis consensus conference were included in the study. The approval of the ethical committee was taken prior to the commencement of the study.

Two mL of blood was collected through a clean venipuncture from children admitted in Paediatrics Department for whom blood investigations were planned and samples were sent immediately to clinical laboratory. HS CRP was measured at admission and on day 5 of admission. Presenting symptoms and signs with which those children were admitted to the hospital were recorded as per the structured and prevalidated pro forma.

HSCRP was interpreted as follows

Normal	<10
Mild inflammation and viral infection	10-40
Active inflammation and bacterial infection	40-200

The study data were processed using SPSS 16.0. Estimated sample size calculated assuming a 95% confidence level, 0.5 standard deviation and a margin of error of 0.1 is around 100. For the analysis of patient data, descriptive statistics were used. Comparisons of continuous variables between groups were applied using Mann- Whitney and Wilcoxon tests. The chi- square test was used in analysis of categorical variables between groups. A p-value <0.05 was considered statistically significant

RESULTS

- According to International Sepsis Consensus conference definition criteria a total of 136 cases formed the study group. Out of 136, seven cases were discharged against medical advice in moribund state within 5 days of admission, hence were excluded.129 cases were analyzed. 23.2% (n=30) were 1month – 1year, 24.8%(n=32) were 1-5yr , 34.1% (n= 44) were 6-12yr, and 17.8% (n=23) were 13-18yr.In present

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study the mean age group of presentation was 6.74 years. The age group in other studies was 2 years -8 years.[1,2,9]

- Fever with abnormal count of leukocyte was noted in 76.7% (n= 99).Fever with tachycardia at least 2 SD above normal age values was found in 84.4 % (n=109) Fever with respiratory rate increased by more than 2 SD above normal age values was found in 48.8% (n=63). Among 129 children 30 satisfied the criteria for severe sepsis, 17 for septic shock and 82 for sepsis.

- In present study infection was proven by positive body fluid culture in 31 %(n=40) of the study group, others had positive findings on clinical examination, imaging and laboratory studies.The source of sepsis was pneumonia, meningitis, urinary tract infection etc. Among culture positive, most common organism isolated was E .Coli followed by Pseudomonas. CRP > 40mg/l was found in 90% (n=36), abnormal leukocyte count in 85% (n= 34) and Bands > 10% in 70% (n=28) of culture positive cases .All three inflammatory markers were elevated in 62% (n=25) of culture positive cases and 28% (n=25) of culture negative cases. CRP > 40mg/l had a sensitivity of 90% and specificity of 46.06% in differentiating between culture positive and culture negative groups which is statistically significant(p-<0.0001). Suprin et al[10] had demonstrated sensitivity 92% and specificity of 42%. Annick Galetto- Lacour et al[11] found to have sensitivity of 89% and specificity of 75%.Combination of CRP, Total Leukocyte count and Bands had less sensitivity but more specificity compared to CRP alone in differentiating between culture positive and negative group.CRP concentration, WBC and Bands% were significantly different between the 2 groups. In a multivariate logistic regression analysis, CRP was better predictor of culture positive sepsis {Beta2.180 and P-0.005 (Exp B-8.8) 95% CI 1.94, 40.21}. Receiver operating characteristic analysis demonstrated CRP (area under curve [AUC] 0.733, standard error [SE] 0.045, 95% CI: 0.644, 0.821) to be superior to WBC (AUC 0.716, SE 0.051, 95% CI: 0.617, 0.816) and to bands% (AUC 0.677, SE 0.050, 95% CI: 0.579, 0.775). The mean CRP level was significantly higher in culture positive group compared to culture negative group at admission (p-<0.001) and day 5 of admission(0.018) The mean CRP levels decreased significantly after 5 days of treatment compared to the levels at diagnosis (p < 0.001).

CONCLUSIONS

In present study, following observations were made with respect to CRP as diagnostic marker of sepsis. CRP is more sensitive marker of sepsis with sensitivity of 90 %(95% CI 76.32% to 97.15%) and NPV of 91.11 % (95% CI 78.76% to 97.47%). However specificity was 46.06 %(95% CI 35.44% to 56.96%). The sensitivity and specificity of abnormal leukocyte count and bandemia as a marker of sepsis were 85.01% & 44.9% and 70.00% & 44.90% respectivelyCRP concentration, WBC and Bands% were significantly different between the 2 groups. In a multivariate logistic regression analysis, CRP was better predictor of culture positive sepsis {Beta2.180 and P-0.005 (Exp B-8.8) 95% CI 1.94, 40.21}. When CRP was evaluated as prognostic marker of sepsis, following observation were made. The mean CRP level in septic shock group on Day 1 of admission was 217.5+143.85 compared to 155.5 + 152.56 in no shock group which was not statistically significant {p-0.122(NS)} However, the mean CRP level in septic shock group on Day 5 of admission was 102.4 +129.29 compared to 45.80+87.52 in no shock group which was statistically significant {p-0.025(S)}In the present study, increasing trend of CRP on Day 5 of admission compared to Day 1 had statistically significant correlation with more number of febrile days {p-0.045(S)}, prolonged duration of antibiotic therapy {p-0.004(S)} and prolonged duration of hospital stay {p-0.001(S)}.

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