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C-reactive protein as diagnostic tool for sepsis and fever in paediatrics

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ABSTRACT

C-reactive protein (CRP) is an acute phase substance, produced in hepatocytes. It appears in sera of Pneumonia patients and also occurs in some other pathological conditions. The present study investigated 100 childrens between the age group of 1 day - 12 years. In this study 52% were males and 48% were females. All the patients were suspected clinically to have either sepsis or fever or both. The CRP levels were found to be positive in 46.43% of children clinically diagnosed to have sepsis, the maximum range of CRP was greater than or equal to 48mg/L. In children with fever 40% of the cases were positive while the maximum range was only greater than or equals to 6mg/L.

KEYWORDS

C-reactive protein;
Paediatrics;
Fever;
Sepsis;
Hepatocytes.

INTRODUCTION

C-reactive protein (CRP) is an acute phase substance, produced in hepatocytes. It appears in sera of Pneumonia patients and also occurs in some other pathological conditions. An abnormal protein (beta globulin) precipates with somatic "C" antigen of Pneumococci and produces C - reactive protein has apparent antibody like relation to the "C antigen of *Pneumococci*. CRP testing by passive agglutination using latex particles coated with anti-CRP antibody is a routine diagnostic tool[1]. Bacterial infections, inflammation, malignancies and tissue destruction decreases/ disappears when the inflammatory reactions subside CRP is used as an index of response of treatment to anti-rheumatic fever drugs.[1]

CRP is an acute reacting protein which increases dramatically up to a thousand fold. It is nonspecific, can be used as a supplement in or complement to erythrocyte sedimentation rate (ESR) studies, as elevated CRP in turn elevates ESR, CRP levels more closely approximate the degree of ongoing tissue damage. CRP responds quickly to inflammation (6-10hrs) and has a short life (5-7hrs). CRP was found to be elevated in the serum of patients with bacterial meningitis but not in patients with viral meningitis or meningoencephalitis. CRP may be useful in monitoring the course of bacterial meningitis, CRP level characteristically returns to normal with in seven days in non-complicated bacterial meningitis. It has also been used to distinguish between a variety of bacterial and viral disorders in children. At least two CRP levels, obtained 24 hrs apart in infants with levels

less than or equal to 6 mg/l, indicates unlikliness of infection. The use of CRP to exclude infection may allow clinician to discontinue antibiotics at 48hrs, limiting extended unnecessary antibiotic exposure. The present study was undertaken to assess CRP levels quantitatively in paediatrics suffering from sepsis, fever and both.

MATERIALS AND METHODS

Specimen collection

The study is a prospective study, 100 children aged between one day to 12 years, clinically suspected of sepsis or fever visiting Niloufer Hospital for women and children, Hyderabad were included. The study was conducted during January and February, 2007.

Single blood sample was collected aseptically with disposable syringe and needle. The test was done by latex agglutination method using the commercial KIT supplied by TULIP DIAGNOSTICS PRIVATE LIMITED, Goa, India. The kit was used for both qualitative and semi- quantitative method[2].

Qualitative method

The test plate was cleaned and allowed to dry. About 50µl of the undiluted sera was applied on the test plate. The reagents were brought to room temperature and one drop of well mixed Rhelax CRP reagent was added with the dropper provided, holding it exactly vertical over the sample. Using the stirring rod, the antigen and the sample was mixed until a uniform distribution of latex particles was achieved. This was spread over the entire circle on the slide taking care not to touch the periphery. The test plate was rocked gently to and fro, manually for two minutes and observed under direct light for agglutination of latex particles. Both positive and negative controls were used periodically to check the efficiency of the kit.

Semi-quantitative

Separated sera was diluted with 0.5 ml of isotonic saline to make the dilutions 1:2, 1:4, 1:8, 1:16 and so on. About 50µl of the undiluted sera was taken into a micro pipette and applied on to the first circle, 50µl of the sample was taken from this circle and transferred to 2nd circle. Procedure was repeated for 3rd, 4th, 5th time and lastly 50µl of sample was discarded. One drop of well mixed Rhelax CRP reagent was added with the dropper provided holding it exactly over the sample. Using the stirring rod, the antigen and the sample were mixed until a uniform distribution of latex particles was achieved. This was spread over the entire circle on the slide taking care not to touch the periphery. The test plate was rocked gently to and fro, manually for two minutes and observed under light for agglutination of latex particle. Both positive and negative controls were used periodically to check efficiency of the kit.[2]

RESULTS

One hundred children tested in the present study. All the children were clinically suspected to have either septicaemia, or fever. The age group of the selected children are that from among the total of 100 children, 52% were males, and 48% were females, shown in TABLE 1.

TABLE 1 : Percentage of positive and negative cases of CRP

Total percentage tested	% CRP positive cases	% CRP negative cases
100	47%	53%

The results of the CRP levels of children showed that 47% of children clinically detected as positive and 53% of children clinically detected as negative CRP levels as shown in TABLE 2. With in the 47% children those showed positive to CRP levels, 60% had sepsis, 40% had fever as shown in TABLE 3. Among the children with sepsis (28%), the maximum age group of CRP positive was observed in neonates as shown in TABLE 4 and the children with fever, the maximum age group of CRP positivity was observed in neo-

TABLE 2 : Age and sex distribution of CRP positive children

AGE GROUP	TOTAL	MALE	FEMALE
Neonates(<4 week) to 3 yrs	77	41	36
4 to 7 yrs	14	6	6
8 to 12 yrs	9	3	6
	100	52	48

TABLE 3 : Percentages of CRP positive cases with sepsis or fever

TOTAL NO. OF CRP CASES	NO.OF CASES WITH SEPSIS	NO. OF CASES WITH FEVER
47(47%)	28(59.57%)	19(40.42%)

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TABLE 4 : Percentage of cases CRP positive in children with sepsis

AGE GROUP	TOTAL	MALE	FEMALE
Neonates (< 4 weeks)	13 (46%)	9	4
2 months to 3 years	12 (43%)	7	5
4 to 7 years	3 (11%)	2	1

TABLE 5 : Percentage of CRP positivity in children with only fever

AGE GROUP	TOTAL	MALE	FEMALE
Neonates to 6 yrs	13(68%)	7	6
6yrs to 12 yrs	6(32%)	1	5

TABLE 6 : Maximum levels of CRP in sepsis

	CRP level mg/l			
AGE GROUP	>6	>12	>24	>48
Neonates	2	-	4	2
2 month to 3 yrs	-	1-	2	3
4 yrs to 7 yrs	2	2	-	1

TABLE 7 : Age and maximum levels of CRP in fever

	CRP level mg/l			
AGE GROUP	TOTAL	MALE	FEMALE	>48
Neonates to 6 yrs	4	1	4	3
6 to12 yrs	2	1	-	2

nates as shown in TABLE 5. The maximum age of the sepsis children was shown in TABLE 6. The rate of children suffering with fever was graded based on their age and resulted in TABLE 7.

DISCUSSION

An abnormal protein (beta globulin) precipitating with the somatic "C" antigen of *Pneumococci* is known as C-reactive protein. CRP is an "acute phase" substance, produced in the "hepatocytes". Its production is stimulated by bacterial infections, inflammation, malignancies and tissue destruction[1]. The bacterial infection is a condition that demands an early diagnosis and immediate specific therapy, there is a definite need for a test which is simple to perform and gives early results. Detection of CRP in serum can be utilized for this purpose. Over recent years, a wealth of knowledge has been accumulated regarding CRP and its role in acute phase septicaemia[3]. The present study comprised of hundred children admitted to the paediatric units with clinically suspected to have sepsis or fever, out of them 47% were CRP positive.

CRP was detected and was found comparable to blood culture by latex agglutination test in 254 clinically suspected cases of bacteraemia in neonates admitted to neonatology unit of Niloufer hospital, Hyderabad[2]. It was found that serum CRP had the highest sensitivity, and the range was more than 6mg/ml in 97 of 110 (81.4%) cases showing positive blood culture[4], clinically, biochemically and microscopically assessed CRP protein in adults and children admitted in Indira Gandhi Medical College and General Hospital, Nagpur. The detected CRP was found comparable to blood culture by latex agglutination test. It was also found that serum CRP had the highest sensitivity; observations are comparatively more similar as Parikh *et al.*,[2] and Wood[5].

Though there are many other ways of detecting CRP in serum, latex agglutination method is convenient readily available, simple to perform, interpret and above all relatively cheap. Thus, the present study emphasizes the need for including the detection of serum CRP by latex agglutination method as a routine diagnostic tool in the early detection of sepsis.

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