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Original Research Article

C-reactive protein levels in children with uncomplicated malaria

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ABSTRACT

Background: Malaria is one of the biggest burden in terms of morbidity and mortality among all infectious diseases and continues to be a major health problem in India. The objective of this study was to study the levels of C-reactive protein in children with uncomplicated Malaria. To correlate C-reactive protein levels with malaria parasite density and species of Malaria.
Methods: Retrospective study was done in Father Muller Medical College, Mangalore, Karnataka. 50 patients below 15 years of age malaria parasite positive by fluorescent test (MPFT) and by Peripheral smear formed the subjects and CRP levels and parasite densities was noted down into the proforma.
Results: The age group predominantly was children more than 10 years. Plasmodium vivax was the type of malaria in 60% children. Most common symptoms were fever (100%), chills and rigors (41%), vomiting (48%) and headache (24%). Clinical signs observed were hepatomegaly (30%) and splenomegaly (64%). Mean levels of C reactive protein (CRP) were 42.91%with standard deviation of 31.62. Mean CRP levels were high in children with Falciparum malaria (44.51±34.19).58% had CRP levels ranging from 6-50 mg/l. 50% children with CRP levels >50 mg/L had parasite density of (++++) which is 100 parasites per 1 field of quantitative buffy coat.
Conclusions: C-reactive protein levels are markedly elevated in acute malarial infection in paediatric age group.It correlates well with disease severity.

Keywords: C-reactive rotein, Uncomplicated malaria

INTRODUCTION

Malaria is one of the biggest burden in terms of morbidity and mortality among all infectious diseases and continues to be a major health problem in India.[1] Malaria has caused 214 million infections and 4,38,000 deaths worldwide; of which 90% deaths were in Africa among which 70% were in children <5 years in 2015.[2] In India out of 1.1 million malaria cases, around 561 deaths were reported in 2014 as per National Malaria programme.[3] It is caused by protozoa of the genus Plasmodium of which Plasmodium falciparum and Plasmodium vivax are important.

Following inflammation and tissue injury there are increase or decrease of certain serum proteins called as acute phase reactants. They are mainly synthesized in the liver. C-reactive protein is a positive acute phase protein that is involved in complement activation and initiation of phagocytosis by its anti-inflammatory action.[4]

C-reactive protein secretion in malaria is induced by pro - inflammatory cytokines that are produced by host mononuclear cells and there have been strong correlations between its levels and parasitemia.[5] It also has an important role in malaria, ie it clears the infected erythrocytes from circulation by immune activation.[6]

Malaria is endemic in Mangaluru with a reported incidence of 7360 cases out of 12,335 cases in Karnataka in 2014.[7] Studies involving acute phase reactants in children with uncomplicated malaria in India are limited. This study is designed to find out the levels of C-reactive protein levels as a measure of acute phase response and its correlation with parasite density and species in children affected with uncomplicated malaria.

METHODS

It is a retrospective study done using data collected from case records. Children aged less than 15 years, admitted in a Medical College Hospital in Mangaluru, a city in coastal Karnataka. Malaria parasite positive by fluorescent test (MPFT) and by peripheral smear formed the study group. Study period was from October 2014 to December 2015. Children with other infections, chronic diseases, on drugs like steroids, antimalarials, immunosuppressants and whose C-reactive protein was not done were excluded. Ethical clearance from the Institutional ethical committee was obtained. Uncomplicated malaria was defined as a patient who presents with symptoms of malaria and has a positive parasitological test (microscopy or rapid diagnostic tests) but with no features of severe malaria.[8]

Parasite density from the malarial parasite flouroscent test was noted down as + (1+) - 1 parasite per QBC field; ++ (2+) - 1-10 parasites per QBC field; +++ (3+) - 11-100 parasites per QBC field;++++ (4+) - 100 parasites per QBC field.[9] C-reactive protein levels (done by immunoturbidometric method in automated Cobas 6000 analyser) were noted. Details of clinical history, examination and investigations were entered in the pre-designed proforma. The data obtained was analysed by frequency, percentage, mean, standard deviation and fisher exact test.

RESULTS

A total of 50 patients meeting the inclusion criteria were included in the study. Their demographic characteristics are given in the Table 1. Children between 10-15 years were predominantly affected, and 32% were under 5 years of age.

Table 1: Demographic characteristics.

Characters	No. of patients	Percentage (%)
Age in years		
<5 years	16	32.0
5-10 years	13	26.0
10-15 years	21	42.0
Total	**50**	**100.0**
Sex		
Male	34	68.0
Female	16	32.0
Total	**50**	**100.0**

Fever was the chief complaint in all children affected and other symptoms were chills with rigors (82%), headache (24%), myalgia (6%), vomiting (48%) and pain abdomen (6%).

Table 2: Type of malaria and mean levels of CRP.

	Number	Mean(mg/l) ±SD
Falciparum	4	44.51 ±34.19
Vivax	30	42.00 ±32.4
Mixed	16	42.91 ±31.62
Total	**50**	

On clinical examination 22% had pallor, 2% icterus, 30% had hepatomegaly, 64% with splenomegaly and 30% with hepatosplenomegaly.

Plasmodium vivax was the most common type of malaria (60%) followed by mixed malaria (32%) and plasmodium falciparum (8%). Mean C-reactive proteins levels were found to be more in children affected with P. falciparum malaria (44.51±34.19) followed by mixed malaria (42.9±31.62) (Table 2).

Table 3: Parasite density and CRP levels of falciparuma and vivax species.

Parasite density	Type of malaria	<6 mg (mg/l)	6-50 (mg/l)	>50 (mg/l)	P value	Total
+	Falciparum	0	0	0	-	0
	Vivax	0	3	1	-	4
++	Falciparum	1	1	0	0.95	2
	Vivax	0	1	1		2
+++	Falciparum	0	0	1	0.958	1
	Vivax	1	5	5		11
++++	Falciparum	0	0	1	0.577	1
	Vivax	1	6	6		13
	Total	**3**	**16**	**15**	**-**	**34**

Table 4: Parasite density and CRP levels of mixed malaria.

Parasite density	6-50 (mg/l)	>50 (mg/l)	Total
V (+) F (+)	6	0	6
V (+) F (++)	3	0	3
V (+) F (++++)	2	2	4
V (++) F (+)	1	0	1
V (++) F (++)	0	1	1
V (+++) F (+)	1	0	1
Total	**13**	**3**	**16**

P value -0.123.

Mean C-reactive protein levels were also correlated with parasite density (Table 3). CRP levels were more than 50mg/l when parasite density was +++ and ++++ in vivax and falciparum. In vivax malaria there were 13 children (43%) with CRP >50 mg/l and 46% of them had parasite density of ++++. In falciparum malaria 2 (50%) had CRP >50 mg/l, out of which 50% had parasite density of ++++. In mixed malaria, there were 13 (81%) children with 6-50 mg/dl of CRP and parasite density was variable (Table 4). No mortality was noted in the study population.

DISCUSSION

Malaria is a major infectious disease affecting children in this part of the country with significant mortality and morbidity. C-reactive protein is a non-specific biomarker of inflammation. It is widely used acute phase reactant as its levels rise rapidly following an infection or inflammation. Predominant age group involved was children between 10 to 15 years. Male to female ratio was 2:1. There are very few studies done in pediatric age group.[5,11]

Plasmodium vivax malaria was found in majority of the children affected. Clinical features observed in our study were fever with chills and rigors, headache, vomiting and myalgia. Similar observations were seen in other studies.[5,10,11] Duration of fever was 3-5 days in this study. Results showed C-reactive protein was elevated significantly in malaria infection. Very high levels were measured during acute attacks of malaria in a study by Hurt et al.[11] Mean C reactive protein levels in this study were 42.91 g/dl. Chatriwala et al had observed mean C-reactive protein levels of 34.85±19.90 mg/L. Levels of C-reactive proteins were higher in children affected with plasmodium falciparum compared to vivax group. However smaller number of falciparum makes it difficult to interpret. Agrawal et al and Chhatriwala et al had similar observations in their studies.[5,10]

Paul R et al in his study found no difference in CRP levels in vivax and falciparum malaria.[12] C-reactive protein levels increased with levels of parasitemia in our study both in falciparum and vivax but were not statistically significant. In studies done by Naik et al and Felix Y et al, they found that biochemical parameters increase with increasing parasite density in falciparum malaria.[13,14] We noted the levels of CRP only on the first day of admission, but study by Agrawal et al had done serial measurements of CRP, which is a better marker for assessing the disease severity.[5]

CONCLUSION

C-Reactive protein levels are markedly elevated in uncomplicated malarial infection in paediatric age group and the levels increase with parasite density.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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