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Original Research Article

Clinical and haematological parameters in malaria caused by different plasmodium species in children

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ABSTRACT

Background: Malaria is a disease of global importance and affects more than ninety countries in both the tropical and subtropical regions. Clinical and haematological parameters vary with type of malaria, although data relating to different species of malaria in children is limited. This study aims to understand the clinical and haematological profile of malaria and to correlate these with different malarial species among children.
Methods: This is a descriptive cross-sectional study involving 130 proven malaria cases done over 18 months from October 2014 to April 2016. A detailed history and clinical examination along with haematological parameters were analysed and correlated with different types of malaria.
Results: Among 130 children, 97 children were *vivax* positive, 4 were *falciparum* and 27 were mixed malaria. Fever was present in all, whilst other symptoms were chills and rigors (86.15%), vomiting (39.52%), headache (19%), pain abdomen (6.84%), myalgia (4.56%) and convulsions (1.52%). Clinical signs were pallor (29.64%), icterus (0.76%), splenomegaly (65.36%), hepatomegaly (23.56%) and hepatosplenomegaly (21.28%).75% of children with *falciparum* malaria had splenomegaly and pallor whereas hepatomegaly was observed in 34% of mixed malaria cases. Haematological parameters observed were anaemia (47.6%), severe anaemia (2%), leucocytosis (11.5%), leukopenia (39.2%), thrombocytopenia (87%) and severe thrombocytopenia (30%). Severe thrombocytopenia was seen with *vivax* malaria (70%). No mortality was noted in the studied population.
Conclusions: Fever and splenomegaly are important clinical features, whereas anaemia and thrombocytopenia are the most noted haematological parameters in malaria. The parameters vary with different species of malaria knowledge of clinical and haematological parameters aid us in early diagnosis and prompt initiation of treatment and prevention of associated complications.

Keyword: Malaria, *Plasmodium falciparum*, *Vivax*, Clinical, Haematological changes, Children

INTRODUCTION

Malaria is a major health problem in overpopulated countries. It is one of the most prevalent human infections worldwide, causing significant morbidity and mortality. There were 241 million cases and around 6,27,000 malaria deaths worldwide in 2020 during pandemic wherein WHO African region had witnessed majority of cases and deaths (95% and 96%) as per latest world malaria report, 83% of malaria deaths in WHO South-East Asia region are from India. Children under age of 5 account for 77% of total malarial deaths worldwide.[1] Haematological manifestations are invariably associated with malaria. They are the most common complications encountered in malaria and play major role in its pathogenesis.[2]

Compared to adults, very few studies have been done in paediatric age group. Even in this age group, most are related to only one plasmodium species [3] and there are

hardly few comparative studies.[4] Malaria is endemic in the Mangaluru city, a coastal city in south India in the state of Karnataka with a reported incidence of 4,741 cases in 2018. But in recent years, the incidence in Mangaluru has dropped to 689 cases in 2022.[5] Hence this study was taken up with the objectives to describe the clinical and haematological profile of children with *Plasmodium falciparum*, *Plasmodium vivax* and mixed malaria and to correlate clinical and haematological parameters with type of malaria in children of different age groups.

METHODS

The study was a descriptive cross-sectional observational study done in Father Muller's medical college hospital, a tertiary centre for a period of 18 months starting from October 2014 to April 2016. 130 children from birth to less than 15 years, admitted in the hospital with history of fever and malaria parasite positive by fluorescent test (MPFT), confirmed by peripheral smear were included in the study. Children who have already received treatment or completed the full course of treatment for current episode of malaria and those with other coexisting illnesses like dengue or leukaemia, that can affect haematological parameters were excluded from the study. The study was approved by institutional ethical committee. Written informed consent was obtained from the parents at the time of enrolment. Samples were selected using purposive sampling technique. Complete history was taken from the parent and the child regarding the symptoms and detailed clinical examination was done and entered in the pre-structured questionnaire.

Haemoglobin, total count, differential count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), MCH concentration (MCHC). Platelets were estimated using automated electronic cell counter. ESR and blood groups were also noted. Peripheral blood smear examination was done using Leishman's stain and examined under oil immersion lens. MPFT (malarial parasite fluorescent test) was done by using quantitative buffy coat (QBC) fluorescent test and reconfirmed with thick smear for identification and thin smear for species differentiation. Mixed malaria was considered when children were positive with both *falciparum* and *vivax* species. The data obtained was an analysed by frequency, percentage, and mean. Chi square test and ANNOVA were used in the analysis. SPSS version 21.0 software was used.

RESULTS

Total of 130 children admitted with MPFT positive for malaria and confirmed by peripheral smear were included in the study. Blood investigations were carried out before starting the antimalarials. Male to female ratio was 1.8:1 with 84 (65%) boys and 46 (35%) girls. Predominantly infected age group was between 11 and 15 years. Most of the children had *vivax* malaria (75%) followed by mixed malaria (22%) and 4 children had *falciparum* malaria (Table 1).

Type of malaria with clinical symptoms and signs

Fever was the presenting complaint in all the patients (100%) and chills and rigors in 86.15% of the cases. Headache was observed in 25 (19.00%) subjects which was of diffuse type. Other symptoms were myalgia (4.56%), vomiting (39.5%), pain abdomen (6.84%), diarrhoea (1.5%) and convulsions (1.5%). All children (100%) with *falciparum* malaria, 72% in *vivax* group and 86% of mixed malaria group had less than 5 days duration of fever. Chills and rigors were predominant symptoms in majority cases with *vivax* malaria. Headache and vomiting were seen in all types of malaria. Diarrhoea and convulsions were present in *vivax* malaria cases. (Table 2).

Pallor, icterus, hepatomegaly, and splenomegaly were the important clinical signs. Pallor was present in 75% of cases with *falciparum* malaria followed by 44% of mixed malaria cases and these results were highly significant (p=0.0127). Icterus was present in one child with mixed malaria. Hepatomegaly was a predominant finding in children with mixed malaria (34%) followed by *falciparum* (25%). Splenomegaly was a main feature in all three types, 31% children with mixed malaria had hepatosplenomegaly followed by *falciparum* (25%) and *vivax* malaria (18%) (Table 2).

Haematological parameters in different types of malaria

Severe anaemia is defined as haemoglobin less than 7gm% and was seen in 3 children, among them 2 had *vivax* malaria and 1 had mixed malaria. All the 4 *falciparum* malaria cases had leukocytopenia (<4000 cells/cumm) 49% of all infected cases had total counts of 4000-11000 cells/cumm (Table 3). Neutrophils and lymphocytes were within normal range. Monocytosis was seen in all three types of malaria and eosinopenia in *falciparum* cases.

Severe thrombocytopenia (<50,000) was seen in children with *vivax* malaria (70%).16 children had normal platelet counts. Majority of the children affected (40%) had platelet counts ranging from 50,000-1,00,000. There was thrombocytopenia in all three types of malaria and mean platelet was 73,750 in *falciparum* cases (Table 4).

Most of the children had O positive (50%) followed by A positive (25%) blood group in the study. Children with O blood group majorly had *vivax* malaria followed by mixed malaria whilst AB positive blood group cases had only *vivax* malaria, 3 out of 4 *falciparum* cases belonged to B positive blood group. These results were significant with p=0.0215 (Table 3). Mean haemoglobin in children with *falciparum* malaria was 11.15 gm%. MCV was 72 in *falciparum*, 75 in mixed malaria and 79.67 in *vivax*. This was highly significant with p=0.0089 (Table 4).

Table 1: Gender and age distribution of malaria positive children based on its types.

Variables		*Falciparum* (%)	*Vivax* (%)	Mixed malaria (%)	Total (%)
Gender	Male	4 (4.76)	59 (70.23)	21 (25)	84 (65)
	Female	0 (0)	38 (82.6)	8 (17.4)	46 (35)
Age group (In years)	<5	1 (2.94)	24 (70.58)	9 (26.47)	34 (26.10)
	6-10	2 (6.06)	23 (69.69)	8 (24.24)	33 (25.38)
	11-15	1 (1.58)	50 (79.36)	12 (19.04)	63 (48.46)
	Total	4 (3)	97 (75)	29 (22)	130 (100)

Table 2: Types of malaria with clinical parameters.

Symptoms		*Falciparum*, (n=4)	*Vivax*, (n=97)	Mixed, (n=27)	Total (%)	X^2	P value
Fever	<5 days	4	70	25	99 (76.1)	3.716	0.155, NS
	>5 days	0	27	4	31 (23.8)		
Chills and rigors	Yes	3	84	25	112 (86.1)	0.433	0.805, NS
	No	1	13	4	18 (13.9)		
Headache	Yes	2	19	4	25 (19.2)	2.99	0.223, NS
	No	2	78	25	105 (80.7)		
Myalgia	Yes	0	4	2	6 (4.6)	0.5896	0.744, NS
	No	4	93	27	124 (95.3)		
Vomiting	Yes	2	39	11	52 (40)	0.2201	0.895, NS
	No	2	58	18	78 (60)		
Abdominal pain	Yes	0	6	3	9 (6.92)	0.9063	0.6356, NS
	No	4	91	26	121 (93.07)		
Diarrhoea	Yes	0	2	0	20 (1.5)	0.691	0.7078, NS
	No	4	95	29	128 (98.4)		
Convulsions	Yes	0	2	0	2 (1.52)	0.691	0.7078, NS
	No	4	95	29	128 (98.4)		
Signs							
Pallor	Yes	3 (75)	23 (23)	13 (44)	39	8.72	0.0127, NS
	No	1	74	16	91		
Icterus	Yes	0	0	1 (3.44)	1	3.5098	0.1729
	No	4	97	28	129		
Hepatomegaly	Yes	1 (25)	20 (20)	10 (34)	31	2.3661	0.306
	No	3	77	19	99		
Splenomegaly	Yes	3 (75)	62 (63)	21 (72)	86	0.864	0.6492
	No	1	35	8	44		
Hepato-splenomegaly	Yes	1 (25)	18 (18)	9 (31)	28	2.0861	0.3523
	No	3	79	20	102		

NS-Not significant.

Table 3: Haematological parameters with type of malaria.

Parameters		*Falciparum* (%)	*Vivax* (%)	Mixed (%)	Total (%)	X^2	P value
Haemoglobin (gm%)	<7	0	2 (1.52)	1 (0.76)	3 (2)	1.5864	0.811 NS
	7-10	0	21 (15.96)	7 (5.32)	28 (21)		
	>10	4 (3.04)	74 (56.24)	21 (15.96)	99 (76)		
TLC (cells/ cumm)	<4000	4 (100)	39 (40.2)	8 (27.5)	51 (39.2)	8.3756	0.078 NS
	4000-11000	0	48 (49.4)	16 (55.1)	64 (49)		
	>11000	0	10 (10.3)	5 (17.2)	15 (11.5)		
Platelet count	>150000	0	12 (9.12)	4 (3.04)	16 (12.16)	4.857	0.5622 NS
	100001-150000 (Mild)	2 (1.52)	23 (17.48)	6 (4.56)	31 (23.56)		
	50000-100000 (Moderate)	0	41 (31.16)	12 (9.12)	53 (40.28)		
	<50000 (Severe)	2 (1.52)	21 (15.96)	7 (5.32)	30 (22.8)		

Continued.

Parameters		*Falciparum* (%)	*Vivax* (%)	Mixed (%)	Total (%)	X^2	P value
Blood group	O+	0	52 (39.52)	14 (10.64)	66 (50)	14.837	0.0215, S
	A+	1 (0.76)	22 (16.72)	10 (7.6)	33 (25)		
	B+	3 (2.28)	14 (10.64)	5 (3.8)	22 (18.16)		
	AB+	0	9 (6.84)	0	9 (6.84)		

NS-Not significant, S=significant.

Table 4: Correlation of mean values of haematological parameters and type of malaria.

Variables	*Falciparum*, (n=4)	*Vivax*, (n=97)	Mixed, (n=27)	ANOVA	P value
Hb (g/dl)	11.15	10.912	10.94	0.03	0.97
MCV (fl)	72.02	79.67	75.82	4.89	0.0089
MCH (pg)	21.97	25.65	26.53	1.18	0.31
MCHC(g/dl)	33.5	32.82	33.02	0.29	0.748
Platelet (microlitre)	73750	96084.53	90655.17	0.25	0.779
WBC (microlitre)	3200	6394.84	6903.44	2.26	0.108
Neutrophils (%)	58.25	57.618	55.44	0.18	0.835
Lymphocytes (%)	28.25	31.257	33.13	0.21	0.810
Eosinophils (%)	1	15.938	15.82	1.53	0.22
Monocytes (%)	8	7.896	9.37	1.15	0.3199
Basophils (%)	0	0	0	0	1
ESR	10	15.938	15.82	0.41	0.664

DISCUSSION

Malaria being a vector borne disease that is endemic in tropics and subtropics, continues to be on the rise due to resistance to drugs and vector resistance to the insecticides.

vivax was the most common type of malaria in our study (75%) and in studies by Jairajpuri et al (84.8%), Bafghi, et al (90.78%) and Shetty, et al (66%).[6-8] Study done by Kotepui et al in Thailand showed not much difference between *falciparum* (51.2%) and *vivax* malaria (48.8%).[2] There are regional variations in the prevalence of type of malaria.

Gender and type of malaria

Most of the studies showed male preponderance probably because of boys being active in outdoor activities and higher health seeking behaviour for male children. Male to female ratio in our study was 1.8:1 as well as Goyal et al (1.5:1) and Singh et al (2.2:1).[9,10] Hussain et al had male to female ratio of 2:1 in all three types of malaria similar to our results.[11]

Age distribution and type of malaria

Children aged 11-15 years were the predominant age group affected in our study probably due to increased exposure to mosquito bites (Table 1) and Singh et al had similar results. Study by Goyal et al observed that children from 4-6 years were more commonly affected.[9,10]

Presenting symptoms and type of malaria

Clinical features like fever (100%), chills and rigors (86.5%), vomiting (39.52%) and headache (19%) were common in our study (Table 2). Kumari et al had similar results except that history of pain abdomen (14%) was more than that of our study (6.84%).[12] Study by Patil et al did not have, body ache, pain abdomen, diarrhoea as symptoms.[13] History of headache was seen in 96.7% children in study done by Muwonge et al, Geleta et al had higher number of patients with diarrhoea (35.74%) and vomiting (61%) compared to other studies.[14,15] There was higher incidence of headache, diarrhoea and vomiting in these studies as majority of children had *falciparum* malaria.

Fever, chills with rigors, headache and vomiting were presenting complaint in all three types of malaria. Myalgia was present in mixed and *vivax* types whilst pain abdomen was predominant in *falciparum* cases. As per study done by Geleta et al vomiting and diarrhoea was present in 70% children with *falciparum*.[15]

Clinical signs and malarial types

Pallor, splenomegaly and hepatomegaly was a consistent feature in all studies. Bhattacharjee et al had all children with pallor, unlike our numbers (29.64%).[16] Pallor was present in 75% children with *falciparum* and 44% children with mixed malaria. (Table 3). We had 21% children with hepatosplenomegaly whereas Kumari, et al evidenced it in 50% cases.[12] Hepatomegaly and hepatosplenomegaly were more in mixed malaria in our study. Icterus was seen only in mixed malaria cases in our

study. Patil et al had 61% children with icterus, 53% of hepatomegaly which was higher than our results (Icterus-0.76%, hepatomegaly-23.56%).[13] Splenomegaly was a major feature (65.36%) and was present in 75% of *falciparum*, 72% of mixed and 63% of *vivax* cases. In a study done by Joseph, et al 70% children with *falciparum* mono-infection and 30% with mixed infection had splenomegaly. Bhattacharjee et al study had splenomegaly and hepatosplenomegaly in 19% and 44% of *vivax* cases.[16,17] The clinical findings in *vivax*, *falciparum* and mixed infections were similar and was not statistically significant in our study.

Complications

In our study, increased severity due to mixed malarial infection was not noticed. Convulsions were present in a child with *vivax* malaria and cause for convulsion could be fever. We did not get any cerebral malaria cases or cases with bleeding manifestations. There were no deaths in our study.

Haematological parameters and type of malaria

Anaemia: Mean haemoglobin in this study was 10.92 gm% whilst study by Geleta et al observed mean haemoglobin of 7.78 gm%.[15] Anaemia was present in 23% of *vivax* malaria and 25% of mixed malaria infection, and Joseph et al, Mittal et al had similar results.[17,18] Anaemia results from haemolysis, splenic clearance, splenic sequestration and suppression of haematopoiesis by TNF alpha.[19] Three children (2%) had severe anaemia in our study (Table 3) of which two were *vivax* affected and comparable to observations by Kochar et al (75%) and Bhattacharjee et al (83%).[16,20] Probably this is due to higher number of children affected with *vivax* malaria than *falciparum* in our study. MCV, MCH, MCHC were decreased in *falciparum* malaria compared to *vivax* malaria in our study. But Kotepui et al had raised indices in *falciparum* malaria than with *vivax* malaria due to the increased release of immature red cells in *falciparum* malaria.[21] We found low to normal ESR compared to significantly raised values in all three types of malaria in a study done by Hussain et al mainly because they had more anaemic cases.[11]

Leukopenia: In this study, mean total count was 6410 cell/cumm, lowest count was 1300 cells/cumm and highest count was 20,000cells/cumm. All 4 children with *falciparum* in our study had leukopenia similar to findings by Rasheed et al (20.9%) and Castano et al (18%).[22,23] We had 40.2% *vivax* cases and 27% of mixed malaria cases also with low counts. Leukopenia has been proposed due to the sequestration of leukocytes that causes its decline. On the other end, leucocytosis was a seen in 66.6% of *vivax* infected cases. It is a marker of poor prognosis in terms of morbidity and mortality in children with *falciparum*. Leukocyte count may vary due acuteness of infection, disease severity, concurrent infections that may have been missed.[24]

Changes in differential count: Our results comparable to study by Fotedar et al except monocytosis.[24] Correlation between differential count and type of malaria was not statistically significant. Neutrophilia was seen more in *falciparum* and *vivax* compared to mixed malaria. Tobon Castano et al had observed normal neutrophils in 91% malaria cases.[23] Normal lymphocyte counts were seen in our study. Tobon Castano et al had 54% children with lymphopenia and Geleta et al evidenced lymphocytosis in *falciparum* and lymphopenia in *vivax* malaria.[15,23] In our study, *falciparum* had significant eosinopenia whilst *vivax* and mixed malaria had eosinophilia, as also observed by Kotepui et al.[21] Our mixed malaria cases had monocytosis whilst Geleta et al had seen monocytosis in *vivax* malaria.[15]

Thrombocytopenia: Mean platelet level in our study was 94,186 cells/cumm. (Table 4). The lowest platelet count was 10,200 cells/cumm and had no signs of bleeding, 50% children with *falciparum* malaria had severe thrombocytopenia followed by 24% of *vivax* cases. Severe thrombocytopenia in *falciparum* was also seen in studies by Joseph et al (51%) and Chhawchharia et al (43.7%) while Singh et al (29.5%) had evidenced it with *vivax* malaria.[17,25] Goyal et al had equal number of cases of *falciparum* and *vivax* with severe thrombocytopenia.[9,10] Mixed malaria cases also had severe thrombocytopenia (23%) similar to study by Shetty, et al (18%).[8] In a study by Kochar et al 10.77% had bleeding manifestations due to the enhanced haemostatic responses to hypersensitive platelets in acute malaria.[20] Thrombocytopenia occurs due to increased platelet destruction from platelet associated IgG antibody and its consumption.

Blood group and type of malaria: This did not show a specific pattern except that *falciparum* cases in our study had no children with blood group O (Table 4). This goes in comparison to other studies which had similar findings i.e. Afoakwah et al and Tekeste et al.[26,27] These studies also showed that people with blood group O were less susceptible to severe *falciparum* malaria, probably due to decreased resetting feature of RBCs with O blood group.

Strengths and limitations

This is a study involving children with different types of malaria describing clinical features and haematological parameters spanning over 18 months with a large sample size. However, restricting to hospital admitted patients is a major limitation of study. Smaller number of *falciparum* malaria cases and not checking serial haematological parameters were other limitations of study.

CONCLUSION

Clinical and haematological parameters vary in acute malaria with different plasmodium species. Fever and splenomegaly are the important clinical features, whereas anaemia and thrombocytopenia are the most noted

haematological parameters in malaria. Knowledge of clinical and haematological parameters aid us in early diagnosis and prompt initiation of treatment and prevention of associated complications. Children with fever, pallor and thrombocytopenia in an endemic area should get relevant investigations for the detection of malaria and management.

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