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ORIGINAL ARTICLE

AGE-RELATED MANIFESTATIONS OF MALARIA AND FACTORS ASSOCIATED WITH TYPE AND SEVERITY OF MALARIA

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ABSTRACT

Aim: To study age related manifestations, type and severity of malaria in children.

Methods: Retrospective study of 30 malarial patients. Clinical features were analyzed as per age-groups, severity and type of malaria.

Results: Mean age was 6.5+4 yrs ranging from 1–14 yrs. Male: female ratio was 2.3:1. Vomiting was common in children >10 yrs of age (p=0.03), anemia and splenomegaly were common in children <5 yrs of age (p=0.002 and p=0.025 respectively). Mean hemoglobin in children <5 yrs age was 7.19±2.21 gm% as compared to 8.55±3.34 gm% in 5-10 yrs and 11.14±2.18 gm% in >10 yrs (p=0.035). Plasmodium falciparum was seen in 7 (23.3%), p. vivax in 18 (60%) and mixed (falciparum+vivax) in 5 (16.7%) children. Mixed malaria was prevalent (100%) in children aged between 5-10 yrs (p=0.041). All patients with P. falciparum and mixed malaria had thrombocytopenia and hepatomegaly (p=0.048 and p=0.026 respectively). Thirteen (43.3%) children had severe malaria. Common features in severe malaria were thrombocytopenia (100%) and hepatomegaly (p=0.010 and p=0.047 respectively). In severe malaria, hemoglobin was lower (7.0+3.0 gm vs 9.4+2.5 gm%) (p=0.025) and serum creatinine was higher (0.9+0.3 vs 0.7+0.2 mg/dl) (p=0.019).

Conclusion: In children <5 yrs, anemia and splenomegaly are common. In children between 5-10 yrs, mixed malaria is common whereas in >10 yrs vomiting is predominant. Falciparum and severe malaria are associated with hepatomegaly and thrombocytopenia.

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malaria, children, severe malaria

Introduction

Malaria is one of the oldest infestations known to man. It accounts for more than one million child deaths globally every year.[1] In 1990's, it was suggested that 90% of all malarial cases and deaths took place in Sub-Saharan Africa which is an endemic region and severe disease and mortality occurred primarily in infancy and childhood.[2] In recent times South and South-East Asia has emerged as one of the major portals for this disease where India contributes majorly in this part of the world.[3] Though, clinical features of malaria are quiet well defined, there is a lack of data comparing age related clinical features as well as the severity of malaria and the species of Plasmodium causing it.

Methods & Materials

A retrospective study was conducted in 2012 at a tertiary referral hospital in Maharashtra, India from case records of 30 patients of malaria (peripheral smear proven or rapid dipstick proven). Their demographic details in the form of age and gender were included. The clinical features observed were fever, vomiting, headache, bodyache, diarrhea, decreased appetite, abdominal pain, cough, itching, convulsion, blood-stained stools, cola-colored urine, and epistaxis. The examination findings included anemia, hepatomegaly, splenomegaly, and abdominal distension. The investigations carried out were peripheral smear (both thick and thin films), parasitic index, hemoglobin levels, platelet counts, white blood cell counts, serum transaminase levels and serum creatinine levels. Treatment in form of antimalarials and ionotropes and blood component therapy was given as and when necessary. The data analyzed also included information regarding prophylaxis, primary treatment, treatment failure, secondary treatment, and combination therapy.

Cerebral malaria was defined as unrousable coma (Blantyre coma score ≤2); persistent, generalized convulsions for at least one hour with hypoglycemia and other causes of coma excluded clinically. If the child had received a sedative or anticonvulsant drug before admission, the coma score was assessed at one hour and six hours after the drug was given. Severe malaria was considered if any of the following was present: cerebral malaria, severe anemia, respiratory distress, hypoglycemia (blood glucose <2.2 mmol/litre), mucosal bleeding, hyperparasitaemia (peripheral parasitaemia of ≥20%), renal failure and jaundice.[2]

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Thrombocytopenia was defined as platelet counts less than 1,50,000 platelets/cumm. Anemia was defined as Hemoglobin less than 10 gm/dl Raised serum alanine transaminase (SGOT) levels were taken as 40 IU/L and serum aspartate transaminase (SGPT) levels above 25 IU/L. Other co-infections such as bacteremia, dengue, leptospirosis, and typhoid were excluded by doing a blood culture, Dengue IgM, Leptospirosis IgM and Widal test respectively.

A statistical analysis of the data was done using SPSS version 13.0 and Open Epi software. Chi square test and Fisher's exact test were used for comparison of proportions. P value <0.05 was taken as significant.

Results

The mean age of presentation was 6.5+4 yrs with patients ranging from 1-14 yrs. Male: female was 2.3:1. The common clinical findings were fever (100%), hepatomegaly (73.3%) and splenomegaly (70%). Common laboratory findings were thrombocytopenia (76.7%), anemia (73.3%) and elevated aspartate transaminase (63.3%). Other clinical and laboratory findings are depicted in Figures 1 and 2. *Plasmodium falciparum* was seen in 7 (23.3%) children, *plasmodium vivax* in 18 (60%) patients and mixed (*falciparum*+ *vivax*) in 5 (16.7%) children. The significant findings in children with falciparum malaria were thrombocytopenia and hepatomegaly (100% each) (p=0.048 and p=0.026 respectively). Also mixed malaria was more common in children in more than 10 years of age (100%) (p=0.041) Clinical and laboratory features in different types of malaria are depicted in Table 1a and 1b respectively.

Thirteen (43.3%) children had severe malaria. The significant findings in children with severe malaria were thrombocytopenia (100%) (p=0.010) and hepatomegaly (92.3%) (p=0.047). The mean hemoglobin (7.0+3.0 gm/dl) in children with severe malaria was lower than that (9.4+2.5 gm/dl) in children with non-severe malaria (p=0.025). Also, serum creatinine values in children with severe malaria (0.9+0.3 mg/dl) were significantly higher than in children with non-severe malaria (0.7+0.2) (p=0.019). Out of 17 children with non-severe malaria, 14 (82.3%) children had P. vivax malaria (p=0.016). Clinical and laboratory features with severity of malaria are depicted in Table 2a and 2b.

Thirteen children (43.3%) were below 5 years. of age, 12 (40%) belonged to the age group of 5-10 years while 5 (16.7%) children were more than 10 years of age. All 13 (100%) children younger than 5 years of age had anemia (p=0.002) while 11 out of 13 belonging to this age group (84.6%) had splenomegaly (p=0.025). Vomiting was particularly more common in older children above 10 years of age. Four out of 5 children in this age group had vomiting (80%) (p=0.03). Common clinical and laboratory features in different age groups are depicted in Table 3a and 3b.

Blood transfusion was needed in 10 (33.3%) children, platelet transfusion in 3 (10%) children and inotrope support in 2 (6.7%) children. Primaquine prophylaxis was given to 21 (70%) children. Combination therapy was implemented in 17 (56.7%) children. Various combinations given were chloroquine + artesunate in 5 (16.7%) children, artesunate + mefloquine in 3 (10%) children, artesunate + sulfadoxine-pyrimethamine in 3 (10%) children, chloroquine + mefloquine, artesunate + doxycycline and artesunate and lumefantrine in 1 (3.3%) child each. Treatment failure was observed in 2 (6.7%) patients. Both patients were on chloroquine and then were treated with quinine and artemether respectively following which they responded. Twenty-nine (96.7%) patients recovered while 1 (3.3%) died.

Figure 1. Clinical findings in malaria.

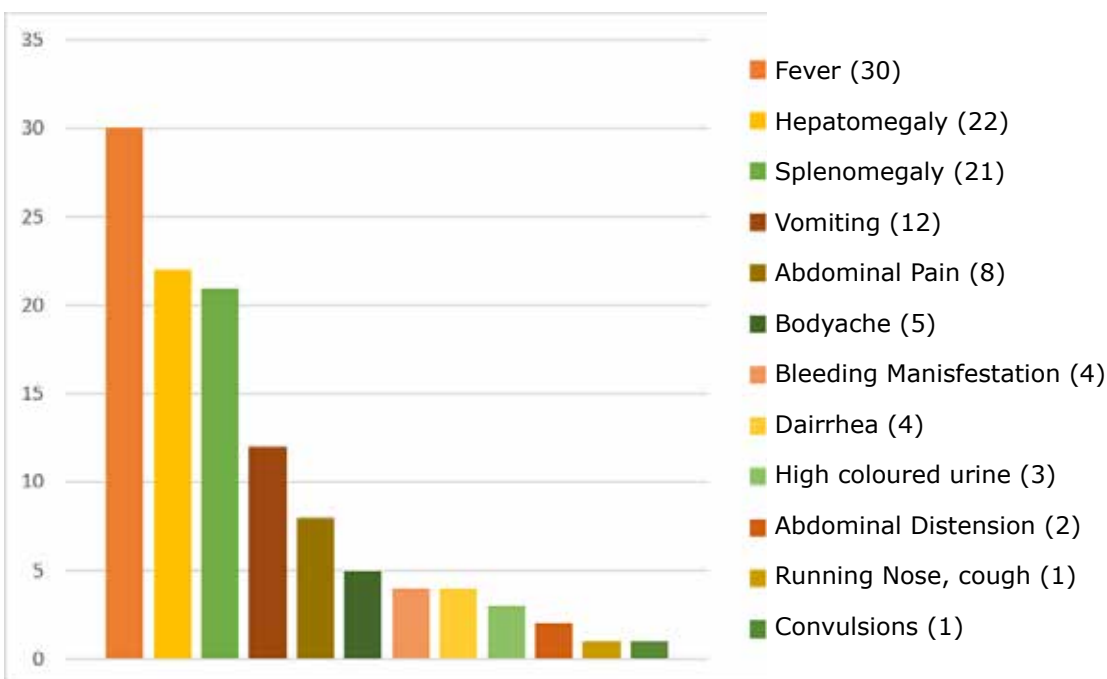

Figure 2. Laboratory Findings.

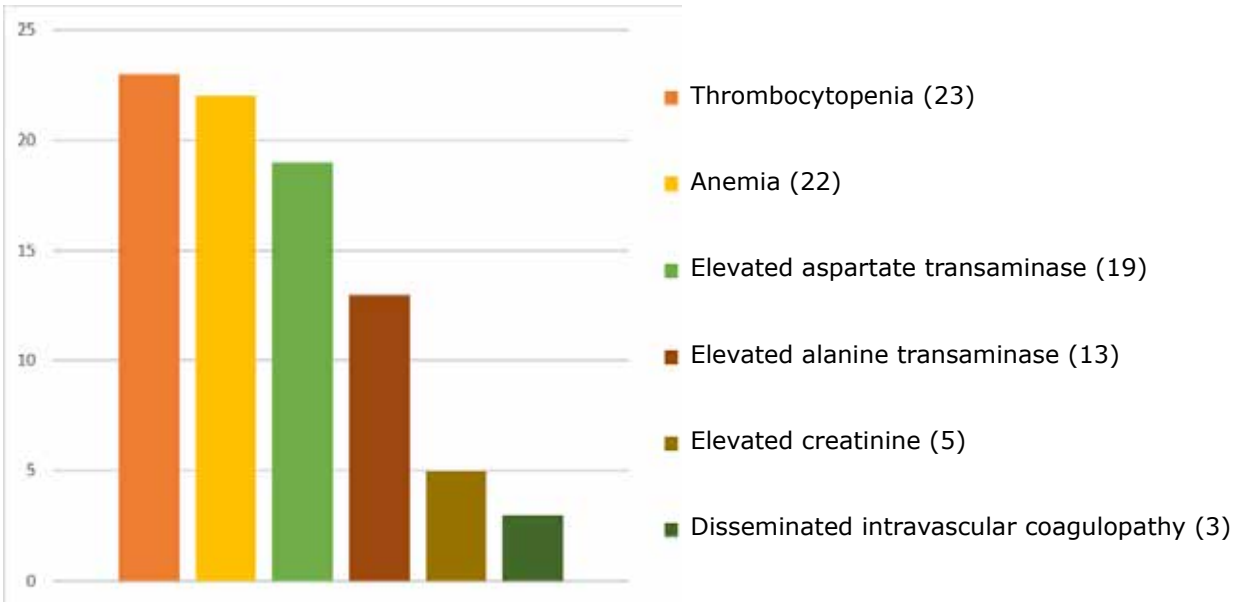

Table 1a. Clinical and laboratory features and type of malaria.

Clinical and laboratory features	Pl. falciparum malaria (n=7)	Pl. vivax malaria (n=18)	Mixed (n=5)	P values
Age group <5 years 5-10 Years >10 Years	 4(57.1%) 1(14.3%) 2(28.6%)	 9(50%) 6(33.3%) 3(16.7%)	 0 5(100.0%) 0	**0.041**
Gender Male Female	 3(42.85%) 4(57.1%)	 5(27.8%) 13(72.22%)	 1(20%) 4(80%)	0.660
Fever	7(100%)	18(100%)	5(100%)	-
Vomiting	3(42.85%)	7(38.88%)	2(40%)	0.984
Diarrhea	2(28.57%)	2(11.11%)	0(0%)	0.324
Anemia	4(57.14%)	13(72.22%)	5(100%)	0.251
Thrombocytopenia	7(100%)	11(61.11%)	5(100%)	**0.048**
Hepatomegaly	7(100%)	10(55.5%)	5(100%)	**0.026**
Splenomegaly	5(71.42%)	11(61.11%)	5(100%)	**0.243**
Elevated SGOT	7(100%)	10(55.5%)	2(40%)	0.058
Elevated SGPT	4(57.14%)	7(38.88%)	2(40%)	0.701
Elevated serum creatinine	1(14.28%)	3(6.67%)	1(20%)	0.966

Table 1b. Clinical and laboratory features in respect to type of malaria.

Clinical and laboratory features	Pl. falciparum malaria (Mean ± SD)	Pl. vivax malaria (Mean ± SD)	Mixed (n=5) (Mean ± SD)	P values
Age (years)	5.84 ± 5.38	6.45 ± 4.12	7.6 ± 0.54	0.769
Days of fever	6.7 ± 5.5	10.7 ± 9.7	11.4 ± 6.9	0.151
Days of Vomiting	1.4 ± 1.8	2.2 ± 7.0	1 ± 1.4	0.535

Days of Diarrhea	1.3 ± 2.6	0.1 ± 0.3	-	0.880
Hemoglobin (gm%)	8.1 ± 3.7	9.1 ± 2.7	6.2 ± 2.3	0.108
Platelets (/cumm)	72571 ± 33029	221533 ± 463779	54200 ± 35294	0.528
SGOT (IU/L)	107 ± 76.8	74.2 ± 124.3	70.8 ± 79.5	0.778
SGPT (IU/L)	64.6 ± 62.8	53 ± 68.6	37.6 ± 34.7	0.77
Creatinine (mg/dl)	0.8 ± 0.2	0.7 ± 0.3	0.8 ± 0.2	0.87

Table 2a. Clinical and lab features in respect to severity of malaria.

Clinical and laboratory features	Severe malaria (n=13)	Non severe malaria (n=17)	P values
Age group <5 years 5-10 Years >10 Years	 5 (38.5%) 6 (46.1%) 2 (15.4%)	 8 (47.1%) 6 (35.3%) 3 (17.6%)	0.833
Gender Male Female	 3 10	 6 11	0.691
Fever	13(100%)	17(100%)	-
Vomiting	6(46.15%)	6(35.29%)	0.547
Diarrhea	2(15.38%)	2(11.7%)	1.000
Anemia	10(76.92%)	12(70.58%)	1.000
Thrombocytopenia	13(100%)	10(58.82%)	**0.010**
Hepatomegaly	12(92.3%)	10(50.82%)	**0.047**
Splenomegaly	11(84.6%)	10(50.82%)	0.130
Elevated SGOT	9(69.23%)	10(50.82%)	0.421
Elevated SGPT	7(53.84%)	6(35.29%)	0.310
Elevated serum creatinine	4(30.76%)	1(5.8%)	0.138

Table 2b. Clinical and laboratory features in respect to severity of malaria.

Clinical and lab features	Severe malaria (n=13) (Mean ± SD)	Non-Severe malaria (n=17) (Mean ± SD)	P values
Age (years)	6.68 ± 3.65	6.36 ± 4.42	0.831
Days of fever	10.3 ± 6.7	9.7 ± 9.9	0.871
Days of Vomiting	1.2 ± 1.5	2.4 ± 7.2	0.541
Days of Diarrhea	0.7 ± 1.9	0.1 ± 0.3	0.246
Hemoglobin (gm%)	7.0 ± 3.0	9.4 ± 2.5	**0.025**
Platelets (/cumm)	61046 ± 40633	233705 ± 474753	0.203
SGOT (IU/L)	90.2 ± 74.8	74.5 ± 127.5	0.696
SGPT (IU/L)	56 ± 52.2	50.9 ± 69.7	0.828
Creatinine (mg/dl)	0.9 ± 0.3	0.7 ± 0.2	**0.019**
Type of malaria Falciparum Vivax Mixed infection	 5(38.4%) 4(30.8%) 4(30.8%)	 2(11.8%) 14(82.3%) 1(5.8%)	**0.016**

Table 3a. Age related clinical and laboratory manifestations of malaria.

Clinical and laboratory features	<5 years (n=13)	5-10 years (n=12)	>10 years (n=5)	P values
Fever	13(100%)	12(100%)	5(100%)	-
Vomiting	2(15.38%)	6(50%)	4(80%)	**0.03**
Diarrhea	3(23.07%)	0(0%)	1(20%)	0.212
Anemia	13(100%)	8(66.67%)	1(20%)	**0.002**
Thrombocytopenia	10(76.92%)	9(75%)	4(80%)	0.975
Hepatomegaly	10(76.92%)	9(75%)	3(60%)	0.757
Splenomegaly	11(84.6%)	9(75%)	1(20%)	**0.025**
Elevated SGOT	10(76.92%)	6(50%)	3(60%)	0.372
Elevated SGPT	4(30.76%)	5(41.66%)	4(80%)	0.177
Elevated serum creatinine	1(7.69%)	3(25%)	1(20%)	0.498

Table 3b. Clinical and laboratory features in respect to age.

Clinical and laboratory features	Age group <5 years (Mean ± SD)	Age group 5-10 years (Mean ± SD)	Age group >10 years (Mean ± SD)	P values
Days of fever	11.69 ± 9.68	9.41 ± 8.68	6.6 ± 4.28	0.525
Days of Vomiting	0.31 ± 0.75	3.58 ± 8.43	1.8 ± 1.64	0.337
Days of Diarrhea	0.77 ± 1.97	0.00 ± 0.00	0.20 ± 0.45	0.345
Hemoglobin (gm%)	7.19 ± 2.21	8.55 ± 3.34	11.14 ± 2.18	**0.035**
Platelets (/cumm)	240461.5 ± 546569.24	95216.67 ± 89251.32	99600 ± 71538.80	0.579
SGOT (IU/L)	60.61 ± 65.45	71.08 ± 76.35	159.80 ± 209.83	0.194
SGPT (IU/L)	38.76 ± 37.43	51.33 ± 53.58	94.80 ± 112.68	0.230
Creatinine (mg/dl)	0.68 ± 0.17	0.83 ± 0.26	0.89 ± 0.34	0.173

Discussion

Along with six other communicable diseases viz. diarrhea, HIV/AIDS, tuberculosis, measles, hepatitis B and pneumonia, malaria accounts for 85% of global infectious disease burden.[4,5] The WHO estimates 300-500 million cases of malaria annually.[6] Southeast Asia contributed to 2.5 million cases to the global burden of which India contributed a major portion of 76% of cases.[7]

India is an endemic zone for malaria with a wide spectrum of clinical presentation and complications. Fever with chills is the most common symptom of malaria. In our study we observed the common clinical features seen in malaria in specific pediatric age groups and compared them with the severity and type of malaria. In younger children less than 5 years of age, anemia and splenomegaly were significantly common while vomiting was the most common symptom in older children more than 10 years of age. Literature on such age specific findings in malaria is lacking and further research is required to establish a pattern, if any, between age and the symptomatology of malaria. However, it would not be wrong to say that in endemic areas, fever and splenomegaly in young children could be an indicator of malaria. We were unable to establish any significant correlation between gender and any of the clinical findings in our study.

In our study, the significant findings in severe malaria were thrombocytopenia, hepatomegaly, decreased hemoglobin levels and raised serum creatinine values as compared to children with non-severe malaria. Our study did not have a significant correlation of age with severity of malaria unlike the study conducted in Orissa, India according to which children less than 5 yrs had a higher risk of developing cerebral malaria, severe anemia, and seizure while children above 5 yrs had higher risk of acute renal failure and hepatic involvement.[8] Although, bleeding manifestation is included in the definition of severe malaria, WHO does not consider thrombocytopenia as an indicator of severe malaria. Our results show the presence of thrombocytopenia and hepatomegaly in severe malaria which should be further studied as important markers of severe malaria.

In our study 100% children with falciparum malaria had thrombocytopenia and hepatomegaly. There are

studies, however, which have found thrombocytopenia as an important finding in vivax malaria.[9,10,11] A study conducted by Jadhav UM et al found thrombocytopenia more common in falciparum malaria similar to our study.[12] Also, it was found that most cases of non-severe malaria were due to P. vivax as compared to severe malaria which was due to falciparum, vivax, or mixed infection equally. As supported by the above studies vivax malaria can lead to serious complications like thrombocytopenia, a proper watch on these patients should be kept to pick up early signs of severe malaria.

Conclusion

In children less than 5 years of age, anemia, and splenomegaly along with fever could be important indicators of malaria. In older children, vomiting in malaria is a common manifestation. Children between 5 to 10 years of age have higher prevalence of mixed malaria. Thrombocytopenia can be one of the indicators of severe malaria along with the pre-existing bleeding manifestations. Hepatomegaly and thrombocytopenia both are significant findings in severe as well as falciparum malaria.

Compliance with Ethical Standards

Funding: None
Conflict of Interest: None

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