Research Article

Clinical profile and complications of acute malaria caused by different species of Plasmodium

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Abstract

Introduction: Malaria is more severe in children than in adults and 78% of all deaths due to malaria occur in children under 5years. Plasmodium *vivax* has long been considered to have benign course. However during past few years several studies reported severe complicated cases of vivax malaria. **Methodology**: Children in the age group of 6 months to 15 years admitted in the Department of Pediatrics with clinical malaria were tested for malaria using peripheral smear, QBC and rapid diagnostic test. Children with positivity of any of these tests were enrolled in the study. Complete clinical profile is noted. Investigations like complete blood counts, LFT, RFT etc., were done. **Results:** Out of 150 children enrolled in the study 80 had Plasmodium *vivax* monoinfection. 61 had Plasmodium *falciparum* monoinfection and 9 had mixed infection. 41% of them were under 5years of age. The incidence of complications like severe anemia (10% vs. 18%), jaundice (10% vs. 44%), transaminitis (6% vs.13%), azotemia (6% vs. 36%) and thrombocytopenia (12.5% vs. 26%) were more common in P *falciparum* than in P *vivax* malaria with statistical significance ($p < 0.05$). There was no statistically significant difference in the incidence of hypoglycemia and cerebral malaria in P *vivax* and P *falciparum* malaria. **Conclusion:** The incidence of severe malaria in P. *vivax* infection is comparable to that in P. *falciparum* infection and it is no more benign. Hence robust efforts are required for reduction and elimination of P *vivax* transmission.

Key Words: Plasmodium *falciparum*, Plasmodium *vivax*, Clinical Profile, Complicated Malaria,

Introduction

Globally an estimated 3.3 billion people in 97 countries and territories are at risk of being infected with malaria and developing disease and 1.2 billion are at high risk (1 in 1000 chance of getting malaria in year). According to the latest estimates, 198 million cases of malaria have occurred globally in 2013 and the disease leads to 584,000 deaths. 78% of all deaths due to malaria occur in children aged less than 5 years [1].

Because of immature immune system malaria is more severe in children than in adults. Malaria imposes great socioeconomic burden on humanity and with six other diseases (diarrhea, HIV/AIDS, tuberculosis, measles, hepatitis B and pneumonia) accounts for 85% of global infectious disease burden.

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Among cases of malaria, proportion of Plasmodium *vivax* and Plasmodium *falciparum* varies in different parts of India. Areas with more than 30% of Plasmodium *falciparum* cases are categorized as high risk.

P.*vivax* malaria has long been considered to have benign course with multiple relapses. However during past few years several isolated studies from India [2], Indonesia [3,4] and Papua, New Guinea[5] have reported severe complicated cases of vivax malaria. P.vivax is now getting recognized as a major cause of severe and fatal malaria despite its low parasite biomass, increased deformability of infected RBC and apparent paucity of parasite sequestration.

With this background this study was carried out to analyze the clinical profile, laboratory parameters and

complications of malaria caused by different species of plasmodium.

Methodology

The present study was a cross sectional observational study conducted over a period of 18 months from December 2011 to May 2013 in the Department of Pediatrics, Government General Hospital, Kakinada. Children in the age group of 6 months to 15 years who were admitted in pediatric wards/ICU with clinical suspicion of malaria were tested for malaria using peripheral smear, QBC and RDT.

Those children with positivity of any of the above mentioned tests were enrolled in the study.

Exclusion Criteria: Children with infections like enteric fever, pyogenic meningitis, tuberculosis etc., with coincidental smear positivity for malaria were excluded in the study.

A predesigned proforma was used to record the socio-demographic details and clinical manifestations of enrolled children. Detailed clinical examination was done and patients were given anti-malarial treatment and complications and outcome were noted. All the enrolled children were subjected to investigations like hemogram, renal function tests, liver function tests and blood sugar. Other investigations like serum electrolytes, ABG, chest X ray etc., were done whenever required. The results were tabulated and statistically analyzed using SPSS version 17.

Results

During the study period 450 cases of clinically suspected malaria were admitted in the hospital, of which 150 cases were positive for malaria either by peripheral smear or QBC or rapid diagnostic tests. P.*vivax* monoinfection was seen in 80 children (53.3%). P. *falciparum* was seen in 61 (40.6%) children and 9 (6%) had mixed infection.

The demographic profile of patients included in the study was shown in table I. 41.3%, 34% and 24.6% of children were in the age group of < 5 years, 6-10years and 11-15 years respectively. 52% of children were males and 48% were females. 35% of them were from tribal areas and rest from rural and urban areas.

Clinical profile and lab parameters of children with malaria caused by P.*vivax*, P. *falciparum* and mixed infections were given in table II and table III.

All children presented with fever. History of chills was present in 93% of P.*vivax* and 95% of P. *falciparum* malaria cases. Myalgias (40% vs. 70.4%), vomitings (38% vs. 62%), oliguria (12.5% vs. 24.5%), cerebral malaria (25% vs. 33%), jaundice (10% vs. 44%) and organomegaly (54%vs. 84%) were more common in children with P. *falciparum* malaria than in children with P.*vivax* malaria. Elevation of AST and ALT (6% vs. 13%), azotemia (6% vs. 36%), severe anemia <5gm %(10% vs. 18%) and thrombocytopenia (12.5% vs. 26%) were more common in children with P. *falciparum* malaria than with P.*vivax* malaria.

Table I: Demographic characteristics

		No of children	Percentage
Age	6 m - 5 yrs	62	41.4
	6 - 10 yrs	51	34
	11 – 15 yrs	37	24.6
Sex	Male	78	52
	Female	72	48
Residence	Tribal	52	34.7
	Urban & rural	98	65.3

Table II: Clinical profile of children with malaria

Clinical Features	P.*vivax*	%	P.*falciparum*	%	mixed	%	total	%
Fever	80	100	61	100	9	100	150	100
Chills	74	92.5	58	95	8	88.8	140	93.3
Myalgias	32	40	43	70.4	6	66.6	81	54
Vomitings	30	37.5	38	62.2	6	66.6	74	49.3
Oliguria	10	12.5	15	24.5	3	33.3	28	18.7
Hepatomegaly	11	13.7	28	46	8	89	47	31.3
Splenomegaly	43	53.7	51	83.6	9	100	103	68.6
Cerebral malaria	20	25	20	32.7	2	22.2	42	28
Jaundice	8	10	27	44.2	2	22.2	37	24.7

Table III: Lab parameters in children with malaria

Parameter	P.*vivax*	%	P.*falciparum*	%	P value
Anemia	30	37.5	46	75.4	0.000
Thrombocytopenia	10	12.5	16	26.2	0.037
Deranged RFT	5	6.25	22	36	0.000
Elevated transaminases	5	6.25	8	13.1	0.000
Hypoglycemia	2	2.5	3	4.9	0.442
Hyperbilirubinemia (TSB >1.5 mg/dl)	8	10	27	44.2	0.000

Table III shows comparison of morbidity profile of P.*vivax* and P. *falciparum* infections. All the complications of malaria were more common with P. *falciparum* than with P.*vivax* infection.

It was observed that severe anemia, thrombocytopenia, azotemia, transaminitis and jaundice were more common with P. *falciparum* with statistical significance (p value <0.05). There was no statistically significant difference in the incidence of hypoglycemia and CNS manifestations in P.*vivax* and P. *falciparum* malaria.

Table-IV: Clinical features and lab parameters in children of different age groups with P.*vivax* and P. *falciparum* infection

	6 m – 5years		6 – 10 years		>10 years	
	P*v*	P*f*	P*v*	P*f*	P*v*	P*f*
Splenomegaly	17(21%)	15(24%)	14(17.5%)	23(37%)	12(15%)	13(21%)
Hepatomegaly	6(7.5%)	6(9.8%)	3(3.75%)	14(23%)	2(2.5%)	8(13%)
Cerebral malaria	6(7.5%)	5(8%)	7(8.7%)	9(15%)	7(8.8%)	6(10%)
Raised bilirubin	3(3.7%)	8(13%)	4(5%)	13(21%)	1(1.2%)	6(10%)
Elevated transaminases	1(1.2%)	3(4.9%)	3(3.75%)	3(4.9%)	1(1.2%)	2(3.2%)
Abnormal RFT	-	6(9.8%)	4(5%)	11(18%)	1(1.2%)	5(8%)
Anemia	8(10%)	14(23%)	12(15%)	21(34%)	10(12%)	11(18%)
Thrombocytopenia	3(3.7%)	4(6.5%)	3(3.75%)	8(13%)	4(5%)	4(6.5%)

Table IV shows the age wise incidence of various complications of P. *falciparum* and P.*vivax* malaria. There was no significant difference in the incidence of complications of P. *falciparum* and P.*vivax* malaria in different age groups.

Discussion

In the present study highest prevalence of malaria was seen in children of age less than 5 years (41%). This is in contrast with the studies done by Ragini et al[6] and Pankiti D Desai et al[7], where children above 6 years are more commonly affected; this can be explained by high endemicity in this area.

Plasmodium *falciparum* accounted for 40% of hospitalized malaria cases in the present study, whereas Koushik et al[8] from Delhi and Ragini et al from uttarakhand[6] showed lower prevalence of Plasmodium *falciparum* (7.9% and 28% respectively).

In the present study hematological, renal and hepatic complications were noted more commonly in P. *falciparum* infection. The incidence of CNS complications was similar in P.*vivax* and P. *falciparum* infections.

Jaundice was seen in 44% and 10% of P. *falciparum* and P.*vivax* malaria whereas transaminitis was seen in 13% and 6% of P. *falciparum* and P.*vivax* malaria. These results indicate that besides hemolysis, hepatocellular injury is important factor for jaundice.

The occurrence of transaminitis (elevated AST and ALT) indicates "malarial hepatitis", but co-existent infections like hepatitis A also have to be ruled out.

In the present study cerebral malaria was seen in 25% and 33% of P.*vivax* and P.*falciparum* infection. Two studies on children from Bikaner [9] and Uttrakhand [10] showed a comparable incidence of cerebral malaria between P. *vivax* and P. *falciparum* infections.

Thrombocytopenia was seen in 26% and 12% of P.*falciparum* and P.*vivax* malaria in present study. Earlier observations found that thrombocytopenia is quiet rare in P.*vivax* malaria but recently thrombocytopenia has been noted in P.*vivax* monoinfection from many parts of world including India [11,12,13,14].

Renal dysfunction was seen in 6% of P.*vivax* infection in this study. A study from Bikaner reported 10% incidence of renal dysfunction in P.*vivax* malaria. Several other studies [11, 15] reported acute renal failure in P.*vivax* infection

The present study analysis shows that the incidence of severe malaria (including cerebral malaria) in vivax infection is comparable to that in P. *falciparum* infection.

The inability of the infected RBC to adhere to vascular endothelium and the parasite's strict preference for invading reticulocytes could explain the benign nature of P.*vivax* infection.

Infected RBC in P.*vivax* is not as rigid as observed in P. *falciparum* infection which makes capillary blockage in organs less likely in P.*vivax* infection. But several reports of occurrence of severe malaria with P. *vivax* show the need to decipher the pathogenesis of severe malaria caused by P.*vivax*.

The geographical areas that reported severe P.*vivax* malaria are the same that demonstrated P.*vivax* chloroquine resistance [16]. Hence further studies are required to find out the relation between the pathogenesis of severe malaria and its relation to emergence of multidrug resistant strains of P.*vivax*.

The WHO severity criteria formerly only validated for P. *falciparum* infection seem to be applicable to most of the P.*vivax* patients. But certain criteria need to be re-addressed. Severe disease with P. *falciparum* is considered with parasitemia of >2, 00,000/µl, while parasitemia exceeding 50,000/µl is rare in severe P.*vivax* malaria[17]. P.*vivax* causes potentially life threatening infection at relatively low grade parasitemia.

There are abundant data showing that transmission of P. *falciparum* is actually more responsive to malaria control measures. As a result, in areas where two species co-exist, the scale up of integrated malaria control measures generally result in a shift, such that P.*vivax* becomes dominant species [18]. Globally malaria control strategies and action plan needs to re-address the fallacy that P.*vivax* is '*benign*', not fatal. More robust efforts are required for reduction and elimination of P.*vivax* transmission to achieve Millennium Development Goal 6 (the goal of no deaths from malaria and malaria free world), which specifically addresses malaria. Malaria control also helps to achieve other MDGs.

Conclusion

The present study shows that P.vivax monoinfection can result in severe malaria in children and more robust measures are required to reduce the transmission of P.vivax malaria to achieve MDGs.

Abbreviations

QBC: Quantitative buffy coat
RDT: rapid diagnostic test
LFT: liver function tests
RFT: renal function tests
HIV: human immunodeficiency virus
AIDS: acquired immune deficiency syndrome
RBC: red blood cell

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