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Clinico-laboratorical spectrum of malaria in children: Emerging new trends.

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Abstract

Background: Malaria is an endemic in developing countries across the world and is associated with significant morbidity and mortality. Recently, a significant change in clinical presentation and various laboratory parameters has been reported worldwide.

Objective: To evaluate the clinical and laboratory parameters in children with malaria.

Material and methods: This prospective study evaluated 55 children aged 1-17 years admitted at SPMCHI, SMS Medical College Jaipur from July 2013 to October 2014 having malaria. A detailed clinical history, examination and relevant laboratory investigations were recorded on day of presentation.

Results: In severe malaria, *Plasmodium vivax* was the predominant organism in 60.4% cases whereas *Plasmodium falciparum* was present in 16.3% cases. Mixed infection was seen in 23.3% cases. In uncomplicated malaria, *Plasmodium vivax* was observed in 50% cases whereas *Plasmodium falciparum* and mixed infection was seen in 33.4% and 16.6% cases, respectively. Most common clinical presentation was fever (94.5%) followed by splenohepatomegaly (70.9%), pallor (69%) and jaundice (25.4%). Most common complication was prostration (49%) followed abnormal bleeding (30.9%) ,severe anemia (27.3%), renal impairments (20%), shock (16.3%), altered sensorium (16.3%), convulsion (12.7%) and pulmonary edema (12.7%). Among laboratory parameters, thrombocytopenia was observed in 70.9% and deranged hepatic functions were observed in 25.4% children.

Conclusion: In changing clinical spectrum of malaria, *Plasmodium vivax* is predominantly associated with severe malaria. Presence of thrombocytopenia, severe anemia, bleeding tendencies in a patient of acute febrile illness should alert the clinician the possibility of malaria.

Keywords: Malaria, *Plasmodium vivax, Plasmodium falciparum*.

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Introduction

The malaria prevention and control is still challenging in developing countries. India has maximum burden of malaria cases in Southeast Asia [1]. Malaria is causing significant morbidity and mortality in children. Childhood mortality is account about 27% of all death per year due to malaria in India [2].

Historically *P. falciparum* malaria has been associated with severe complications and significant mortality. However *P. vivax* malaria is increasingly being reported as cause of severe malaria and different manifestation of severe malaria as compared to *P. falciparum* malaria from several countries across the world [3]. This study was planned to know the current clinico- laboratorical trends of malaria.

Materials and Methods

This was a prospective observational study conducted at sir padampat mother and child health institute (SPMCHI), SMS Medical College, Jaipur from July 2013 to October 2014. In which we enrolled 55 children hospitalized with malaria aged between 12 months to 17 years. Out of them 35 were male and 20 were female. Approval from the institutional ethical committee was obtained before performing the study.

The diagnosis and confirmation of species of *P. falciparum*, *P. vivax* malaria and mixed infection were established by thick and thin film of peripheral blood smear examination under oil immersion with Giemsa stain and rapid diagnostic test for malarial antigen (RDT). The RDTs were based on detection of specific Plasmodium spp. lactate dehydrogenase and histidine-rich protein [2].

On the basis of results of peripheral smear and/or rapid diagnostic malaria test, cases were classified in to three groups: *P.vivax* malaria, *P. falciparum* malaria and mixed infection (P.V+P.F).

Children with malaria categorized in to two groups: severe malaria and non severe malaria as per world health organization (WHO) criteria [4].

Children with human immunodeficiency virus (HIV) infection, co-existing systemic illness (chronic renal failure, chronic interstitial lung disease, bleeding disorders, chronic liver disease and known progressive neurological illness) and Children with clinical diagnosis of malaria but without any evidence on smear or antigen testing were excluded.

A detailed clinical history, examination and relevant laboratory investigations were recorded on day of presentation. Data thus collected were entered into Excel worksheet and classified as well as analyzed according to objective. Analysis was done using SPSS v 21.0 for Windows (IBM Inc., USA)

Results

In present study, the mean age of study subjects was 6 ± 1.2 year. Out of 55 children, thirty five were male and twenty were female. Forty three (78.2%) had severe malaria and twelve (21.8%) children had non severe malaria. Thirty two (58.2%) children had *P. vivax*, eleven (20%) had *P. falciparum* and twelve (21.8%) had mixed infection. Twenty six (60.4%) children with *P. vivax*, seven (16.3%) children with *P. falciparum* and ten (23.3%) children with mixed infection had severe malaria as shown in Table 1. The most common clinical presentation was fever (94.2%) followed by splenohepatomegaly (70.9%), pallor (69%), weakness (49%), abnormal bleeding (30.9%), icterus (25.4%) and Oliguria (20%) as mentioned in Table 2. The laboratory features of children having malaria are depicted in Table 3. Overall, the most common laboratory finding was thrombocytopenia (70.9%) followed by severe anemia (27.3%), deranged hepatic function (25.4%), renal function impairments (20%), hypoglycemia (10.9%) and Hyperparasitemia was observed in five (9%) children. The most common complication in children with severe malaria was prostration (49%) followed abnormal bleeding (30.9%), severe anemia (27.3%), jaundice (25.4%), AKI (20%) and convulsion (12.7%) as depicted in Table 4.

Discussion

Malaria is one of major health concern of India. Malaria is completely curable if effective treatment started promptly. Delay in effective treatment may lead to devastating consequences including death. In present study the most common causative agent of malaria was *P. vivax*. The *P. vivax* was responsible of more than half (60.4%) of severe malaria cases in our study. Earlier, the *P. vivax* malaria was considered as benign tertian malaria. However recent several studies are challenging this terminology. Studies from Southeast Asia have shown that *P. vivax* is accounted 40% to 60% hospitalization of children with malaria and *P. vivax* is responsible for 30% to 65% of severe malaria in children [5-6].

Table 1. *Demographic data and baseline characteristics of study subjects*

Characteristics		**Observations**	
		No. of Study Subjects	**% Study Subjects**
Sex	Male	35	63.6
	Female	20	36.4
Mean age ± SD (Year)		6 ± 1.2	
Severe Malaria		43	78.2
Non Severe Malaria		12	21.8
Peripheral Blood Smear Positive		46	83.6
Malaria Antigen Test Positive		49	89
P. vivax		32	58.2
P. vivax	Severe malaria	26	60.4
	Non severe malaria	6	50
P. falciparum		11	20
P. falciparum	Severe malaria	7	16.3
	Non severe malaria	4	33.4
Mixed Infections (*P. vivax*+*P. falciparum*)		12	21.8
Mixed Infections	Severe Malaria	10	23.3
	Non Severe Malaria	2	16.6

Table 2. *Distributions of study subjects according clinical features*

Clinical Features		No. of Study Subjects (%)
Fever		52 (94.5%)
Splenohepatomegaly		39 (70.9%)
Pallor		38 (69%)
Abnormal bleeding		17 (30.9%)
Abnormal bleeding	Skin and mucocutaneous	11 (20%)
	Pulmonary bleeding with hematemesis	1 (1.8%)
	GI bleeding	1 (1.8%)
	Hematuria	4 (7.2%)
Icterus		14 (25.4%)
Breathlessness		10 (18.2%)
Oliguria		11 (20%)
Weakness		27 (49%)
Convulsion		7 (12.7%)
Impaired consciousness (GCS<9)		9 (16.3%)

Table 3. *Distributions of study subjects according to laboratory profile*

Laboratory Parameters	No. of Study Subjects (%)
Severe anemia	15 (27.3%)
Thrombocytopenia	39 (70.9%)
Deranged hepatic function	14 (25.4%)
Metabolic acidosis	7 (12.7%)
Hyperparasitemia	5 (9%)
Renal function impairment	11 (20%)
Hypoglycemia	6 (10.9%)
Hemoglobinuria	3 (5.5%)

Table 4. *Distributions of study subjects according to complications of severe malaria*

Complications	No. of Study Subjects (%)
Prostration	27 (49%)
Severe Anemia	15 (27.3%)
Abnormal Bleeding	17 (30.9%)
Jaundice	14 (25.4%)
Shock	9 (16.3%)
Renal Impairments	11 (20%)
Convulsions	7 (12.7%)
Impaired consciousness	9 (16.3%)
Pulmonary Edema/ARDS	7 (12.7%)
Hypoglycemia	6 (10.9%)
Hyperparasitemia	5 (9%)

Another study from India which was done on children who were hospitalized with malaria, shown that the risk of severe disease was greatest with the *P. vivax* infections (63.1%) [7]. The studies from other part of globe also suggested that *P. vivax* is now new emerging challenge because it is also cause severe malaria [8-9].

The most common clinical presentation of malaria in our study was fever (94.5%) followed by splenohepatomegaly (70.9%) and pallor (69%). A study from Mumbai, India which was done on children with malaria, revealed that the most common presentation was fever (96%) followed by pallor (62%) and hepatosplenomegaly (50%) [10].

The thrombocytopenia (platelet counts of $<150 \times 10^3/\mu L$) was most common hematological observation in our study. It was found in 70.9% children with malaria. A study was done from Mumbai, in children with malaria had also reported that thrombocytopenia was detected in 75% of children with severe *P. vivax* malaria [11]. Thrombocytopenia was described as the most common manifestation of malaria in the WHO report. Recent reports from various parts of the world suggest that the incidence of thrombocytopenia, which was earlier considered to be rare in *P. vivax* malaria, is currently similar in vivax and falciparum malaria [12]. The association of severe thrombocytopenia (platelet counts of $<20 \times 10^3/\mu L$) to skin and mucosal bleeding has been observed in children with especially *P. vivax* malaria [13]. In our study, 20% children had petechial rashes while 7.2% children had

hematuria, one child had pulmonary hemorrhage with GI bleed and one child had GI bleeding. The exact mechanism of the *P. vivax* associated thrombocytopenia is not known. Both immunological and non-immunological factors are involved.

The anemia in children with malaria is common manifestation. Present study has reported that pallor was observed in 69% children while severe anemia was found in 27.3% children with malaria. Bhattacharjee [11] did found pallor in 100% children while severe anemia and liver dysfunction were present in 8.3% and 16.7% children respectively with *P. vivax* malaria.

A transient liver dysfunction is common feature of childhood malaria. But it can progress severe hepatic complications like hepatic encephalopathy. Deranged hepatic function was observed in 24.5% children in our study. These all children have icterus, conjugated hyperbilirubinaemia and elevated hepatic enzymes which were suggested malaria hepatitis. Out of all these children with malarial hepatitis, two children had GI bleeding and one developed hepatic encephalopathy.

Shobha [14] did report that icterus with deranged liver functions was present in 25.9% cases in their study. They were also found that abnormal bleeding was seen in 18.5% cases in the form of malena, haematemesis, epistaxis, hematuria, petechiae. 5.6% children with *P. vivax* malaria were presented with ARDS/pulmonary edema. Another study which was done by Sharma and Khanduri, who reported deranged liver functions in 27% of the cases [15].

There were 12.7% children with malaria had repeated convulsions. 16.3% children with malaria had impaired consciousness (GCS $\leq$ 9). Other possible causes of convulsion and altered sensorium were ruled out. Shobha did found impaired consciousness and convulsions in 18.3% and in 7.6% children with *P. vivax* malaria respectively [14].

Acute Respiratory Distress Syndrome (ARDS) was observed in 12.7% children. All these children had *P. vivax* malaria. The exact mechanisms of ARDS is still unknown but it has been thought that the sequestration of infected RBCs within pulmonary microvasculature resulting in alveolar capillary dysfunction. The ARDS in vivax malaria probably results from the cytokine-related increases in the alveolar permeability and from the altered alveolar fluid clearance [16]. ARDS was reported in 9.1% children with *P. vivax* malaria by Bhattacharjee [11].

Renal dysfunction is increasingly being reported in *P. vivax* malaria. Renal function impairment was observed in 20% children with malaria. Out of them 81.8% children had *P. vivax* malaria. All these children had Oliguria and 7.2% children had hematuria. Hemoglobinuria was found in 5.5% children. These all children had *P. vivax* malaria. It was postulated that the possible mechanism of renal dysfunction in *P. vivax* malaria is mechanical obstruction by parasitized RBCs, DIC and hypoxic or immune mediated necrosis of glomeruli [17]. Bhattacharjee were found renal dysfunction in 11.9% children with *P. vivax* malaria [11].

The exact pathophysiology of *P. vivax* malaria is still not well understood. The inflammatory response of *P. vivax* infection is more than that seen in *P. falciparum* infection with similar or greater parasite load [18]. The cytokine production and release is also greater than that which observed in the *P. falciparum* infection [19].

Conclusion

Plasmodium vivax was most common etiology of severe malaria in children. It should no longer be considered as benign malaria. Thrombocytopenia was most common hematological observation. Abnormal bleeding, severe anemia, hepatorenal functions impairment and pulmonary dysfunction are more common complications than cerebral manifestations in children with severe malaria.

Contributions

BSS & MLG designed the study, HMM collected the data and write manuscript, AS & PS interpreted the data; RC helped in interpreting the data.HMM will act as guarantor of the article.

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