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Clinico-hematological manifestations of malaria in hospitalized children.

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Abstract

Background: Malaria is a disease of global importance and affects more than 90 countries in both the tropical and subtropical regions. Malaria is one of the important causes of mortality in pediatric age groups. This study aims to understand the clinico-haematological profile of malaria and its correlation with different malarial species among hospitalized children in tertiary care hospital, Surat, India.

Methods: A retrospective study was carried out at a tertiary care hospital of a medical college in Surat over a period of 6 months from July 2024 to December 2024. Children below 18 years admitted with acute febrile illness with peripheral smear and/or rapid malaria antigen test positive were included in the study. A detailed history and clinical examination along with biochemical and hematological parameters were analyzed using different statistical tests.

Results: Out of 154 children admitted with malaria, majority of cases were due to *P. vivax* (66.2%) compared to *P. falciparum* (28.6%) and mixed infection (5.2%). Case fatality rate was 1.94%, all due to severe *Vivax* malaria. Incidence of malaria was found to be more in males (63.6%) and 1-5 years age group. Fever was the presenting complaint in all the patients (100%) and chills and rigors in 77.2% of the cases. Other symptoms were vomiting 64 (42.8%), headache 38 (24.7%), abdominal pain 24 (15.6%), yellowish discolorations of eyes 3 (1.9%), diarrhea 2 (1.2%) and convulsions 2 (1.2%). Clinical signs were pallor (52.5%), icterus (16.8%), splenomegaly (42.2%), hepatomegaly (24%) and hepatosplenomegaly (9.09%), abdominal distension (16.2%), oedema (7.1%), shock (1.9%), ARDS (2.5%). Haematological parameters observed were anaemia (47.4%), severe anaemia (5.8%), leucocytosis (16.8%), leukopenia (24%), thrombocytopenia (65%) and severe thrombocytopenia (22.7%). Severe thrombocytopenia was seen with vivax malaria (65.7%).

Conclusion: The study highlights that is a common cause of malaria in Surat, Gujarat and can result in a severe disease. Fever with chills and rigor and splenomegaly are important clinical features, whereas anemia and thrombocytopenia are the most noted hematological parameters in malaria. The parameters may vary with different species of malaria. Knowledge of clinical and hematological parameters aids us in early diagnosis and prompt initiation of treatment and prevention of associated complications.

Keywords: Malaria, *P. vivax*, *P. falciparum*, Children, Clinico-hematological changes.

Introduction

Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bite of anopheles' mosquito. Malaria is endemic in the tropics and subtropics with highest prevalence in Africa followed by South East Asia. India contributes to 80% of South East Asia malaria burden (24 million cases per year). Malaria is causing significant morbidity and mortality in children. Childhood mortality is accounted in about 27% of all deaths per year due to malaria in India. Children under age of 5 accounts for 77% of total malarial deaths worldwide. Haematological manifestations are invariably associated with malaria. They are the most common complications encountered in malaria and play major role in its pathogenesis.

The proportion of *P. vivax* and *P. falciparum* varies in different parts of India. *Vivax* malaria has long been considered to have a benign course with multiple relapses. The typical complications seen in falciparum malaria were not usually found in *Vivax* mono-infections. However, during the past few years, the trend in the clinical manifestations of *Vivax* malaria has been changing [1-5].

Hence, this study was carried out to outline the clinico-hematological profile and outcome in children with malaria admitted to a tertiary care hospital in Surat, Gujarat.

Materials and Methods

This study was a retrospective study of children aged between 0-18 years admitted in pediatric ward and pediatric intensive care unit in SMIMER hospital, a tertiary care centre from July 2024 to December 2024. A total of 154 cases of malaria under 18 years were enrolled in the study.

Inclusion criteria

- Children in age group 1 month-18 years.
- Any acute febrile illness lasting for 2-7 days.
- Peripheral blood smear and/or rapid malaria antigen test positive for *P. vivax* and/or *P. falciparum* malaria.

Exclusion criteria

- Patients presenting with fever with Peripheral Smear (PS) and/or rapid malaria antigen test negative for malaria but treated empirically like malaria.
- Chronic illnesses, bleeding disorders, renal disorders, progressive neurological diseases.
- Co-infection with dengue (dengue antigen or dengue serology positive), typhoid (serum widal, typhi dot).

Diagnosis

Diagnosis and confirmation of species of *P. falciparum* and *P. vivax* malaria were established by thick and thin film of Peripheral Smear (PS) examination under oil immersion with Giemsa stain and malaria rapid card test which is a chromatographic immunoassay for qualitative determination of malarial parasite (*P. vivax*/*P. falciparum*), pLDH and aldolase. Diagnostic methods used were conventional thick and thin peripheral smear stained with Leishman stain, examined under oil immersion. The slide was considered negative when there were no parasites in 100 HPF. Rapid diagnostic tests were based on detection of specific plasmodium antigen, LDH (optimal test) for *Vivax* and HRP2 for *Falciparum*. Xamin malaria (one step malaria antigen rapid test device) was used as rapid diagnosis. Other lab investigations were undertaken like hemoglobin, total leukocyte count, platelet count, G6PD, renal function tests, liver function test, blood sugar, CSF examination and other investigations wherever needed.

Data collection and analysis

Records of all the patients who were discharged or expired with the diagnosis of malaria were retrieved. Data regarding patient's age, sex, clinical presentation, investigation and outcome were recorded. The clinical features and lab reports were analyzed to label severity based on WHO guidelines for classification of severe malaria. The qualitative variables were expressed in terms of percentages, frequency and mean and analyzed using *chi-square* test. A p-value of <0.05 was considered as statistically significant.

Treatment

Patients were treated according to National Vector Borne Disease Control Program (NVBDCP) guidelines for malarial treatment.

Outcome

Out of 154 patients admitted with malaria, 151 patients had recovered and discharged while 3 patients died due to severe vivax malaria.

Results

During the study period total of 154 children were admitted with malaria. Blood investigations were carried out before starting the anti-malarials. Majority of cases, 102 (66.2%) were found to have *P. vivax* infection, while 44 (28.6%) and 8 (5.2%) patients had *P. falciparum* and mixed infections respectively. Incidence of malaria was found to be more in males (63.6%) than females (36.4%). Male to female ratio was 1.75. Majority of patients with *P. vivax* malaria, with *P. falciparum* and mixed infection were in the age group (>5) years. Predominantly infected age group was between 11 and 15 years (Table 1) [6,7].

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

Variables		*Falciparum* (%)	*Vivax* (%)	Mixed malaria (%)	Total (%)
Gender	Male	23 (23.5)	69 (70.4)	6 (6.1)	98 (63.6)
	Female	21 (37.5)	33 (58.9)	2 (3.6)	56 (36.4)
Age groups (In years)	<5	5 (17.8)	22 (78.6)	1(3.6)	28 (18.2)
	6-10	11 (27.5)	26 (65)	3 (7.5)	40 (25.9)
	11-15	19 (32.2)	37 (62.7)	3 (5.1)	59 (38.4)
	>15	9 (33.3)	17 (62.9)	1 (3.7)	27 (17.5)

Type of malaria with clinical symptoms and signs

Fever was the presenting complaint in all the patients (100%) and chills and rigors in 77.2% of the cases. Headache was observed in 38 (24.7%) subjects. Other symptoms were vomiting 64 (42.8%), abdominal pain 24 (15.6%), yellowish discoloration of eyes 3 (1.9%), diarrhoea 2 (1.2%) and convulsions 2 (1.2%). 93% Children with *Falciparum* malaria, 94% in *Vivax* group and 100% 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. Abdominal pain, yellowish discolouration of skin, diarrhoea

was more common in *Vivax* malaria cases. Convulsion was seen with *Falciparum* malaria. Pallor, icterus, hepatomegaly and spleomegaly were the important clinical signs. Pallor was present in 70% of cases with *Vivax* malaria followed by 24.6% of *Falciparum* malaria cases. Icterus was present more with *Vivax* malaria (84.6%). Hepatomegaly was a predominant finding in children with *Vivax* malaria (78.3%) followed by *Falciparum* (21.6%). Splenomegaly was present in all three types, 71.4% children with *Vivax* malaria had hepatosplenomegaly followed by *Falciparum* (28.5%) abdominal distention, oedema, shock, respiratory distress were more common with *Vivax* malaria (Tables 2 and 3) [8,9].

Table 2. *Types of malaria with clinical parameters.*

Symptoms		***Falciparum*, (n=44)**	***Vivax*, (n=102)**	**Mixed, (n=8)**	**Total (%)**	**X^2**	**P value**
Fever	<5 days	41 (28.3)	96 (66.2)	8 (5.1)	145 (94.1)	0.573	0.751
	>5 days	3 (33.3)	6 (66.7)	0 (0)	9 (5.8)	0.573	0.751
Chills and rigor	Yes	35 (29.4)	78 (65.5)	6 (5.1)	119 (77.2)	0.19	0.909
	No	9 (25.7)	24 (68.6)	2 (5.7)	35 (22.7)	0.19	0.909
Headache	Yes	9 (23.6)	28 (73.6)	1 (2.6)	38 (24.7)	1.483	0.477
	No	35 (30.1)	74 (63.7)	7 (6.03)	116 (75.3)	1.483	0.477
Vomiting	Yes	19 (28.8)	44 (66.7)	3 (4.5)	66 (42.8)	0.099	0.952
	No	25 (28.4)	58 (65.9)	5 (5.6)	88 (57.2)	0.099	0.952
Abdominal pain	Yes	8 (33.3)	15 (62.5)	1 (4.2)	24 (15.6)	0.343	0.842
	No	36 (27.6)	87 (66.9)	7 (5.3)	130 (84.4)	0.343	0.842
Yellowish discolouration of skin	Yes	0 (0)	3 (100)	0 (0)	3 (1.9)	1.56	0.458
	No	44 (29.1)	99 (65.5)	8 (5.2)	151 (98)	1.56	0.458
Diarrhoea	Yes	0 (0)	1 (50)	1 (50)	2 (1.2)	8.49	0.014
	No	44 (28.9)	101 (66.4)	7 (4.6)	152 (98.8)	8.48	0.014
Convulsions	Yes	1 (50)	1 (50)	0	2 (1.2)	0.512	0.774
	No	43 (28.8)	101 (66.4)	8 (5.2)	152 (98.8)	0.512	0.774
Signs							
Pallor	Yes	20 (24.6)	57 (70.3)	4 (4.9)	81 (52.5)	1.363	0.506
	No	24 (32.8)	45 (61.6)	4 (5.4)	73 (47.4)	1.363	0.506
Icterus	Yes	3 (11.5)	22 (84.6)	1 (3.84)	26 (16.8)	4.882	0.087
	No	41 (32)	80 (62.5)	7 (5.5)	128 (83.1)	4.882	0.087
Hepatomegaly	Yes	8 (21.6)	29 (78.3)	0 (0)	37 (24)	4.438	0.109
	No	36 (30.7)	73 (62.3)	8 (6.8)	117 (75.9)	4.438	0.109
Spleenomegaly	Yes	19 (29.2)	42 (64.61)	4 (6.1)	65 (42.2)	0.261	0.878
	No	25 (28)	60 (67)	4 (4.5)	89 (57.7)	0.261	0.878
Hepato-spleenomegaly	Yes	4 (28.5)	10 (71.4)	0	14 (9.09)	0.863	0.65
	No	40 (28.57)	92 (65.7)	8 (5.7)	140 (90.9)	0.863	0.65
Abdominal distension	Yes	11 (27.5)	13 (52)	1 (4)	25 (16.2)	3.481	0.175
	No	33 (25.5)	89 (68.9)	7 (5.4)	129 (83.7)	3.481	0.175
Oedema	Yes	3 (27.3)	8 (72.7)	0	11 (7.1)	0.698	0.705
	No	41 (28.6)	94 (65.7)	8 (5.5)	143 (92.8)	0.698	0.705
Shock	Yes	0	2 (66.7)	1 (33.3)	3 (1.9)	5.538	0.063
	No	44 (29.1)	100 (66.3)	7 (4.6)	151 (98.1)	5.538	0.063

Respiratory distress	Yes	1 (25)	3 (75)	0	4 (2.5)	0.279	0.87
	No	43 (28.6)	99 (66)	8 (5.3)	150 (97.5)	0.279	0.97
Note: Ns: Not significant							

Table 3. *Haematological parameters with type of malaria.*

Parameters		***P. falciparum* (%)**	***P. vivax* (%)**	**Mixed (%)**	**Total (%)**	**X^2**	**P value**
Haemoglobin (gm %)	<7	0 (0)	8 (5.1)	1 (0.6)	9 (5.8)	4.29	0.117
	7-10	19 (12.3)	50 (32.4)	4 (2.5)	73 (47.4)	10.58	0.005
	>10	25 (16.2)	44 (28.5)	3 (1.9)	72 (46.7)	6.73	0.034
TLC (cells/cumm)	<4000	10 (6.4)	26 (16.8)	1 (0.6)	37 (24)	5.21	0.074
	4000-11000	23 (14.9)	62 (40.2)	6 (3.8)	91 (59)	9.36	0.009
	>11000	11 (7.1)	14 (9.09)	1 (0.6)	26 (16.8)	3.18	0.204
Platelet count	>150000	5 (3.2)	15 (9.7)	1 (0.6)	21 (13.6)	2.83	0.243
	100000-150000 (Mild)	8 (5.2)	17 (11)	0	25 (16.2)	5.94	0.051
	50000-100000 (Moderate)	20 (12.9)	47 (30.5)	6 (3.8)	73 (47.4)	8.27	0.016
	<50000 (Severe)	11 (7.1)	23 (14.9)	1 (0.6)	35 (22.7)	7.83	0.019

Hematological parameters in different types of malaria

Severe anaemia is defined as haemoglobin less than 7 gm% and was seen in 9 children, among them 8 had *Vivax* malaria and 1 had mixed malaria. 24% malaria cases had leukocytopenia (<4000 cells/cumm). 59% of all infected cases had total counts of 4000-11000 cells/cumm.

Majority of the children affected (47.4%) had platelet counts ranging from 50,000-1,00,000. There was thrombocytopenia in all three types of malaria. Severe thrombocytopenia (<50,000) was seen in children with *Vivax* malaria (14.9%). 21 children had normal platelet counts.

Mean haemoglobin in children with *Falciparum* malaria was 11.15 gm% and with *Vivax* 9.6 gm%. Pallor, leucopenia and thrombocytopenia were statistically significant (Table 4).

Table 4. *Malaria parasite in children.*

	***P. falciparum* (+)**	***P. vivax* (+)**	**Both (+)**	**None**	**Total**
PSMP+	2	9	-	-	11
PSMP++	21	45	-		66
PSMP+++	11	26	-		37
PSMP++++	5	5	-		10
PSMP NEGATIVE	-	-	-	30	30
MPRDT	40	93	8	13	154

Majority of patients with *P. vivax* malaria had MP++ , MP+++ of malaria parasite seen in the thick peripheral blood smear while only 10 patients had 4 plus (MP++++) seen in the peripheral blood film. 13 patients had negative MPRDT.

Out of 154 patients, 53 patients had severe malaria, 35 were infected with *P. vivax*, 17 were *P. falciparum* and 1 were mixed infection. Some patients had more than 1 parameter of severe malaria. Among them, bleeding was present in 2 cases, both patients were expired [10].

Discussion

Malaria continues to be on the rise due to resistance to drugs and vector resistance to the insecticides. The present study highlights the clinico-hematological profile of malaria in pediatrics age group in Surat. We analyzed patients admitted

with proven malaria (Peripheral smear positive and/or RDT), admitted to our hospital. *P. vivax* was the most common cause of malaria and its complications as compared to *P. falciparum* and mixed infection. A similar findings was seen in other studies from Uttarpradesh, Karnataka, Haryana.

Most of the studies showed male predominance as in the present study. This is possibly due to increased outdoor activity and exposure to mosquitoes in males as compared to females. Male to female ratio in our study was 1.75:1 as well as in studies by Castelino DN et al., (1.8:1), Hassan N et al., (1.9:1). The results show the transmission of malaria in Surat is seasonal with peak incidence in months of July to November.

Predominantly infected age group was between 11 and 15 years probably due to increased exposure to mosquito bites and Castelino DN, et al., had similar results. In our study majority of patients were in the age group (>5) years. On the contrary, a study by Hassan N et al., observed that children from 1-5 years were more commonly affected.

Clinical features like fever (100%), chills and rigors (77.2%), vomiting (42.8%), headache (24.7%) were common in our study (Table 2). Castelino DN, et al., had similar findings. Abdominal pain was higher in our study (15.6%) as compared to Castelino DN, et al. Majority of the children affected (47.4%) had platelet counts ranging from 50,000-1,00,000. There was thrombocytopenia in all three types of malaria (6.84%). Abdominal pain, diarrhoea were more common in *Vivax* malaria cases similar to other study.

Pallor, icterus, hepatomegaly and splenomegaly were consistent feature in all studies. Pallor was present in 70.3% children with *Vivax* malaria and 24.6% of *Falciparum* malaria similar to Castelino DN, et al. Severe anemia on blood test was present in 6% cases similarly in Hassan N, et al. Icterus was present more with *Vivax* malaria (84.6%) as compared to other study in which it was more common in mixed malaria. Hepatomegaly (24%) was a predominant finding in children with *Vivax* malaria (78.3%) followed by *Falciparum* (21.6%). Splenomegaly (42.2%) was present in all three types. Hepatosplenomegaly was 9.09% whereas Castelino DN, et al., evidenced it in 21% cases (Table 2).

Convulsions were noted in 2 patient infected with each of *P. falciparum* and *P. vivax* compared to Castelino DN, et al., study in which 3.47% patients infected with *Vivax* malaria. Respiratory distress was observed in both *Falciparum* and *Vivax* malaria compared to Hassan N et al., study in which respiratory symptoms were with *Vivax* malaria only. 2 patients with *Vivax* malaria were presented with shock. Abdominal distention, oedema were more common with *Vivax* malaria.

Mean heamoglobin in this study was 9.9 gm% while study by Castelino DN, et al., observed mean heamoglobin of 10.9 gm%. Anaemia was present in 56.8% of *Vivax* malaria and 43% of *Falciparum* malaria. Anaemia results from haemolysis, splenic clearance, splenic sequestration and suppression of haematopoiesis by TNF alpha. 9 children (5.8%) had severe anaemia in our study (Table 3) of which 8 were *Vivax* affected and comparable to observations by Castelino, DN, et al., (2%). Probably this is due to higher number of children affected with *Vivax* malaria than *Falciparum* in our study.

In this study, mean total count was 7380 cell/cumm, lowest count was 1940 cells/cumm and highest count was 33,000 cells/cumm. We had 25.4% *Vivax* cases and 12.5% of mixed malaria cases also with low counts. Leukopenia has been proposed due to the sequestration of leukocytes that causes its decline. Leukocyte count may vary due acuteness of infection, disease severity, concurrent infections that may have been missed.

Mean platelet level in our study was 96,080 cells/cumm. The lowest platelet count was 11,600 cells/cumm and had no signs of bleeding, 25% children with *Falciparum* had severe thrombocytopenia followed by 22.54% of *Vivax* malaria cases. While Castelino DN, et al., study had severe thrombocytopenia in *Falciparum* (50%) cases followed by *Vivax* (24%) malaria. Thrombocytopenia occurs due to increased platelet destruction from platelet associated IgG antibody and its consumption.

3 patients were died due to severe *Vivax* malaria. Case fatality rate was 1.94%. All patients had thrombocytopenia, ARDS, multiorgan dysfunction, shock. Patients had CNS involvement with convulsions and intracranial hemorrhage.

This is a study involving children with different types of malaria describing clinical and hematological parameters over 6 months. All these observations of this study definitely indicate that a significant proportion of severe malaria morbidity is caused by *P. vivax* infections in this region where both these species coexist. However, restricting to hospital admitted patients is a major limitation of study. Smaller number of falciparum malaria cases and not checking serial hematological parameters were other limitations of study.

Conclusion

The present study thus reflects the epidemiology of malaria in pediatric age group Surat, India. The study highlights that *P. vivax* is more common and affects younger age group (<5 years) and can result in a severe complication and death. It can no longer be considered a benign condition. However, there is a need for further studies to establish mortality and severity predictor specific to *P. vivax* malaria. Clinical and hematological parameters vary in acute malaria with different plasmodium species. Knowledge of clinical and hematological parameters aids us in early diagnosis and prompt initiation of treatment and prevention of associated complications.

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