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Study of Clinical Profile And Lab Parameters Of Vivax And Falciparum Malaria In Children: Data From A Northern Rural Centre

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Abstract

Background: Malaria is one of the most widespread infectious diseases in humans. Plasmodium falciparum and plasmodium vivax cause the maximum morbidity and mortality. The present study was done prospectively, to note the clinical profile and lab parameters in children infected with P. falciparum.

Methods: A total of 100 pediatric patients with confirmed malarial infection (falciparum or vivax) and under the age of 18 years were enrolled. All the patients were well examined with a detailed history and all necessary hematological and biochemical investigations done were noted. Data was compiled and compared between both forms of malarial infections.

Results: Out of 100 patients enrolled with positive rapid diagnostic tests for malaria, 85% were positive for plasmodium vivax, 13% for plasmodium falciparum and 2% for mixed infection with both these species. The age ranged from 0-18 years with M:F ratio of 1.94 : 1. The most common symptom noted was fever (98%) and finding present on examination was pallor (56%). Splenomegaly was found in 42% while bot hepatomegaly and splenomegaly was present in 20% of cases. Lab investigations revealed statistically significant difference (p= 0.03 & 0.005) of deranged renal function tests (S. urea and creatinine) in P. falciparum (50% and 66.7%) as compared to P. vivax (50% and 33.3%). None other lab parameters had significant difference between the two species of infection.

Conclusion: Our study highlights that the plasmodium vivax is a commoner form of malarial infection in children but the risks and deranged renal functions are more seen in falciparum malaria which is finally responsible for higher morbidity and mortality.

Keywords: Malaria, Falciparum, Vivax, Pallor, Organomegaly, Urea, Creatinine.

Introduction: Malaria, one of the most widespread infectious diseases in humans is caused by the Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale and Plasmodium knowlesi species. Most severe form of malaria is caused by Plasmodium falciparum where the infected red blood cells (RBCs) have distinct antigenic properties generally with cytoadherent phenotypes. The parasites spread to people through the bites of infected female *Anopheles* mosquitoes, called "malaria vectors", which bite mainly

between dusk and dawn[1]. The majority of patients experience fever (>92% of cases), chills (79%), headaches (70%), and diaphoresis (64%). Other common symptoms include dizziness, malaise, myalgia, abdominal pain, nausea, vomiting, mild diarrhea, and dry cough. Physical signs include fever, tachycardia, jaundice, pallor, orthostatic hypotension, hepatomegaly, and splenomegaly. Clinical examination in non-immune persons may be completely unremarkable, even without fever[2]. Thrombocytopenia is the most common laboratory abnormality (60%), followed by hyperbilirubinemia (40%), anemia (30%), and elevated hepatic aminotransferase levels (25%). The leukocyte count is usually normal or low, but neutrophilia with a marked increase in band forms (left shift) is present in the majority of cases[3]. This study highlights the various clinical and lab parameters in falciparum and vivax malaria infection in a prospective cohort of children from a rural Indian setting.

Methods: The present study was conducted in the department of paediatrics, M.M Hospital MMIMSR, Mullana, Ambala. 100 cases of malaria under 18 years of age were taken up for study in two years period. All cases with clinical picture consistent with malaria along with slide and or rapid diagnostic test positive were included. Proper history taken with emphasis on the chief complaints relating to all systems. General examination was done in detail and following parameters were noted-

- Vital parameters like temperature, pulse rate, respiratory rate, blood pressure and oxygen saturation
- Abnormalities like pallor, icterus, clubbing, cyanosis, lymphadenopathy and edema.
- Systemic examination was done in detail and abnormalities related to abdominal examination on percussion for various organomegaly. Other systems were also examined in detail and abnormalities noted. Presence of organomegaly was classified as per standard criteria.

Following laboratory investigations were also done in each case to assess the presence or absence of any complications:

- Complete Blood Count (Hemoglobin, TLC, DLC, Platelet count)
- Liver function Tests (SGOT, SGPT, Direct Bilirubin, Total Bilirubin)
- Renal function tests (Urea and Creatinine)
- Ultrasonography for confirmation of organomegaly.

Statistical analysis was done via parametric test and non – parametric test, where ever applicable. Mean comparison was done using t-test , chi-square test and Mann Whitney U test. Parametric test were used to compare the proportions using Annova test and Yate's test. A proper ethical clearance for this study was taken from Institute's ethical committee.

Results: During the study period of two years, 100 children were included that were positive to malarial species on rapid diagnostic tests. The age stratified composition of different species of malaria **(Figure 1)** was P. vivax monoinfection 85%(85/100) (children aged 0-5 years 10.5%[9/85]; in 5-12 years 47%[40/85]; 13-18 years 42.3% [36/85]) compared with P. falciparum monoinfection 13%(13/100) (children aged 0-5 years 15.3%[2/13]; in 5-12 years 46.1%[6/13]; 13-18 years 61.5% [8/13]). 2% of children suffered mixed infection and were not included in further study. The male to female distribution was 66% to 34% in total.

On analysis of clinical profile between the two forms of malarial infection **(Table 1)**, it was found that the general finding of fever, pallor and body ache were distributed as 100%(13/13), 53.8%(07/13) and 0%(0/13) in P. falciparum respectively compared to 97.6%(83/85), 57.6%(49/85) and 1.17%(01/85) in P. vivax respectively.

Respiratory symptoms were seen in 16 patients in total of which in P. falciparum group 1/13 (7.69%) had cough while none had breathing difficulty compared to P. vivax in whom 14/85 (16.4%) had cough and 1/85(1.17%) had breathing difficulty. Symptoms related to gastrointestinal involvement like vomiting , pain abdomen were seen in 38.8% and 29.4% cases of P. vivax compared to 30.7% and 23% of P. falciparum infected cases. Loose stool and jaundice was seen in only a minority of cases. Bleeding manifestation in the form of hematuria was present in 2 of the total cases, both of which belonged to P. vivax group. CNS symptoms like headache, abnormal body movements and altered sensorium were found in 1/13 (7.6%), 1/13(7.6%) and 0% respectively in P. falciparum compared to 9/85(10.5%), 0% and 1/85(1.17%) in P. vivax respectively. Splenomegaly alone was seen in 41.1%(35/85) and 53.8%(7/13) in P. vivax and P. falciparum while hepatomegaly was not seen in P. falciparum and in only 5.88%(5/85) of P. vivax cases. Hepatosplenomegaly was found in both groups with 21.1%(18/85) in P. vivax and 15.3%(2/13) in P. falciparum.

The details of lab investigations as compared between two groups are highlighted in **Table 2**. Anemia was found in 83.3% (mean 9.9±2.4) of P. vivax and 16.7% (mean 8.9±2.5) of P. falciparum cases but showed no statistical significance on comparison (p=0.39). The mean TLC was seen as 7641.2±6141.6 in vivax and 7500±3228 in falciparum group, comparing the leukopenia(<4000/mm^3) [11/100]; 90.9%[10/11] with vivax while 9.1%[1/11] in falciparum group and leukocytosis (>10,000/mm^3) [15/100]; 80%[12/15] in vivax and 20%[3/15] in falciparum; the difference was not significant (p=0.618). Thrombocytopenia (<150,000/mm^3) was seen in 75/100; 89.3%[67/75] of P. vivax (mean value 112976±87826.1) and 10.7% [8/75] in P. falciparum (mean value 118461±89544.8); p=0.309. Deranged liver function tests like serum total bilirubin was raised (>1mg/dl) in 8/100 of which 50%(4/8) [mean 1.1±0.4] were in P. vivax and 50%(4/8) [mean 3.7± 6.3] in P. falciparum; p=0.228. However, deranged renal functions showed a significant difference in S. urea and S. creatinine on comparison; **p=0.031 and 0.005** between P. falciparum and P. vivax groups with 66.7% of P. falciparum cases having high serum creatinine compared to only 33.3 % in P. vivax cases.

Discussion: Malaria is one of the commonest infection endemic in our country which can lead to high morbidity and mortality. The common species found in our region is usually plasmodium falciparum and plasmodium vivax . Through this study an attempt was made to identify the clinical patterns associated with these two forms of malarial infection in children. The age of children ranged from 10 months to 18 years. Majority of children were in 5 – 12 years of age group with a mean value and standard deviation of 10.6 ±4.6 years respectively. Different studies in the literature have reported varying age distribution. Taksande et al[4] observed the maximum number of cases were between the age group of 3 – 6 years while Genton B et al[5] reported children who presented with malaria to them were under 5 years of age. Ketema T et al[6] , observed in their study that male children had higher risk of malaria infection as compared to female patient . In our study, two more males were affected with M:F ratio of 1.94:1. However , this needs to be assessed in a larger cohort of cases.

In our study, most of the cases presented with the complaint of fever (98%) which is expected for any infectious illness. Studies by Bhattacharjee et al[7] (2013), Kumari et al[8](2014) and Singh et al[9] (2014) also reported that fever is the commonest complaint seen in patients with malaria positive and is equally seen in both P. falciparum and vivax malaria. Children also presented with other symptoms of discomfort and organ

involvement like vomiting (38%), pain abdomen(28%), cough(15%) and headache(11%). Beg MA et al[10], had observed that vomiting and pain abdomen were the commonest finding in children who were positive for plasmodium falciparum malaria, although our study in our study majority of P. vivax infected cases also had these symptoms. This is likely due to bias because of more number of P. vivax infected cases enrolled as compared to P. falciparum. The least common complaints found in our study were haematuria (bleeding manifestation), convulsions, body ache and loose stool. On clinically examining the patient, pallor was the commonest finding seen in 56% of the total number of cases enrolled. It was almost equally prevalent in both the groups with 57.6% in vivax malaria and 53.8% in falciparum malaria. The second most common clinical finding in the study was splenomegaly(42%) followed by hepato-splenomegaly(20%) and hepatomegaly(5%)seen more commonly in plasmodium falciparum species (53.8% with splenomegaly and 15.3% with hepatosplenomegaly) as compared to plasmodium vivax but no such statistically significant data in literature was found. Beg MA et al[10] also reported that hepatomegaly , splenomegaly and jaundice were mostly seen in plasmodium falciparum malaria as compared to plasmodium vivax malaria . Bhattacharjee P et al[7], Singh R et al[9] and Herrera MA et al[11] also observed splenomegaly, hepatomegaly and hepatosplenomegaly as one of the common examination findings observed in their study but comparison between the malaria species was not done in their study. The reason for organomegaly is the activation and expansion of reticulo-endothelial system macrophages in response to malarial infection.

42(42.8%) children in our study had anaemia on haematological evaluation . The minimum haemoglobin was 2 grams and maximum was 15.7 grams with a mean value (SD) of 9.9±2.4 grams and 8.9±2.5 grams in vivax and falciparum malaria respectively. Beg MA et al[10] did a comparative study of plasmodium species and found out that low haemoglobin levels were common and significantly lower in plasmodium falciparum malaria. Genton B et al[5] also observed low levels of haemoglobin in falciparum malaria in their study. Thrombocytopenia is one of the commonest complication seen in malaria . This complication is mostly seen in plasmodium falciparum but many studies mention that it is now equally prevalent in plasmodium vivax species also. In our study, a total of 75 children had thrombocytopenia(platelet count <150,000) with mean value of 112976.5±87826.1, of these o 8(10.7%) were found in plasmodium falciparum and 67(89.3%) were seen in plasmodium vivax species. On comparison thrombocytopenia was more commonly seen in plasmodium vivax malaria but was not a statistically significant finding. Leucopenia was a finding observed in some studies; Limaye CS et al[12] observed that out of total number of cases enrolled in his study 19% of children positive for plasmodium vivax had leucopenia. Another study by Kumari M et al[8] , observed that children positive for plasmodium vivax only 10% of them had leucopenia. Herrera MA et al[11] observed that leucopenia was more commonly seen in plasmodium falciparum species in their study. In our study, 11 children had leucopenia (Total leukocyte count <4000/mm^3) out of which 9.1% belong to plasmodium falciparum group and 90.9% to plasmodium vivax malaria. Raised serum bilirubin level is a sign of liver dysfunction seen in 8% of cases only with 3(37.6%) belonging to plasmodium falciparum children and 5(62.5%) to plasmodium vivax group. Limaye CS et al[12] observed high bilirubin levels (46%) in plasmodium falciparum species in their study . Another study by Singh R et al[9] also observed raised serum bilirubin levels in 11.1% of the total cases while Herrera MA et al[11] also observed raised serum bilirubin levels in 11% of falciparum malaria group. Our study also compared the

deranged values of both falciparum and vivax malaria but no comparative statistically significant data gained. The reason for low frequency of raised serum bilirubin in our study could be due to very less number of P. falciparum infected cases studied. Deranged renal function tests especially high serum creatinine was seen in 66.7% of P. falciparum cases compared to 33.3% of P. vivax cases in our study and the difference was statistically significant **(p= 0.005)**. Bhattacharjee P et al[7], observed raised urea creatinine levels in children with plasmodium vivax malaria while Beg MA et al[10] found derangement more in P. falciparum cases in their study. However , renal dysfunction as a complication of P. falciparum is well described in literature and is a known cause of morbidity in cases infected with these species. Mortality is commonly seen in children with malarial infection. Earlier it was seen in complicated cases of plasmodium falciparum malaria but now a days it also seen in children with complicated plasmodium vivax species, though in our study amongst the total enrolled cases , no mortality was observed. The average length of stay of the enrolled patients in our study was around 10 days with complete recovery and no post infectious squeal.

Overall, our study highlights complete clinical and basic lab parameter profile in children infected with P. vivax and P. falciparum forms of malarial infection. But it suffers from limitation of small sample size and a less number of P. falciparum infected cases being studied. Larger prospective studies in rural children with malarial infection can shed more light on various complications seen in these groups.

Conclusion: Plasmodium vivax was considered as the benign infection in the earlier times with lesser complication and with least mortality . This present study highlighted that plasmodium vivax is almost equally responsible for the deranged body functions associated with malaria species as is more commonly observed malarial infection in children. Derranged renal function tests are noted both in plasmodium vivax and plasmodium falciparum infections, however are more common in P. falciparum group.

Ethical approval: By the Institute ethical committee.

Conflicts of Interest: None

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Legend of Figure and Tables:

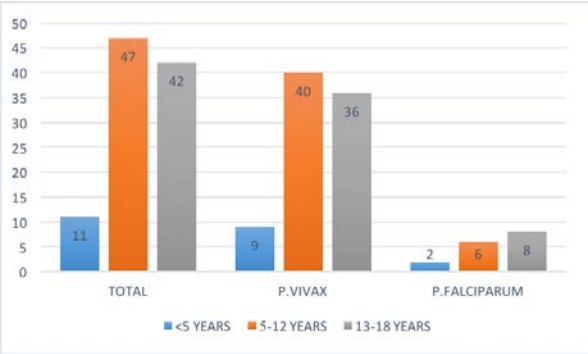

Figure 1: Age specific distribution of the study groups. [Total=100, P. vivax=85, P. falciparum=13].

Parameter	Total (%) N=100	Falciparum Malaria (%) N=13	Vivax Malaria (%) N=85
Age			
<5	11 (11)	02 (15.3)	09 (10.5)
5 -12	47 (47)	06 (46.1)	40 (47.0)
13 -18	42 (42)	08 (61.5)	36 (42.3)
Gender			
Male	66 (66)	08 (61.5)	57 (68.6)
Female	34 (34)	05 (38.4)	28 (32.9)
General			
Fever	**98 (98)**	**13 (100.0)**	**83 (97.6)**
Pallor	**56 (56)**	**07 (53.8)**	**49 (57.6)**
Bodyache	01 (01)	00 (00)	01(1.17)
Respiratory			14 (16.4)
Cough	15 (15)	01 (7.69)	01 (1.17)
Breathing difficulty	01 (1)	00 (0.00)	
Gastrointestinal			
Vomiting	37 (37)	04 (30.7)	33 (38.8)
Pain abdomen	28 (28)	03 (23.0)	25 (29.4)
Loose stools	02 (02)	00 (0.00)	02 (2.3)
Jaundice	02 (02)	01 (7.6)	01 (1.17)
Bleeding Manifestation	02 (2.00)	00 (0.00)	02 (2.35)
CNS			
Headache	10 (10)	01 (7.6)	09 (10.5)
Altered Sensorium	01 (01)	01 (7.6)	00 (0.00)
Convulsions	01 (01)	0 (0.00)	1 (1.17)
Organomegaly			
Splenomegaly	42 (42)	07(53.8)	35 (41.1)
Hepatomegaly	05 (05)	00 (0.00)	05 (5.88)
Hepato-splenomegaly	20 (20)	02 (15.3)	18 (21.1)

Table 2: Comparing various lab parameters between the two groups:

Variable	N	Falciparum malaria (n-13)		Vivax malaria (n-85)		X^2	df	p-value
		No. of cases	%	No. of cases	%			
Anaemic (Hb<7)	42	7	16.7	35	83.3	0.739	1	0.390^{NS}
Non-anaemic	56	6	10.7	50	89.3			
Leukopenia (<4000)	11	1	9.1	10	90.9	0.921	2	0.618^{NS}
Normal TLC	72	9	12.5	63	87.5			
Leukocytosis(>10000)	15	3	20.0	12	80.0			
Platelet Count (<150000)	75	8	10.7	67	89.3	1.037	1	0.309^{NS}
Platelet Count (>150000)	23	5	21.7	18	78.3			
Total Serum Bilirubin (≤1)	60	8	13.6	52	86.4	1.456	1	0.228^{NS}
Total Serum Bilirubin (>1)	8	3	37.5	5	62.5			
Serum Urea (<40)	63	8	12.7	55	87.3	4.627	1	**0.031***
Serum Urea (>40)	8	4	50.0	4	50.0			
Serum Creatinine (≤1)	65	8	12.3	57	87.7	8.010	1	**0.005***
Serum Creatinine (>1)	6	4	66.7	2	33.3			