Research Article

Clinical Spectrum of Plasmodium Vivax Malaria in Children Presenting to a Tertiary Care Hospital, Lahore

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Abstract

Background: Malaria is endemic in Pakistan and physicians should be fully aware of varied clinical and laboratory manifestations of malaria in children to maintain high index of suspicion for diagnosis.

Objective: To describe the clinical features and haematological investigations of children with Plasmodium Vivax malaria in a tertiary care hospital.

Methods: This analytic cross-sectional study consisted of 83 children under15years of age. They had clinical features suggestive of malaria and blood films were positive for Plasmodium Vivax. Data were collected by non-probability convenient sampling technique and were analyzed by SPSS version 21.

Results: Of 83 children, mean age was 5.3±4.4 years and 66% were males. All patients had fever (100%) associated with rigor and chills (94%), vomiting (73.5%) and abdominal pain (32.5%). Splenomegaly was found in 92.8%, pallor in 89%, hepatomegaly in 85% and jaundice in 25% children. It was observed that 77.1% of the children had anaemia with mean haemoglobin as 9.1±2.53 g/dL and 84% had thrombocytopenia with mean thrombocyte count as 114 ± $73\times10^3/mm^3$. Red cell indices and haematocrit were below the normal limits. Splenomegaly was significantly associated with rigors/chills, vomiting, jaundice, abdominal pain and pallor ($p < 0.05$). Hepatomegaly was found to has significant association with abdominal pain only ($p < 0.001$).

Conclusion: High grade fever with chills/rigors and vomiting along with hepatosplenomegaly were main clinical features of Plasmodium Vivax malaria. Anaemia and thrombocytopenia were most frequent haematological disturbances.

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Key Words: Malaria, demographics, haematology, Plasmodium Vivax, clinical features, children, Lahore, Pakistan

Introduction

Malaria is a major public health problem around the globe.[1] It contributes to increase mortality among infants and young children.[2] Plasmodium (P.) genus causes malaria, including P. Malariae, P. Ovale, P. Vivax, P. Falciparum and P. Knowlesi.[3] P. Vivax is the most prevalent in Pakistan.[1] The highest prevalence of malaria is found in Baluchistan, followed by Sindh and Khyber Pakhtunkhwa (KPK), with lower prevalence in Punjab and the city of Islamabad. In Punjab malaria prevalence

ranges from1.2% in Lahore to 5.5% in Bhakkar city.[3]

Clinical features of malaria may resemble other febrile illnesses but there are certain specific clinical features and haematological changes seen in malarial patients' blood.[4] Parasite sporozoites invade human body and causes disease.[5] They enter into liver and red blood cells (RBCs) leading towards pyrexia, sweating, shivering and spleen enlargement. Malarial infection causes decrease in haemoglobin (Hb.), RBCs, packed cell volume (PCV) and platelets counts leading to anaemia and thrombocytopenia.[5] There is usually enhanced production of leukocytes at the early stage of infection to remove malarial parasites from the body. However, both increasing and decreasing tendencies of WBCs has been found.[6]

Clinical features of malaria occur in paroxysms. Duration between paroxysms varies depending upon species of malarial parasite. High grade fever with rigors and chills is the most consistent feature of paroxysms which is commonly associated with P. Vivax infection due to its low threshold of parasitemia for fever.[7] Other common features are headache and loss of appetite while severe manifestations include icterus, bleeding, disorientation and severe anaemia.[8] Thrombocytopenia, anaemia and low PCV are frequently found.[9] Most serious complications like cerebral malaria, black water fever, renal failure, algid malaria, coma, fits etc. are mostly associated with P. Falciparum which is luckily not so prevalent in Punjab, Pakistan.[1,3] However, P. Vivax is also no more benign.[10]

Although some studies are available from Lahore on adult malarious patients but this study was aimed to extend the efforts of understanding changes in clinical and blood profile of malarious children infected by P. Vivax only presenting in a tertiary care hospital in a slum and peripheral area of Lahore. This work may enable the health care professionals to recognize the common presentation which can be used as a diagnostic tool for early detection of malaria in paediatrics community.

Methods

This was an analytic cross sectional study that was conducted at Shahdara Teaching Hospital, Lahore during January to December 2016. All children up to 15 years of age who were brought to the hospital in children outdoor and emergency room with clinical features suggestive of malaria were admitted and recruited consecutively. Non-probability, convenient method was used to collect data. Detailed history was taken regarding symptoms. Patients' clinical examination was done noting temperature, weight, pallor and jaundice. Liver and spleen sizes were also measured by palpation of abdomen. On admission blood samples were taken for complete blood count, red cell indices, peripheral blood smear and thick and thin film for malarial parasites. Three thick and three thin films were prepared on slides according to World Health Organization (WHO) guidelines and were studied by the only available haematologist of the hospital. If parasite was detected on thick blood film, its type was also determined by thin film study. Informed consent was taken from parents/guardians of the children to include in the research work who had P. Vivax malaria on the basis of blood film study. Initially all patients with positive blood film for malarial parasites were noted just to calculate the percentage of various types of parasites responsible for malaria. In next stage only P. Vivax positive patients were included in analysis of the data. So, our study consisted of P. Vivax only. The recruited patients, who did not fulfil inclusion criteria or who were not willing to participate in the study or left the hospital against medical advice due to any cause were excluded from the study. Weight of the patient was measured, its percentage in comparison with standard was calculated and nutritional status was classified according to modified Gomez classifycation of malnutrition.[2] Haemoglobin, haematocrit, Anaemia (Hb <11g/dL)[9] severe anaemia (Hb <5 g/dL)[9] RBCs count, RBCs indices including me-an corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC), thrombocyte count, thrombocytopenia (platelets <150000/mm^3)[9], WBCs count, leukocytosis (WBCs > 11000/mm^3)[9], leukopenia (WBCs < 5000/mm^3),[9] were also calculated. Patients were managed accordingly and monitored for complications of malaria like black water fever, azotemia and also for altered conscious level (Glasgow Coma Scale <10). SPSS version 21 was used for data management. Mean and standard deviation (SD) was calculated for continuous/

numerical variables like age, Hb; WBCs, neutrophil, lymphocytes, platelets count and RBCs indices etc. Percentages were calculated for nominal variables like gender and different clinical findings etc. The associations of rigors & chills, vomiting, jaundice, abdominal pain and pallor with splenomegaly, hepatomegaly and malnutrition were examined by using Pearson chi squared test and Fisher's exact test. P value of less than 0.05 was considered as statistically significant. Permission was sought to conduct the study followed by ethical approval of the Research Ethics Committee of Shahdara Teaching Hospital Shahdara, Lahore on completion of the study.

Results

We detected 90 patients whose blood films were parasites positive for malarial parasite. However, our study consisted of 83 patients infected with P. Vivax because 7 (7.8% of all malarial children) were excluded being infected by P. Falciparum. Out of 83 patients, 55 (66.3%) were males and 28 (33.7%) were females. Mean age of patients was (5.3±4.4, range: 0.2-14) years. Mean weight of the patients was 85.5±12.4 % of standard weight for age and gender of the children according to modified Gomez classification.[2] Mean duration of stay in the hospıtal was (9.2 ± 5.2, range: 2-27) days.

All patients were febrile. Two patients developed black water fever and disturbed renal functions. Table 1 depicts other symptoms and signs including splenomegaly in 77(92.8%) and hepatomegaly in 71(85.5%) patients. Malnutrition was found in 60.2% patients. Splenomegaly showed significant positive association with rigors & chills ($p < 0.001$), vomiting ($p < 0.001$), jaundice ($p < 0.001$), abdominal pain ($p < 0.013$) and pallor ($p < 0.017$). Similarly, we observed association of these clinical features with hepatomegaly which was significant only with abdominal pain ($p < 0.001$). We found no association of these factors with malnutrition (Table 2).

We found mean Hb. 9.1±5.3 g/dL, anaemia (Hb. <11 g/dL) in 60 (72.3%) and severe anaemia (Hb. <5g/dL) in 4 (4.8%) patients. Normal white blood cells (WBCs) (5-11 $x10^3/mm^3$) was found in 51 (61.4%), leukocytosis (WBCs >11 $x10^3/mm^3$) in 13 (15.7%) and leukopenia (WBCs <5$x10^3/mm^3$) in 19 (22.9%) malarial patients. Table 1 shows the other investigation results.

Table 1: *Clinical and Haematological Features of Children with Malaria (n=83).*

Clinical feature	Number (%)	Haematological feature	Mean ±SD
Chills and rigors	77 (92.7)	Haemoglobin (g/dL)	9.1 ±2.53
Vomiting	61(73.5)	WBCs count ($x10^3/mm^3$)	7.3 ±2.73
Abdominal pain	27 (32.5)	Neutrophil (%)	49.6 ± 15
High grade fever	78 (93.9)	Lymphocyte (%)	39.93 ± 18
Low grade fever	05 (6.1)		
Pallor	74 (89.2)	Platelets ($x10^3/mm^3$)	114 ± 73
Jaundice	21 (25.3)	MCV (fL)	69.14±8.74
Hepatomegaly		MCH (pg)	25.1 ±4.56
• No	12 (14.5)		
• 1-2 cm	51 (61.4)		
• 3-5 cm	20 (24.1)		
Malnutrition¥		MCHC (g/dL)	31.97 ± 3.13
• No	33 (39.8)		
• 1st degree	38 (45.8)		
• 2nd degree	5 (6.0)		
• 3rd degree	7 (8.4)		
Splenomegaly		Haematocrit (%)	33.58±6.6
• No	6 (7.2)		
• 1-2 cm	29 (35.0)		
• 3-5 cm	48 (57.8)		

¥- According to modified Gomez classification of malnutrition.[2] SD- Standard deviation, g/dL - Gram per deciliter, uL- Micro liter, fL- Femtoliter, pg – Peco gram, WBCs- White blood cells, MCV- mean corpuscular volume, MCHC- Mean corpuscular haemoglobin concentration

Table 2: *Associations of Rigors & Chills, Vomiting, Jaundice, Abdominal Pain and Pallor with Splenomegaly, Hepatomegaly and Malnutrition.*

Features	Splenomegaly (Cm)				Hepatomegaly (Cm)				Malnutrition		
	0	1-2	>2	P*	0	1-2	>2	P*	Yes	No	P*
Rigor				**.001**				.255			.76
Yes	3(50%)**	29(100%)	45(93.8%)		12)100%)	45(88.2%)	20(100%)		44(88%)	33(100%)	
No	3(50%)	0	3(6.3%)		0	6(11.8%)	0		6(12%)	0	
Vomiting				**.000**				.088			.163
Yes	0	21(72.4%)	40(83.3)		6(50%)	38(74.5%)	17(85%)		34(68%)	27(81.8%)	
No	6(100%)	8(27.6%)	8(16.7%)		6(50%)	13(25.5)	3(15%)		16(32%)	6(18.2%)	
Jaundice				**.000**				.65			.857
Yes	0	0	21(43.8%)		0	16(31.4)	5(25%)		13(26%)	8(24.2%)	
No	6(100%)	29(100%)	27(56.3)		12(100%)	35(68.5)	15(75%)		37(74%)	25(75.5%)	
Abdominal pain				**.013**				**.000**			.302
Yes	0	10(34.5%)	27(56.3%)		0	23(45.1)	14(70%)		20(40%)	17(51.5%)	
No	6(100%)	19(65.5)	21(43.8%)		12(100%)	28(54.9%)	6(30%)		30(60%)	16(48.5%)	
Pallor				**.017**				.081			1
Yes	3(50%)	26(89.7%)	45(93.8%)		9(75%)	45(88.2%)	20(100%)		44(88%)	30(90%)	
No	3(50%)	3(10.3%)	3(6.3%)		3(25%)	6(11.8%)	0		6(12%)	3(9.1%)	

P* = P value was calculated using Chi squared test provided individual cell values were >5. In other case Fisher's exact test was used. ** = % ages are column percentages

Discussion:

Malaria is a global disease of varying severity. Due to resources constraints in developing countries, the physicians usually have to rely on clinical manifestations for diagnosis.[9] Strengthening this clinical experience was the motive of this study.

P. Vivax is the most common species in Asia.[11,12] In an Indian work it was found 94%.8 WHO reported P. Vivax in Pakistan 80-90%,[1] while in a Lahore study it was 99%,[13] in various districts of KPK it was reported as 91%-100%,[14] in Orakzai 86%,[11] in Karachi 83%[15] and in Quetta 72%.[16] Our findings of 92% P. Vivax also supported the previous literature results.

Mean age of our children was 5.5±3.4 years corroborating the results of a Karachi study as (5.3±4.4 years)[17]. Our 2/3rd (66%) children were male. Male predominance was also noted in studies from Quetta (60%)[18], Khuzdar, Baluchistan (57%),[19] Karachi (67%)[15] and Lahore (71%).[13] Male outnumber in malarial patients in Indian studies as well (64% & 57%)[8,20]. Most of these studies were on adults, although our patients were children but gender variation pattern was similar to adults. These studies explained that males are involved in outdoor /agricultural activities and being less covered as compared to female counterparts are more exposed to mosquito biting. Same pattern was seen in male children too. In our study mean hospital stay was nine days while it has been noted as four days in Karachi Study.[15] and five days in an Indian study.[8] This difference may be because our hospital drain community from peripheral/ rural areas who have difficult emergency access to health facilities. So, they want to be discharged only when they are satisfyied that treatment has been completed.

Our study revealed that most common symptom was fever (100%) along with chills and rigors (93%). Similar report of fever is from Quetta as100% and also 99% in an Indian work by Surve et

al.[20] However, Krishna et al. reported 94% fever with 81% chills in another study from India.[8] We found vomiting in 3/4th children corroborating with findings of two studies from India (67 & 69%).[8,9] Abdominal pain was the least common symptom (32%) in our study, same finding is reported by other studies as 34% & 39%.[9,21] We found significant association of abdominal pain with hepatomegaly ($p < 0.05$).

Pallor was the most common (89%) sign in our patients mainly it is due to anaemia but may visible as a result of dehydration and toxicity of the patient. Malaria is an important cause of anaemia in endemic countries.[17] Frequency of anaemia (72.3%) in our patients was almost consistent with findings of an Ethiopian study as (73.8%).[21] Our 1/4th children were icteric. This finding is comparable to an Indian study which describes jaundice in 15-38% patients, depending upon the age with low frequency in younger patients.[21] While same finding was noted 17 % in a Karachi and 34% in a Quetta study.[17,19]

The frequency of splenomegaly (92.7%) was comparatively higher in our study as compared to other researchers' findings as 74%, 65%, 71% and 60%[17,8,20,21]. In malaria, spleen enlarges as a result of phagocytosis of parasitized red cells and their accumulation in spleen for clearance. In contrast to Ahmed's report from Karachi[17] as 57% we found hepatomegaly in 85.5% patients. The difference in hepatosplenomegaly may be due to variable individual reaction to the infection.

In our work, mean size of palpable spleen was found larger than that of liver size. We found splenomegaly significantly associated with rigors, vomiting, abdominal pain, jaundice and pallor ($p < 0.05$).

In our study frequency of anaemia [22] was 72.3% with mean haemoglobin 9.1±2.53g/dL. An Indian study corroborating our findings showed anaemia as 79%.[20] We found severe anaemia (Hb. < 5g/dL) 5% and exactly similar finding was reported in another study from Karachi[15] while it was reported 9% from India[20] and 10% from Orakzai, Pakistan.[11] In contrast, a research from Northwest Ethiopia showed mean hemoglobin 7.7 g/dL and severe anaemia in 14% patients with P. Vivax malaria.[21] This differences may be justifiable on the basis of geographical variation and pre-malarial haematological status of patients. Malarial infection leads to anaemia and thrombocytopenia in our research and same was reported by a study from Sheikh Zayed Hospital (SZH) Lahore.[5] Our patients' red blood indices MCV, MCH and MCHC were decreased and these findings are consistent with a report from Iran as well.[22] Studies from Lahore and Lower Deer KPK also mentioned low number of red blood indices leading to anaemia.[5,24]

Thrombocytopenia often accompanies malaria and is usually mild to moderate. In our study mean platelet count was found114 $\times 10^3/mm^3$ while in SZH Lahore it was 74 $\times 10^3/cmm^5$ and at Agha Khan University, Karachi this figure was noted as $55 \times 10^3/cmm$.[15] Majority of our patients (84%) had platelets in thrombocytopenic range (<150 x $10^3/cmm$). Other studies with almost comparable results include two studies from Karachi as 92% and 86%, one from Quetta as 70% and an Indian study as 75% thrombocytopenia in P. Vivax malaria.[15,17,19,20]. Majority of our patients (61%) had WBCs count in normal range ((5-11 $x10^3/mm^3$). However, we found leukocytosis (>11 $x10^3/mm^3$) in 16% and leukopenia (<5 $x10^3/mm^3$) in 23% of patients. Almost coinciding our findings an Indian study reported these findings as 72%, 10% and 18% respectively.[20] However, both increasing and decreasing WBCs trends in malarious patients has been witnessed in the literature.[5]

Regarding complications, 11% patients had altered consciousness while this finding was declared as 8% in another work from Pakistan,[11] and 14% in an Indian study.[23] Our 2.4% patients developed black water fever who also manifested as deranged renal functions in addition to other common findings. In a study from AKU Karachi, 3.4% patients of P. Vivax malaria developed renal impairment[15] while an Indian study reported the same findings as 2%.[23] Black water fever and impaired consciousness are although frequently encountered in P. Falciparum but with low frequency it is seen in P. Vivax malaria as well.[23]

This study is an endeavor to extend the efforts of understanding the clinical and blood profile of malarial patients in Lahore. This can act as a

diagnostic tool for early detection of malaria in children. Anyhow, extensive research is needed to establish reliability of clinical and haematological profile of patients for early diagnosis of malaria.

Limitations:

The results of this study cannot be generalized due to small sample size and public hospital based work. As, study is cross sectional and sampling was convenient so, we don't know whether patients in private hospitals may come up with different spectrum. Large community based studies are recommended to explore the authentic clinical and haemotological presentation of the disease.

Conclusion:

Common symptoms of plasmodium Vivax were high grade fever with chills/ rigors, vomiting and abdominal pain. Pallor, splenomegaly and heaptomegaly were frequently encountered physical findings. Anaemia and thrombocytopenia were most frequent haematological disturbances.

Ethical Approval: Given
Conflict of Interest: The authors declare no conflict of interest
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