Original Article

Clinical Profile and Spectrum of Complications of Malaria in Hospitalized Children at a Tertiary Care Hospital

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Abstract

Introduction: In children, the clinical profile of malaria may vary from nearly asymptomatic disease to febrile illness leading to life-threatening complications. The mortality among children is largely due to complications like cerebral malaria, severe anemia, and pulmonary complications. The current study was conducted to study the clinical profile of malaria, its complications, and factor associated with its complications.

Materials and Methods: This observational study was conducted at Children's Hospital, PIMS from March 2018 to March 2021. All patients with positive immunochromatographic tests and needing hospitalization due to unsettled fever or other troublesome symptoms were included. A total of 53 patients were included in the study. All patients underwent routine investigations which included ICTMP, complete blood picture, ultrasound abdomen, chest x rays, and routine urinary analysis. Severe malaria was characterized upon WHO guidelines. Patients were treated with chloroquine while those resistant to chloroquine were given artemisinin-based therapy. Data were analyzed by applying appropriate statistical tests via SPSS v20.

Results: Mean age of the patients was 5.80±3.5 years with male predominance (n=32, 60.4%). Majority of the patients had *P.vivax* (n=45, 84.9%) infection followed by *P.falciparum* (n=5, 9.4%), while 3 patients (5.7%) had positive immunochromatographic test for both *P.vivax* and *P.falciparum*. Severe malaria developed in 17 (32.1%) of the patients. Most common complication was severe anemia (n=10, 18.8%) followed by blackwater fever, ADEM disease, pneumonia, and convulsions. Patients with *P.falciparum* infection had a higher risk (OR=8.00, P-value=0.07) of developing complications compared to *P.vivax* one.

Conclusion: The rate of severe malaria was found to be 32.1% in children of the current study which is quite high. Therefore, every child with malaria should be properly investigated for complications and treated accordingly.

Keywords: Malaria, Plasmodium Falciparum, Plasmodium Vivax, Cerebral Malaria, Anemia.

Introduction

Globally, malaria is responsible for almost 300 to 500 million cases resulting in approximately 1 to 3 million deaths per year. Malaria is caused by the bite of female Anopheles mosquitoes resulting in the transmission of the Plasmodium parasite in the human bloodstream. Almost all cases of malaria in mankind are caused by four species of Plasmodium i.e. *Plasmodium vivax*, *Plasmodium falciparum*, *Plasmodium ovale,* and *Plasmodium malariae*.[1]

According to the World malaria report 2019, Pakistan is the fourth biggest contributor of Malaria in the Eastern Mediterranean region.[2] Malaria possesses endemic status in Pakistan, and the majority of the cases (64%) in Pakistan are caused by *Plasmodium vivax* whereas the rest (36%) are caused by *Plasmodium falciparum*.[3] Another study reported *P.Vivax* infection to be 81.3% (1). However, few studies have reported an increase in *Plasmodium falciparum* cases in different regions of Pakistan.[4] Rise in *P. falciparum* infection is associated with an increase in complications leading to increased morbidity. Compared to *P. falciparum*, *P, vivax* has been observed to follow a benign course. However, recent reports of severe life-threatening disease with multi-organ involvement due to *P. vivax* have also been noted.[5]

Morbidity in malaria is usually due to its associated complications. WHO has classified severe malarial patients into three groups. Group 1 includes prostrate children either conscious or comatose and those with respiratory distress. Group 2 includes children who can be treated with oral anti-malarial however require supervision, they include children with hemoglobin less than 5mg/dL, children with hemoglobinuria, children with persistent jaundice, and children with 2 or more episodes of convulsions in 24 hrs. Group 3 includes children requiring parenteral treatment due to persistent vomiting but lacking features of group 1 and group 2.[6]

This study is conducted to check the prevalence of severe malaria in the paediatric population. Patients were differentiated based on the Plasmodium strain responsible for the disease and then the clinical features, and disease severity of the patients were analyzed in order to assess its association with a type of strain.

Materials and Methods

This observational study was conducted at Children Hospital, Pakistan Institute of Medical Sciences from March 2018 to March 2021. All patients with positive immunochromatographic tests and needing hospitalization due to unsettled fever or other troublesome symptoms were included. A total of 53 patients were included in the study. Patients having other associated illnesses like enteric fever, hepatitis A and other chronic illnesses with concomitant enteric fever were excluded from the study. All patients underwent routine investigations which included ICTMP, complete blood picture, ultrasound abdomen, chest x rays, and routine urinary analysis. Severe Malaria was characterized upon WHO guidelines. Patients were treated with chloroquine while those resistant to chloroquine were given artemisinin-based therapy.

Data were analyzed by applying appropriate statistical tests via SPSS v20. Firstly, data were arranged and values labels were given. Frequencies and percentages were calculated. Dispersion in quantitative data was analyzed by standard deviation. ODDs ratio was applied to check associations. Statistical significance was checked by $P>0.05$ values.

Results

Mean age of the patients was 5.80±3.5 years with male predominance (n=32, 60.4%). Majority of the patients had *P. vivax* (n=45, 84.9%) infection followed by *P. falciparum* (n=5, 9.4%), while 3 patients (5.7%) had positive immunochromatographic test for both *P. vivax* and *P. falciparum*. Majority of the patients had intermittent (n=47, 88.7%) fever while 6 patients (11.3%) had continuous fever. Other symptoms of malarial infection included vomiting (n=29, 54.7%), anorexia (n=24, 45.3%), body aches (n=14, 26.4%), headache (n=12, 22.6%), hematuria (n=6, 11.3%), rash (n=3, 5.7%) and fits (n=2, 3.8%). (Figure 1)

Complete blood picture of malarial patients showed a mean TLC count of 6885.47±3702.9, platelet count of 108924.52 ± 85952.7, and hemoglobin levels of 7.97±2.49g/dL. Table 1 showed a detailed analysis of CBC in different malarial types. Bone marrow suppression was present in 31 (58.5%) patients. Thirty-one (58.5%) of the children had splenomegaly on ultrasound examination. Twenty (37%) had positive urine routine examination for infection. Six (11.3%) had hematuria. Thrombocytopenia was present in thirty-nine (78%) of the patients while severe thrombocytopenia i.e. platelets less than 50000 were present in twelve (22.2%) of the patients. (Figure 2)

Severe malaria developed in 17 (32.1%) of the patients. Most common complication was severe anemia (n=10,

18.8%) followed by blackwater fever (n=3, 5.6%), ADEM disease (n=2, 3.7%), pneumonia (n=2, 3.7%) and convulsions (n=2, 3.7%). Figure 3 shows the complications in both types of malarial infections. Patients with *P. falciparum* infection had a higher risk (OR=8.00, P-value=0.07) of developing complications compared to *P. vivax* one. No significant association (OR=1.13, P-value=0.8) was found between gender and risk of severe malarial infection.

The mean duration of illness was 9.94±6.6 days. Fever of majority (n=32, 60.4%) of the patients settled on the third day of hospital stay. The majority (n=32, 60.3%) of patients stayed in the hospital for more than days.

Table 1: Blood Picture

	ICTMP	N	Mean	Std. Deviation	T-Score
TLC (/uL)	**vivax**	45	6887.8	3975.7	-0.137(P-value=0.25)
	falciparum	5	7136.0	1652.1	
	vivax +falciparum	3	6433.3	1692.1	
	Total	**53**	**6885.4**	**3703.0**	
Neutrophils (%)	**vivax**	45	54.8	17.1	0.693(P-value=0.21)
	falciparum	5	58.0	14.3	
	vivax +falciparum	3	47.3	8.1	
	Total	53	54.7	16.4	
Lymphocytes (%)	**vivax**	45	37.2	15.2	0.335(P-value=0.35)
	falciparum	5	34.8	13.0	
	vivax +falciparum	3	41.7	2.1	
	Total	**53**	**37.2**	**14.5**	
Platelets (/uL)	**Vivax**	45	111711.1	86037.7	0.737 (P-value=0.85)
	falciparum	5	82000.0	79928.0	
	vivax +falciparum	3	112000.0	120216.5	
	Total	**53**	**108924.5**	**85952.8**	
Hb (gm/dL)	**Vivax**	45	8.1	2.4	1.567(P-value=0.34)
	falciparum	5	6.3	3.5	
	vivax +falciparum	3	8.9	1.7	
	Total	**53**	**8.0**	**2.5**	

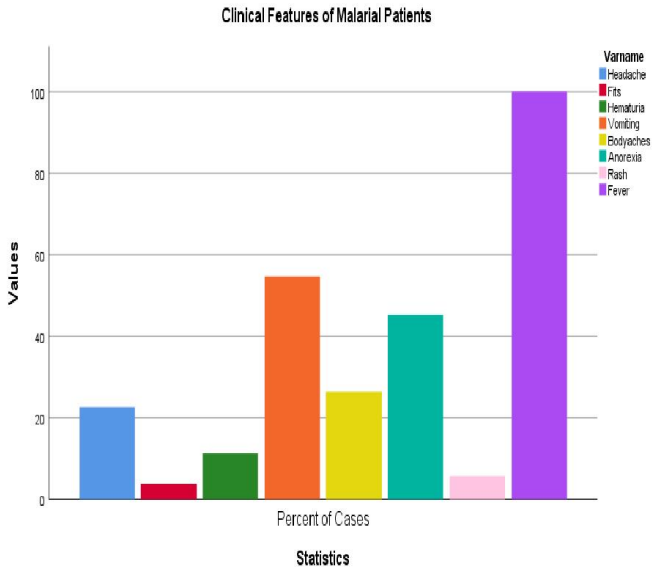

Figure 1: Clinical Features of Malarial Patients

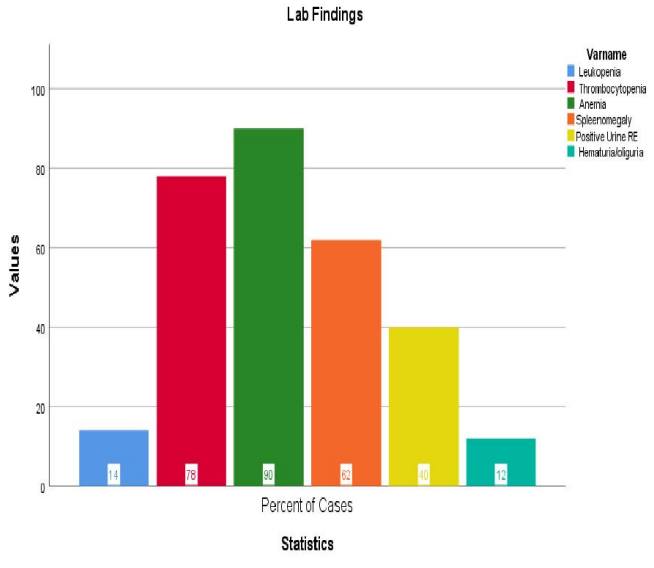

Figure 2: Lab findings in Malarial patients

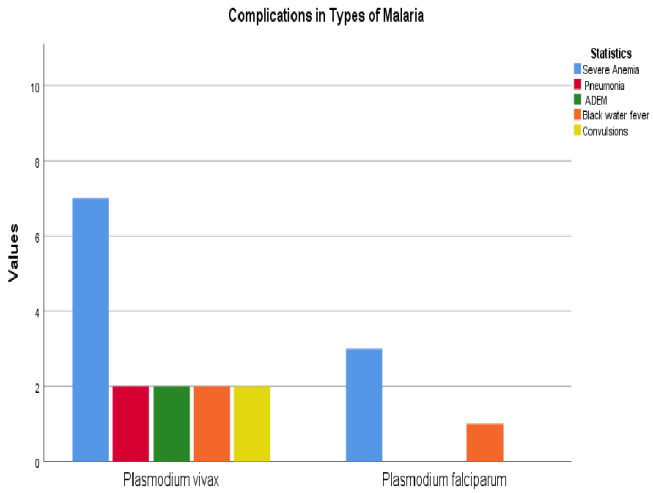

Figure 3: Severe Malaria Complications according to WHO criterion in both types of Malarial Infection

Discussion

Malaria is the largest vector-borne disease affecting nearly 300 million people worldwide.[1] Around 80% of the cases occur in malaria-endemic countries i.e. Ethiopia, India, Indonesia and Pakistan.[5] Sixty percent of the Pakistani population lives in malaria-endemic regions with 3.5 million cases each year. Among four Plasmodium species, *P. vivax* contributes to around 81.3% of the cases occurring in the region. *P. falciparum* infection contributes about 14.7% and other mixed species infection around 4% of the malarial burden (1). The results of the current study were also in agreement with the above-mentioned values with *P. vivax* infection present in 84.9% of the patients.

In children, the clinical profile of malaria may vary from nearly asymptomatic disease to febrile illness leading to life-threatening complications. The mortality among children is largely due to complications like cerebral malaria, severe anemia, and pulmonary complications.[7] Presentation of malaria often resembles other viral infections with fever being the most cardinal feature accompanied by myalgia, anorexia, headache, diarrhea, and vomiting.[8] In the current study, all patients presented with fever with 88.7% having intermittent while 11.7% having continuous fever. Other accompanying symptoms of malarial infection included vomiting, anorexia, body aches, headache, hematuria, rash, and fits. Fits were present in patients with patients having cerebral complications.

Hematological changes are evident in malaria and help in the diagnosis of suspicious cases. Different studies have been conducted on hematological parameters in malaria. Anemia, thrombocytopenia, leukopenia and reduced RBCs count are frequent in malaria.[9] Latif et al found thrombocytopenia, leukopenia, and anemia to be more common in *P. falciparum* compared to *P. vivax* infection.[10] In the current study, the mean platelet count was found to be low in both groups, with a mean of 80000 in *P. falciparum* and 11171.1 in *P. vivax* infections. Similarly, anemia was also invariably present in both groups however mean hemoglobin count was lower for the *P. falciparum* group compared to *P. vivax* one.

The worldwide prevalence of severe malaria is around 3%.[11] However, the rate is higher in malaria-endemic countries with a study reporting rate of severe malaria up to 17% in Ethiopia.[12] In the current study rate of severe malaria was very high reaching up to 32%. This high rate could be due to the inclusion of only indoor patients in the study.

WHO defines severe malaria in children as children having hemoglobin levels less than 5mg/dL, children having persistent jaundice, 2 or more convulsions in 24 hours, children with hemoglobinuria (black fever), or respiratory distress. All such children should be managed with antimalarial drugs under strict supervision to avoid life-threatening complications.[6]

In the current study severe malaria developed in 17 (32.1%) of the patients. Most common complication was severe anemia followed by blackwater fever, ADEM disease, pneumonia, and convulsions. The rate of these complications was higher in patients with *P. falciparum* infection having eight times more risk compared to *P. vivax* infection. Ahmed S et al conducted a study in Karachi and found rates of P. falciparum to be 57%, P. Vivax 11%, and mixed 32% with complications of Thrombocytopenia (86%), splenomegaly (74%), MOD (70%), severe anemia (42%), cerebral malaria (31%), respiratory distress (24%) and convulsions in 20% of the patients.[13] In another study by Asma U et al in India with a P. Vivax rate of 64%, the most common complications were thrombocytopenia followed by anemia, convulsions, and respiratory distress.[14] However, in Ethiopia with the majority of P. Falciparum infections (67.36%), the most common complication was respiratory distress (15.8%), severe anemia (42%).[15]

Globally with *P. vivax* infections rarely lead to life-threatening complications. Worldwide, almost all the deaths due to malaria are attributed to a complication caused by *P. falciparum*.[6] In a study by Herrera with

P. Falciparum rates of 70%, Hepatic dysfunction was found in 40% of the patients along with severe thrombocytopenia in 43% and severe anemia in 34%, two deaths were also reported.[16] In the current study, all of the patients were managed successfully with anti-malarial. No death was reported.

Conclusion

The rate of severe malaria is higher in children of the current study. Therefore, every child with malaria should be properly investigated for complications and treated accordingly. Early diagnosis and prompt treatment can save these children from life-threatening complications.

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