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PLASMODIUM VIVAX MALARIA AND ITS EFFECT ON CHILDREN IN AFRICA

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ABSTRACT

Background: Malaria is highly cognitive disease in African continent, where it is considered to be severe death causing disease. Plasmodium vivax are the main causes of disease and death from malaria. P. falciparum and P. vivax can cause severe anemia. The initial symptom of malaria the sequence high fever with muscle fatigue and weakness. Insight into the complexity of malaria pathogenesis is vital for understanding the disease and will provide a major step towards controlling it. **Aim**: To assess the effect of plasmodium vivax malaria in children. **Material and Methods:** This was prospective study conducted at Kenyatta hospital in Kenya. We used questionnaire to collect data, a total of 2465 patients were admitted to hospital during our study period, out of which 350 children affected with malaria were included in our study. **Results:** Our results revealed that, children in 0–5 year age group had more predilection for severe P. vivax monoinfection (OR = 5.73 [95% CI = 2.36–13.91], P < 0.0001), whereas children in 5–10 year age group were more predilicted to P. falciparum monoinfection (OR = 2.48 [95% CI = 1.09–5.63], P = 0.035). **Conclusion:** Plasmodium vivax malaria is more prominent in children under 5 years, hence, an increased risk to getting malaria associated effects and mortality in children under 5 years.

KEYWORDS: Plasmodium Vivax; Malaria Effects; Children; Africa.

INTRODUCTION

Malaria is a tropical disease which proves to be fatal if it is not treated on time, causing 247 million infections worldwide and 3.3 billion world's population were at risk in 2006 causing nearly a million deaths of which 88% occurred in sub-Saharan African children < 5 years of age (Snow, et al. 2005). Malaria is transmitted into humans through the mosquito of genus Anopheles. Out of the 400 species of Anopheles mosquitoes, almost 60 species are the carrier of malaria. It is caused due to Plasmodium parasite which is transferred to the red blood cells in the human body through the bite of an infected female anopheline mosquito. They are P.ovale, P. falciparum, P.vivax, P.malariae, and P.knowlesi. P.knowlesi is considered to be to the rarest form of malaria parasite and is commonly known as monkey malaria parasite (Commons, et al. 2018) (Guidelines for the treatment of malaria, 2015). The organism that causes malaria is known as endoparasite. Endoparasites are smaller organisms that live inside the nutrient supply of their hosts. The endoparasites do not have to worry about finding their meal or getting attacked by other animals. However, the problem arises when their host dies. If the host dies, then the parasite also dies. In such a case, some of the end parasites transfer from one host to another through an ectoparasite. A similar situation happens in malaria where it is transferred from one host to another through a mosquito (Marcus & Babcock, 2009).

Almost 100 million cases of malaria materialize each year with the death toll rising to 1 million every year. Unfortunately, this death toll includes almost 850,000 children. Due to its dangerous after-effects, malaria is considered to be a complicated disease. It usually occurs in four different forms and causes severe illness, pain, and death. Even though medical science has entered an advanced phase, still, malaria remains the greatest challenge in most parts of the world including Africa (Marcus & Babcock, 2009). In sub-Saharan Africa the overwhelming majority of malaria-associated morbidity and mortality occurs with Plasmodium falciparum infections. However, Plasmodium vivax accounts for 50% of the malaria prevalence in Asia, and yet the morbidity associated with this infection and its spectrum of disease is largely ignored.

Plasmodium vivax is the parasite that is considered to be the causative agent of human malaria. Although it is less dangerous than P. falciparum, still it can lead to death due to splenomegaly. It accounts for almost 9% of the malaria cases occurring throughout the world. It

is one of those malaria species that are quite dominant outside Africa. Majority of the P. vivax cases are discovered in Central America, Asia, South America, Oceania, and the Middle East. It is quite uncommon throughout Africa except for some places such as the Horn of Africa or in Mali and Mauritania in West Africa. In the areas where P.vivax prevails, the transmission of malaria is quite low due to which the patients gain little immunity. However, people belonging to all age groups are at risk of getting attacked by P.vivax (White, et al. 2018) (Guidelines for the treatment of malaria, 2015).

The estimated global burden of malaria due to Plasmodium vivax is approximately 70-80 million cases annually. Probably approximately 10-20% of the world's cases of P. vivax infection occur in Africa, south of the Sahara. In eastern and southern Africa, P. vivax represents around 10% of malaria cases but < 1% of cases in western and central Africa. Outside of African, P. vivax accounts for > 50% of all malaria cases (Mendis, et al. 2001). About 80-90% of P. vivax outside of Africa occurs in the Middle East, Asia, and the Western Pacific, mainly in the most tropical regions, and 10-15% in Central and South America.

Although P. vivax is widely regarded as benign, its propensity to recur is increasingly recognized by clinicians in endemic areas to result in appreciable disease, particularly in young children.(Hulden and Hulden 2011), Moreover, most of the published literature consists of case reports or small descriptive clinical series on severe P. vivax lacking denominators.(Baird 2007; Tan, et al. 2008). P.vivax can put children at risk for coma, severe anemia, hypoglycemia, abnormal bleeding, academia, circulatory collapse, hyperpyrexia, hyperparasitemia and impaired consciousness (Kumari & Ghildiyal, 2018). Children falling ill due to P.vivax malaria also face a grave issue of re-attack by the disease sometime after it has been cured. In such an instance, malaria prevention seems like the only strategy that can protect the children from the painful effects of P.vivax (Schumacher & Spinelli, 2012).

Plasmodium falciparum and P. vivax develop over 48 hours in RBCs, producing around 20 merozoites per mature parasite, with each merozoite able to invade other RBCs. A small proportion of asexual parasites converts to gametocytes that are essential for transmitting the infection to others through female anopheline mosquitoes, but cause no disease. Here, the strategy of P. vivax differs from that of P. falciparum. P. vivax develops into gametocytes soon after the release of merozoites from the liver; P. falciparum gametocytes develop much later. The early treatment of clinical attacks of malaria by anti-bloodstage chemotherapy for P. falciparum also kills the developing gametocytes; P. vivax transmits before the symptomatic stage of the disease (Price, et al. 2007).

P. vivax invades only Duffy blood group positive RBCs and is largely limited to reticulocytes. In West Africa, where RBCs are Duffy blood group negative, P. vivax has essentially disappeared. The Duffy negative blood group has arisen independently in Papua New Guinea — a region in which P. vivax is highly endemic (Ventura, et al. 2018). Previously, P.vivax malaria was considered to be a benign disease due to which it was not considered to be a serious issue. However, recently due to the findings from molecular diagnosis, it has become evident that P.vivax can cause dysfunction of multiple organs, especially in children. Even though, it can be treated with a fourteen-day course still there are various issues attached to this treatment. First of all, most of the patients lose their commitment due to the long duration of the treatment. Secondly, it can re-emerge even after it has been treated. Due to the fact that the transmission rate is low in most of the P.vivax regions so the patients in those areas do not achieve high-level immunity against this parasite. The lack of immunity against this disease has turned P.vivax into a great risk factor for the people of all ages especially children and infants. (Watson, et al. 2018). By considering the problems we investigate the primary and secondary symptoms of malaria in children and learn to differentiate between the initial symptoms of malaria and the common cold, precautionary measures that can help in the prevention of malaria and specifically P.vivax treatment children. We investigate the primary and secondary symptoms of malaria in children and learn to differentiate between the initial symptoms of malaria and the common cold, the treatment procedure of P.vivax in children in Africa.

MATERIAL AND METHODS

A retrospective case study was conducted in the Kenyatta Hospital from doctors, pea medical staff, over those patients who were admitted to hospital or diagnosed with malaria. Over a period of one year, the questionnaire was used to collect both qualitative and quantitative data. The objective of the study was to collect information about the symptoms, dispersal, mortality rate of Malaria and specifically for P. vivax.

During the duration of study total of 2465 patients were admitted to hospital, out of which 350 children affected with malaria were our study subject. Patient inclusion criteria, only neonates were included, who were admitted during a year, age less than 14 years. Total numbers of included patients and their ways of exclusion have been shown in the **Table 1** below.

The data about the Malarial susceptibility testing by fully automatic microbial identification and drug sensitivity analysis system was collected. And the

results were analyzed by using the statistical software SPSS.

RESULTS

Distribution of the malaria

The consolidated analysis revealed the presence of severe anemia (hemoglobin < 5 g/dL) in 81% (64/79), 75.4% (49/65), and 33.3% (2/6) children having P. falciparum, P. vivax, and mixed infections, respectively. Among children in 0–5 year age group this proportion was 26% (13/50), 75.6% (31/41), and 16.7% (1/6), whereas in 5–10 year age group it was 44.2% (42/95), 22.7% (10/44), and 14.3% (1/7) and in > 10 year age group it was 22.5% (9/40), 44.4% (8/18), and 0%, respectively. Thus, children in 0–5-year age group had more predilection for severe P. vivax monoinfection (OR = 9.3 [95% CI = 3.68–23.46], P < 0.0001), whereas children in 5–10-year age group were more predilicted to P. falciparum monoinfection (OR = 2.88 [95% CI = 1.33–6.22], P = 0.007). In children of severe anemia caused by P. vivax malaria, mean ± SD hemoglobin level was 4.142 ± 0.662 mg % and mean reticulocyte count was 1.1 ± 0.422% (normal range 0.5–1.5%). Type of anemia was normocytic normochromic in 35 (71.43%) and microcytic hypochromic in 14 (28.57%) children (OR = 6.3 [95% CI = 3.39–11.52], P < 0.0001). In children of severe P. vivax malaria, mean ± SD level of total leukocyte count was 9743.1372 ± 4710.839 cells/mm3.

Table 1: The distribution of malaria in different species.

Markers of severity	P. falciparummonoinfection		P. vivaxmonoinfection		Mixed (Pf + Pv) infection		Total	
	N	%	N	%	N	%	n	%
All patients	185		103		15		303	
Severe illness	79	42.7	65 †	63.1	6	40		
Anemia alone	16	8.6	18	17.5	1	6.6	37	12.2
Thrombocytopenia alone	5	2.7	9	8.7	4	26.7	19	6.3
Cerebral malaria alone	3	1.6	2	1.9	0	0	8	2.6
ARDS * alone	2	1.1	1	0.9	0	0	7	2.3
Hepatic dysfunction alone	3	1.6	2	1.9	0	0	7	2.3
Renal dysfunction alone	1	0.5	1	0.9	0	0	4	1.3
Abnormal bleeding alone	1	0.5	1	0.9	0	0	3	0.9
Multiorgan dysfunction	48	25.9	31	30.1	1	6.6	65	21.4

Table 2: The age wise distribution of malaria in children.

Category	Age group in years						Total	
	0–5		5–10		> 10			
	N	%	N	%	N	%	N	%
Total malaria patients	97		146		60		303	
Plasmodium falciparum monoinfection	50		95		40		185	
Plasmodium vivax monoinfection	41		44		18		103	
Mixed (Pf + Pv) infection	6		7		2		15	
Total severe malaria patients	46	47.4	79	54.2	25	41.7	150	49.5
Severe P. falciparum monoinfection	14	28	52	54.7	13	32.5	79	42.7
Severe P. vivax monoinfection *	31	75.6	23	52.3	11	61.1	65	63.1
Severe mixed (Pf + Pv) infection	1	16.7	4	57.1	1	50	6	40

Thrombocytopenia (platelet count < 1,00,000/µL) was present in 60.8% (48/79), 61.5% (40/65), and 83.3% (5/6) children having P. falciparum, P. vivax, and mixed infections, respectively. Among children in 0–5 year age group this proportion was 18% (9/50), 61% (25/41), and 50% (3/6), whereas in 5–10 year age group it was 34.7% (33/95), 18.2% (8/44), and 14.3% (1/7) and in > 10 year age group it was 15% (6/40), 38.9% (7/18), and 50% (1/2), respectively. Thus, children in 0–5 year age group had more predilection for severe P. vivax monoinfection (OR = 5.73 [95% CI = 2.36–13.91], P < 0.0001), whereas children in 5–10 year age group were more predilicted to P. falciparum monoinfection (OR = 2.48 [95% CI = 1.09–5.63], P = 0.035). In children of severe P. vivax malaria, thrombocytopenia was found in 40 (61.54%) children with mean ± SD platelet count 54175 ± 21256.537/µL and minimum platelet count of 13,000/µL. Platelet count < 20,000/µL were present in 3 (7.5%); between 20,000/µL and 50,000/µL in 12 (30%) and between 50,000/µL and 1,000,000/µL in 25 (62.5%) children. Out of these 40 children, bleeding manifestations were present only in 7 children (10.77%) in the form of epistaxis (57.1% [4/7]) and hematemesis (42.9% [3/7]). All of these 7 children required platelet transfusion.

Cerebral malaria was present in 21.5% (17/79) and 13.9% (9/65) children having P. falciparum and P. vivax infections, respectively. Among children in 0–5

year age group this proportion was 20% (10/50) and 12.2% (5/41), whereas in 5–10 year age group it was 4.2% (4/95) and 6.8% (3/44) and in > 10 year age group it was 7.5% (3/40) and 5.6% (1/18), respectively. Thus, the risk of CM was not different in different species and in different age groups. There were a total of 9 children (13.85%) of cerebral malaria caused by P. vivax infection with Blantyre coma scale ≤ 2. Multiple convulsions were present in 77.8% (7/9) children and bilateral upper motor neuron (UMN) lesion signs in 66.7% (6/9). Four (44.4%) children presented with semi-dilated pupil reacting to light and 3 (33.3%) children had pallor optic disc in fundus examination. No children had evidence of hemorrhage and papilledema in fundus examination. The CSF examination, CT scan of the head, and EEG were unremarkable in all the children. Out of these 9 children, 4 (44.4%) had multiorgan derangement. Comparing the rate of each neurological sign between P. vivax and P. falciparum severe malaria, multiple convulsions were as frequent in both species (22% for both, $\chi 2 = 0$, P = 0.96); and coma (4% versus 2%, respectively, $\chi 2 = 1.25$, P = 0.26).

Respiratory distress was present in 17.7% (14/79) and 10.8% (7/65) children having P. falciparum and P. vivax infections, respectively. Among children in 0–5-year age group this proportion was 2% (1/50) and 14.6% (6/41), whereas in 5–10 year age group it was 12.6% (12/95) and 2.3% (1/44) and in > 10 year age group it was 2.5% (1/40) and 0% (0/18), respectively. Thus, children in 0–5 year age group had more predilection for severe P. vivax mono-infection (OR = 9.43 [95% CI = 1.4–61.59], P = 0.039), whereas children in 5–10 year age group were more predicted to P. falciparum mono-infection (OR = 7.23 [95% CI = 1.16–44.31], P = 0.034). In arterial blood gas analysis of severe P. vivax children, PaO2 (mean value 91.1 mm/Hg) and O2 saturation (mean value 93.4%) were low in 28.6% cases showing hypoxemia. All the patients had a lower level of PaCO2 with a mean level of 25.6 mm/Hg caused by hyperventilation and CO2 washout showing respiratory compensation for metabolic acidosis. The mean arterial pH was 7.14 with mean bicarbonate level 12.1 mmol/L and mean base excess level 17.9 mmol/L. The metabolic acidosis was presented clinically as vomiting (7/7 [100%]), diarrhea (3/7 [42.9%]), and dehydration (7/7 [100%]). None of the children showed hypoglycemia, and urinary sugar and ketone bodies were also not present in any case.

Hepatic dysfunction was present in 44.3% (35/79), 26.2% (17/65), and 16.7% (1/6) children having P. falciparum, P. vivax, and mixed infections, respectively. Among children in 0–5-year age group this proportion was 16% (8/50), 36.6% (15/41), and 16.7% (1/6), whereas in 5–10 year age group it was 25.3% (24/95), 2.3% (1/44), and 0% and in > 10 year age group it was 7.5% (3/40), 5.6% (1/18), and 0% (0/2), respectively. Thus, children in 0–5 year age group had more predilection for severe P. vivax mono-infection (OR = 3.01 [95% CI = 1.18–7.70], P = 0.031), whereas children in 5–10 year age group were more predicted to P. falciparum mono-infection (OR = 16.9 [95% CI = 2.79–100.90], P < 0.0001). Out of the 17 children of hepatic dysfunction in severe P. vivax monoinfection mean ± SD level of serum bilirubin was 4.829 ± 2.229 mg/dL. Mild jaundice (3–5 mg/dL) was present in 12 children (70.6%), whereas moderate jaundice (5–10 mg/dL) in 4 (23.5%) and severe jaundice (> 10 mg/dL) was present in only 1 (5.9%) child. Jaundice was predominantly the conjugated type (82.4% [14/17]) with a mean level of conjugated bilirubin of 2.953 ± 2.243 mg/dL. The mean level of AST (537.471 ± 776.373 IU/L) was higher than that of ALT (484.059 ± 699.020 IU/L). Total protein and serum albumin level were also decreased with a mean level of 4.512 ± 0.507 gm/dL and 2.364 ± 0.609 gm/dL, respectively. The mean level of serum alkaline phosphatase (SAP) in children having severe P. vivax monoinfection and hepatic dysfunction was 602.706 ± 237.263 IU/L. On clinical examination, it was associated with hepatosplenomegaly (47%), splenomegaly (17.6%), and hepatomegaly (5.9%), which was also confirmed by ultrasonography of abdomen without any evidence of a parenchymal lesion. Six (35.3%) children were having signs of hepatic encephalopathy, four in grade II and two in grade I.

Renal dysfunction was present in 30.4% (24/79) and 15.4% (10/65) children having P. falciparum and P. vivax infections, respectively. Among children in 0–5 year age group this proportion was 6% (3/50) and 19.5% (8/41), whereas in 5–10 year age group it was 14.7% (14/95) and 2.3% (1/44) and in > 10 year age group it was 15% (6/40) and 5.6% (1/18), respectively. Thus, children in 0–5 year age group had more predilection for severe P. vivax mono-infection (OR = 4.28 [95% CI = 1.14–15.92], P = 0.049), whereas children in 5–10 year age group were more predicted to P. falciparum mono-infection (OR = 8.64 [95% CI = 1.40–52.57], P = 0.020). Out of the 10 children of renal dysfunction in severe P. vivax monoinfection the mean level of blood urea and serum creatinine was 193.9 ± 47.153 mg/dL and 3.680 ± 0.653 mg/dL, respectively. The mean serum potassium level was 5.13 ± 0.967 meq/L. Seven (70%) children were having oliguric renal failure, whereas 3 (30%) were of nonoliguric renal failure. Urine examination showed granular cast (50%), pus cell (50%), microscopic hematuria (20%), albuminuria (20%), and hemoglobinuria (10%). Ultrasonography of the abdomen showed normal kidneys without any parenchymal lesion.

CONCLUSION

Males were more affected than females, which is possibly due to increased outdoor activity and increased exposure to mosquitoes in males as

compared to females. Age distribution among various age groups was 33.9% in 0–5 years, 30.1% in 5–10 years, and 30% in >10 years, which was almost similar in all age groups. A study done in East Delhi studied population of 1 to 12 years which shows 59.7% males and 40.3% females having P. vivax malaria, as compared to our study which shows 69% males and 31% females having P. vivax malaria in similar age group of 1 to 12 years. Plasmodium vivax is an important cause of malaria outside Sub-Saharan Africa. The WHO estimates that P. vivax comprises 41% of the malaria burden outside of Africa. Globally, there are challenges in the prompt diagnosis and treatment of malaria infections with both P vivax and P falciparum. We propose an agenda for future research. Some of these challenges include low sensitivity of diagnostic tests and restrictions on antimalarial agents to be used for treatment, prevention, and elimination in pregnant women, such as antirelapse therapy for P vivax. the risk of early recurrence of P vivax after chloroquine monotherapy is high, it can be reduced by a modest increase in the dose of chloroquine, particularly in children younger than 5 years, and by the additional administration of primaquine. As reports of chloroquine treatment failure for P vivax increase, we recommend that the dose of chloroquine be increased to 30 mg/kg in children younger than 5 years, and health-care providers should be encouraged to provide adjunctive primaquine radical therapy to reduce the risk of both recrudescent and relapsing infections. Alternatively, a universal policy of ACT for uncomplicated malaria, with additional primaquine for vivax malaria, should be considered in regions where there is a high risk of recurrent P vivax after chloroquine treatment.

CONFLICT OF INTEREST

There was no conflict of interest.

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