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Original Research Article

Clinico-epidemiological features of malaria among children attending a tertiary care hospital: a two year study

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ABSTRACT

Background: Malaria caused by Plasmodium species and transmitted by Female anopheles mosquito, still remains as a major public health concern around the world. India is one of the major contributors of malaria cases in South East Asia. Malaria accounts for 205,000 deaths with 55,000 deaths occurring in early childhood. In endemic areas, children under 5 years are particularly susceptible to infection, illness and death. The present study was aimed to study the clinical, epidemiological profile of malaria cases among children (<12 years) attending a tertiary care hospital. We also assessed the complications associated with non-severe and severe malaria.
Methods: The study was conducted at a tertiary care hospital for a period of two years and all children <12 years of age diagnosed with malaria were enrolled in the study. The demographic, clinical and laboratory parameters were observed and noted. Cases were categorized into severe and non-severe malaria based on the WHO guidelines.
Results: A total of 2420 cases were observed and 250 cases of malaria were diagnosed, of which 136 were p. vivax mono infections, 82 falciparum malaria and 32 had evidence of mixed infections. Males were predominant in the study (58.8%) and 1-5 years was the common age group. Fever was the most common symptom (100%) in all cases and pallor, edema was common in falciparum malaria. jaundice was observed in 62% of mixed infections and altered sensorium in 43% of mixed infections. Severe malaria was observed almost equally in *vivax* and *falciparum* cases. Hyperparasitemia, cerebral malaria was common in falciparum cases than vivax. Thrombocytopenia, hypoglycemia and impaired consciousness were more common in mixed infections than falciparum and *vivax* cases.
Conclusions: Present study finally concludes that there is a significant change in the trends of vivax malaria in this region where both species coexist. The spectrum of complications seen in *vivax* and *falciparum* follow a similar pattern, then mentioned earlier that complications are less frequently seen in vivax than falciparum malaria. Hence more number of studies is required to generate the differing patterns associated with *vivax* and compare them with different studies from geographic regions.

Keywords: Altered sensorium, Malaria, *P. falciparum*, *P. vivax*, Thrombocytopenia

INTRODUCTION

Malaria caused by Plasmodium species and transmitted by Female anopheles mosquito, still remains as a major public health concern around the world. As per the WHO report April 2017, 91 countries and areas had ongoing malarial transmission. The African region shares 90% of total malaria cases and 92% of malarial deaths throughout the world.[1] India is one of the major contributors of malaria cases in South East Asia. Malaria accounts for

205,000 deaths with 55,000 deaths occurring in early childhood. In endemic areas, children under 5 years are particularly susceptible to infection, illness and death, 70% of all malarial deaths occurs in this age group. Among the five species of *Plasmodium (Vivax, falciparum, ovale, malariae* and *knowlesi), P. falciparum* and *P. vivax* accounts for majority of infections and deaths.[2] Most of the studies state that falciparum malaria is more virulent and associated with more complications (cerebral malaria, ARDS etc) and deaths in children and pregnant women. Changing trends in the pattern now had made vivax malaria also as virulent as falciparum malaria. Isolated studies from India have reported severe complicated cases from vivax malaria.[3] Several studies have stated that *vivax* malaria also accounts for majority of deaths in children and infants.[4] Microscopy provides a good method in diagnosis of malaria irrespective of the species infected, newer diagnostic techniques like rapid malarial antigen detection tests which is an immunochromatographic method has been developed and widely used in urban settings and hospitals for the diagnosis of malaria cases. However, these RMATs have low sensitivity with more false positives.

Hence the present study was aimed to study the clinical, epidemiological profile of malaria cases among children (<12 years) attending a tertiary care hospital. We have also assessed the contribution of vivax malaria and falciparum malaria in the study and noted the complications associated with non-severe and severe malaria.

METHODS

A hospital based prospective, cross sectional study was conducted at Narayana Medical College, by Dept of pediatrics, for a period of two years from June 2014 to May 2016. All the children between 0 months to 12 years of age attending the OPD of pediatrics, emergency, with history of fever (≥380c and <3 days duration) and symptoms suggestive of malaria were enrolled in the study. The socio demographic data of the cases (age, sex, socioeconomic status, bed net utilization etc), clinical signs and symptoms (temperature, weakness, body ache, prostration, vomiting, jaundice etc) were examined thoroughly and recorded in a predesigned data form by physician. Also, the symptoms of severe malaria as per WHO guidelines were examined thoroughly and recorded. All the guardians of the cases were explained about the study and written informed consent was obtained. The study was approved by the institutional ethical committee and all the ethical practices were followed strictly. Detailed biochemical and hematological parameters were recorded for all the cases diagnosed as malaria regularly.

Diagnosis of malaria

Blood sample was collected from all the suspected cases and a drop was placed on a slide and prepared thin and thick film. Rest of the sample was used for Hb% estimation, Haematocrit (HCT), S.creatinine and blood glucose was estimated using automated BD analyzer. The slides were stained by Geimsa stain and examined under microscope. The smear was screened as per WHO guidelines and parasite count was estimated using the below mentioned formula assuming that mean WBC count of human is 8000/µl.

Parasite count/ µl = Number of asexual parasites observed x 8000WBC count/ µl/200 WBC

Any smear with presence of asexual forms of the parasite on microscopy was considered positive. Rapid Malarial Antigen detection tests were done using Optimal. These were based on detection of Plasmodium specific antigen, Lactate dehydrogenase or Histidine-rich protein-2. Cases were considered positive for malaria if any of this is positive or both positive. Based on the results of peripheral smear and RMDTs cases were categorized as *P. vivax* mono infection, *P. falciparum* mono infection and mixed infection with both *P. vivax* and *falciparum*.

Patient's complications like cerebral malaria, severe anemia was classified as per WHO guidelines and recorded as severe and non-severe malaria.[5] Other investigations like, CSF analysis, Ultrasonography of abdomen and chest, X-ray chest were done when required.

Statistical analysis

All the data was entered in Microsoft excel spread sheet and checked. Mean and medians were calculated for continuous variables. P value <0.005 was considered significant.

RESULTS

In the present study, a total of 2420 presumptive clinical cases of malaria were included and of these 250 were diagnosed as malaria and enrolled in the study. The incidence of malaria in the study was 10.33%. Of the 250 cases, 147 (58.8%) were males and 103 (41.2%) were females, with male to female ratio of 1.43:1. The median age of the children enrolled in the study was 5.2 years (1 month to 12 years). Males outnumbered females in all the age groups. The most common age group in the study was 1-5 years (46.4%) with males (46.26%) and females (46.6%).

Most of the cases (56.8%) were from low socioeconomic status and very few (12.8%) were belonging to upper class. Out of 250 cases enrolled in the study, 57 (22.8%) were graded as PEM-II followed in order by PEM-III (22%) and 19.2% in Grade –I and IV. Most of the cases of malnourishment were in the weaning period. 42 cases (16.8%) were of good nutritional status as graded by physician. 71.6% of cases (179) were belonging to rural community and living in unsanitary neighborhoods,

places where there is breeding zones of mosquitoes (Huts, near drainages etc). However, bed net utilization was 80.4% in our study. Most of the parents were illiterate (78%) and 58% were farmers and agricultural labourers without monthly fixed income. (Table 1).

Table 1: Demographic data of cases in the study.

Age	Male (no) (%)	Female (no) (%)	Total
< 1 year	18 (12.24)	12 (11.65)	30(12)
1 year - 5 years	68 (46.26)	48 (46.60)	116(46.4)
6 years - 12 years	61 (41.50)	43 (41.75)	104(41.6)
Total	147 (58.8)	103 (41.2)	250(100)
Mean age	5.4 years	5 years	5.2 years
Male to female ratio 1.43:1			
Socio economic status			
Low status	95	47	142(56.8)
Middle	38	38	76(30.4)
Upper	14	18	32(12.8)
Nutritional status			
PEM-I	27	21	48(19.2)
PEM-II	43	14	57(22.8)
PEM-III	33	22	55(22)
PEM-IV	20	28	48 (19.2)
Normal	24	18	42 (16.8)
Locality			
Urban	49	22	71 (28.4)
Rural	98	81	179(71.6)
Bed net utilization	64	46	110(44)

Of the 250 malaria cases, 136 (54.4%) were of P. vivax mono infection, 82 were *P. falciparum* mono infection (32.8%) and 32 were mixed infections (*p. vivax* and *falciparum*) (12.8%) (Figure 1). Fever was the commonest presenting complaint in all the cases (100%) with an average duration of 2-9 days. Pallor was observed almost equally in mixed and *falciparum* infections (87%) and comparatively less in vivax malaria (74.24%). Edema was observed maximally in 80.5% cases of *falciparum* malaria than *vivax* (63%) and mixed cases (65%).

Cough and tachypnoea were present predominantly in falciparum cases than *vivax* malaria cases. With regard to gastro intestinal manifestations, vomiting, diarrhea and abdominal pain were more commonly seen in falciparum malaria, whereas abdominal distention is observed maximally in vivax malaria and Jaundice (62.5%) in cases of mixed infections.

Headache was complained maximally (92.68%) in falciparum cases but convulsions (25%), altered sensorium (43.75%) and hypotonia (25%) were seen predominantly in mixed infections than mono infections of *vivax* and *falciparum*. Dizziness was complained maximally (30.5%) in cases of *falciparum* malaria (Table 2).

Table 2: Distribution of clinical presentations in cases of the study.

Features	*P. vivax* (n=136) (NO) (%)	*P. falciparum* (n=82) (No) (%)	Mixed (n=32) (No) (%)
General			
Fever	136 (100)	82 (100)	32 (100)
Pallor	101 (74.24)	72 (87.8)	28 (87.5)
Edema	86 (63.24)	66 (80.49)	21(65.63)
Bodyache	24 (17.65)	31 (37.8)	11(34.38)
Respiratory symptoms			
Cough	56 (41.18)	39 (47.56)	14(43.75)
Tachypnoea.	22(16.18)	32 (39.02)	8 (25)
Gasro-intestinal			
Vomiting and Diarrhoea	24 (17.65)	19 (23.17)	6 (18.75)
Abdominal pain	12 (8.82)	16 (19.51)	4 (12.5)
Abdominal distention	29 (21.32)	14 (17.07)	6 (18.75)
Jaundice	34 (25)	46 (56.10)	20 (62.5)
Bleeding			
Cutaneous bleeding	12 (8.82)	8 (9.76)	4 (12.5)
Pulmonary hemorrhage	6 (4.41)	8 (9.76)	2(6.25)
Haematuria	8 (5.88)	8 (9.76)	2(6.25)
Central nervous system			
Headache	90 (66.18)	76 (92.68)	24 (75)
Convulsions	24 (17.65)	18 (21.95)	8 (25)
Altered Sensorium	36 (26.47)	29 (35.37)	14(43.75)
Hypotonia	28 (20.59)	12 (14.63)	8 (25)
Dizziness and Diplopia	26 (19.12)	25 (30.49)	6 (18.75)

Severe malaria symptoms were classified following WHO guidelines and all the cases were differentiated as severe and non-severe malaria. Among the 250 cases enrolled in the study, 46 cases of *falciparum* malaria had at least one or more than one symptoms of severe malaria which are summarized in Table 4. Hyperparasitemia (>10^5 /µl) was the most common symptom observed in 56.1% of cases, followed by severe anemia in 46.3%, raised S. creatine and hypoglycemia in 29.3% of cases and impaired consciousness in 26.8% of cases. In cases of *vivax* malaria, severe malaria symptoms were observed in 66 cases. Severe anemia (Hb <5mg/dl) was observed in 48.5% of cases followed by Thrombocytopenia (<1.5 lakh/mm^3) in 41.2%, Hypoglycemia in 33.8%, Hyperparasitemia in 30.9% of cases and less common

were impaired consciousness (23.5%), raised S. creatinine (20.6%), and repeated convulsions in 17.6%. In cases of mixed infections, severe malaria was observed in 20 (62.5%) cases with Thrombocytopenia as the commonest character (62.5%) followed by hypoglycemia (56.3%), severe anemia in 50% cases and less commonly impaired consciousness (31.3%) and Hyperparasitemia in 37.5% of cases. All the symptoms of severe malaria with species distribution are summarized in Table 3.

Table 3: Distribution of WHO severity parameters in different cases of malaria.

Characteristics	P.f (n=82)	P.v (n=136)	P.f + P.v (n=32)
Severe Anemia (Hb<5mg/dL)	38 (46.3)	66 (48.5)	16 (50)
Hyperparasitemia (>5%)	46 (56.1)	42 (30.9)	12 (37.5)
Repeated Convulsions (≥3/24 hrs)	18 (22)	24 (17.6)	8 (25)
Raised Serum Creatinine(3mg/dl)	24 (29.3)	28 (20.6)	8 (25)
ARDS	6 (7.3)	3 (2.2)	1 (3.1)
Abnormal bleeding	10 (12.2)	10 (7.4)	4 (12.5)
Hemoglobinuria	8 (9.8)	6 (4.4)	4 (12.5)
Impaired consciusness (Glassgow coma Scale <9)	22 (26.8)	32 (23.5)	10 (31.3)
Hypoglycemia	24 (29.3)	46 (33.8)	18 (56.3)
Thrombocytopenia (150,000/mm3)	18 (22)	56 (41.2)	20(62.5)

Table 4: Comparison of microscopy and RMAT* in different species.

Test method	Pf cases +ve	Pv cases +ve	mix Cases +ve	Negative
Microscopy	76 (92.68)	122 (89.7)	26 (81.25)	26 (10.4)
RMAT	68 (82.92)	112 (82.35)	32 (100)	38 (15.2)

*RMAT = Rapid Malarial Antigen Test

By microscopy and observation of both thick and thin films, 224 cases were positive by microscopy with slide smear positivity of 89.6% (224/250), 92.68% positivity in falciparum malaria (76/82), 89.7% (122/136) in vivax malaria and 81.25% (26/32) in mixed infections. By using rapid malarial antigen detection tests (RMAT), overall positivity was 84.8% (212/250), with 100% positivity in mixed infections and almost equally 82% in cases of *falciparum* and *vivax* malaria cases (Table 4). The difference in percentage of diagnosis by microscopy and RMAT was 4.8%, mentioning microscopy is still a good choice in diagnosis than RMATs.

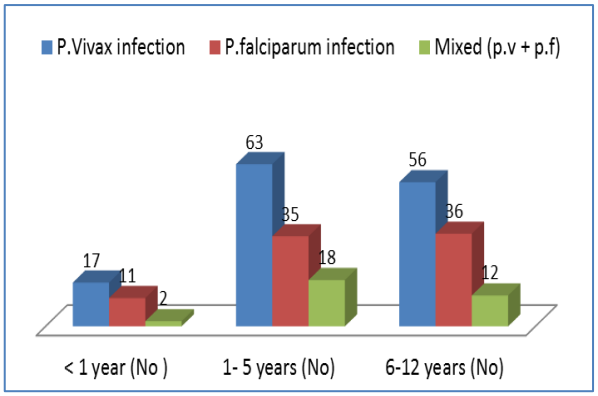

Figure 1: Distribution of cases by age and infected species of plasmodium.

DISCUSSION

In the present study, majority of the cases were of *Vivax* malaria than *falciparum* with a difference of almost 21.6%. Studies conducted previously from the same zone have also stated that vivax is more frequent cause of malaria than falciparum which is on par with our findings, but the difference may be variable based upon multiple parameters like bed net utilization rate, prevalence of mosquitoes etc.[6] In our study, males were affected more than females, which may possibly be due to increased outdoor activity of male children than females. Findings in our study were consistent with findings of Kochar et al who reported increased prevalence of malaria among females but only 33% whereas in our study it was found to be 41.2%.[7] Our findings were on par with findings of Gomber and kabilan who reported the prevalence of malaria as 42% among females in age group of 1-12 years.[8] Most of the cases in our study are from low socioeconomic status and were dwelling from areas with unsanitary neighborhoods which shows a clear indicator of malnutrition because most of them were in the weaning period. Malnutrition was an accompanying condition in many cases but majority of them were in PEM-II followed by PEM-IV. Malnutrition as such due to malaria cannot be made because, children during the weaning period have moderate degree of malnutrition and intestinal parasitic infections are seen in children of low socio-economic status. Bed net utilization is a very significant factor in reduction of cases of malaria by vector prevention, in our study it was only 44%, which might me an important factor in increased incidence of malaria in our study.

Fever was the most common presenting feature in our study as mentioned by many studies globally. Low level of parasitemia in *P.vivax* infections can even produce high fever due to its recognized low fever thresholds (100 infected RBCs/µl). Pallor was noticed maximally in cases of *P.falciparum* and Mixed infections than vivax malaria. Pallor caused by severe anemia is seen most commonly *falciparum* malaria as mentioned in many studies. Anemia may be due to hemolysis of infected RBCs and

decreased production of RBC from bone marrow which is observed mostly in falciparum than vivax. In endemic areas associated factors like malnutrition and intestinal parasitic infections aggravate this condition.[9] Jaundice was noted predominantly in cases of falciparum and mixed infections than vivax malaria, the reason is not clearly known, Findings in the study of Goyal and Makwana also observed similar finding where the reason was mentioned as unknown autoimmune factors which contribute the development of hepatitis more in falciparum than *vivax* cases.[10]

In our study, Involvement of the central nervous system with altered sensorium, convulsions, dizziness and diplopia were observed maximally in mixed infections followed by *falciparum* and *vivax* malaria. These were consistent with studies done in Pakistan and Thailand.[11,12]

Parameters of severe malaria as mentioned by WHO were observed in present study. Severe anemia was the most common parameter observed in our study with almost equal distribution among *vivax* and *falciparum* cases (48%). But the type of anemia observed in vivax malaria was normocytic normochromic anemia whereas in falciparum was microcytic microchromic anemia and this observation was consistent with many of the earlier reports. Most of studies mention severe anemia as a hallmark of *P.falciparum* infection due to intense hemolysis of infected RBCs, high level of parasitemia, but in our study it was shown equally distributed, which is on par with findings of Handayani et al.[13] Hyperparasitemia was observed predominantly in cases of *vivax* malaria than *falciparum* malaria in our study and more in mixed infections than both. This was an unusual finding in our study clearly indicating a change in the trends of vivax malaria which was initially considered benign. Acute respiratory distress syndrome was observed in 3 vivax cases and 6 cases of falciparum malaria in our study, which were associated with hypoglycemia, raised S.creatinine, severe anemia and circulatory failure. Thrombocytopenia with bleeding manifestations in skin, mucous membranes were reported from cases of severe *vivax* and *falciparum* malaria in our study, which is also observed in the studies of Thapa R et al in his study.[14] Thrombocytopenia was found in 41.2% of cases in vivax malaria and 22% in falciparum and 62% in mixed infections, similar findings were also reported by Bhatiua V et al in his study. Bleeding manifestations in severe malaria cases are due to hyperactive platelets which will enhance homeostatic responses.[15] Altered sensorium, impaired consciousness (with Glassgow coma scale <9) were also found in the study and presented as cerebral malaria. Most of the studies report cerebral malaria as a lethal entity and children as most susceptible groups. In our study, cases of cerebral malaria were observed in both *vivax* and *falciparum* malaria almost with equal distribution, stating that vivax malaria is no longer a benign entity, and is almost comparable to falciparum in complications. In our study, 8 cases of cerebral malaria due to vivax and 12 cases of *falciparum* malaria and 2 cases with mixed infections expired and observed with multi-organ dysfunction and shock.

Liver abnormalities with raised liver enzymes and hepatomegaly with associated spleenomegaly were common findings in our study reported from both *vivax, falciparum* and mixed infections. However, findings of our study were almost similar to many earlier studies reported globally.[16]

Our study finally concludes that there is a significant change in the trends of vivax malaria in this region where both species coexists. The spectrum of complications seen in *vivax* and *falciparum* follow a similar pattern, than mentioned earlier that complications are less frequently seen in *vivax* than *falciparum* malaria. Hence more number of studies is required to generate the differing patterns associated with *vivax* and compare them with different studies from geographic regions. However large studies are to be undertaken to justify the findings of our study.

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