

Original Research Article

DOI: <http://dx.doi.org/10.18203/2349-3291.ijcp20192056>

Clinical profile and renal complications among cases of malaria in children attending a tertiary care hospital of South India

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Received: 22 April 2019

Accepted: 27 April 2019

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ABSTRACT

Background: Malaria is one of the major vectors borne disease globally responsible for 1 million deaths a year. Changing trends in the causative species and epidemiological distribution have identified icterus and renal involvement as an emerging complication associated with severe mortality in children. The objectives of this study were aimed to study the clinical profile of malaria cases admitted in a pediatric ward. The study also highlights the involvement of renal manifestations in the cases with regard to species distribution and associated complications in the study group.

Methods: A prospective study for 14 months was conducted, and all positive cases of malaria admitted in paediatric unit were enrolled and socio demographic data, clinical history were collected, and biochemical investigations were performed and analyzed. SPSS software version 12 was used for analysis. Statistical significance was set at $p \leq 0.05$.

Results: About 278 subjects with 55.4% males, 44.6% females and with 5-10 years was most common age group. 102 cases of vivax malaria, 152 cases were falciparum and 24 were mixed cases. Cerebral malaria, hyperparasitemia was identified in 28 cases, DIC in 5.04% of cases. Renal involvement was observed in 38.16% of falciparum infections and 27.45% of vivax infections. 68 cases developed acute renal failure as a severe complication.

Conclusions: Renal involvement is more in falciparum and mixed infections than vivax malaria. Early diagnosis and prompt treatment help in early recovery of cases and halts to progression to renal failure. An urgent need for a biomarker for early identification of renal involvement in malaria before biochemical involvement is detected.

Keywords: Acute renal failure, Cerebral malaria, Hyperparasitoid, Malaria

INTRODUCTION

Malaria is one of the major vectors borne disease globally responsible for 1 million deaths a year and an estimated 200-300 million cases per year. Most of the malaria cases in 2017 were in the WHO African region (200 million), followed by WHO south east Asian region with 5% and WHO Eastern Mediterranean region with 2%.¹ India accounts for around 25% of cases globally, and is associated with a significant decrease in the number of cases and associated mortality in the recent years. Most of deaths due to malaria are associated with

complications like cerebral malaria, DIC and renal complications. Recent studies have identified changing trends in the clinical features and complications due to differences in the species and various internal and external factors. Differing species have been identified as one of the major factors in differences in complications globally.² Malaria accounts for one million deaths among children globally every year. Most of the studies have reported that cerebral malaria and severe anemia are the most common causes of mortality in children. Changing trends in the causative species and epidemiological distribution have identified icterus and renal involvement

as an emerging complication associated with severe mortality in children.³ Recent studies from south East Asian countries have shown that *P. vivax* as a major cause of complications in children. Trends of chloroquine resistant malaria are on surge and are an increasing problem associated with higher rates of mortality. Formulating the drug policies under national malaria control program is essential in management of cases of drug resistant malaria.⁴

The present was aimed to study the clinical profile of malaria cases admitted in a pediatric ward. The study also highlights the involvement of renal manifestations in the cases with regard to species distribution and associated complications in the study group.

METHODS

A prospective study was conducted by department of Pediatrics, Narayana Medical College and Hospital, a tertiary care hospital of South India. All the cases admitted in the pediatric ward of the hospital and diagnosed as malaria by smear positivity or rapid test or by quantitative buffy coat (QBC) examination during the period from January 2018 to February 2019 were included as subjects in the study. The study details and protocol were clearly explained to all the parents or guardians of the subjects and a written informed consent was obtained from all the parents. The study was approved by the institutional ethical committee and was conducted as per the guidelines of the committee. All the children less than 15 years of age were considered in the study. Children with preexisting renal disease, with history of medications known to cause renal impairment or past history of renal disease were excluded from the study.

All the socio demographic data, clinical history was collected by interviewing from the parents and noted in a separate structured project questionnaire. A detailed Clinical examination was done, and findings were elicited and noted in the proforma sheet. Biochemical investigations and complete urine analysis were performed in all the subjects of the study. Biochemical investigations with regard to renal involvement include serum urea, creatinine and electrolytes. Dipstick urinalysis was carried out on all the urine samples of the subjects and samples tested positive for blood were sent for urine microscopy.

Malaria parasite screening

Peripheral blood thick and thin films were made on the same slide for each subject. Methanol fixation was performed for thin film and immediately stained by Giemsa staining. The stained slide was examined under x100 oil immersion objective and x10 eye piece with a total x1000 magnification. The parasites were counted against 200 WBC and parasite density was calculated for

each patient based on an assumed total WBC of 8000/ μ l of blood.

*Identification of *P. falciparum**

Multiple infection of RBC, accolé form of trophozoite, no change in size of infected RBC, sickle shaped gametocytes and two nuclei on same side or opposite side of ring.

*Identification of *P. vivax**

One parasite in an RBC, Thick cytoplasm with single nucleus, Increase in size of RBC and absence of accolé forms.

Table 1: Criteria for renal involvement.

Parameter	Criteria
Serum creatinine	>1.5mg/dL or rise of 0.3 mg/dL from baseline level
Hematuria	>5 RBC/HPF
Proteinuria	>traces by dipstick method
Cast	Granular, RBC and muddy cast
Edema	Peri-orbital edema or pitting edema of lower extremities
Anuria	No urination
Oliguria	<0.5 ml/kg/hour urination

Table 1 illustrates the criteria for renal impairment. Presence of any one of these criteria was considered for renal involvement.

Statistical analysis

Data was entered in a Microsoft excel spread sheet and corrections were noted. Analysis of data was done was using SPSS software version 12 for windows. Continuous variables were expressed as mean or median and categorical variables were in proportions, ratios and percentages. Statistical significance was set at $p \leq 0.05$.

RESULTS

In the present prospective study, a total of 278 children who fulfilled the inclusion criteria were enrolled. All the cases were positive for malaria by either microscopy or rapid test or quantitative buffy coat examination. Of the 278 cases in the study, 154 (55.4%) were males and 124 (44.6%) were females with a male to female ratio of 1.24:1.

The most common age group in the study was 5-10 years with 168 cases (60.43%) followed in order by 10-14 years with 74 cases (26.62%) and 0-5 years (36 cases, 12.95%). The mean age of the study group was 8.2 ± 2.14 years with mean age of the males 7.84 ± 1.8 years and females 8.12 ± 1.8 years (Figure 1).

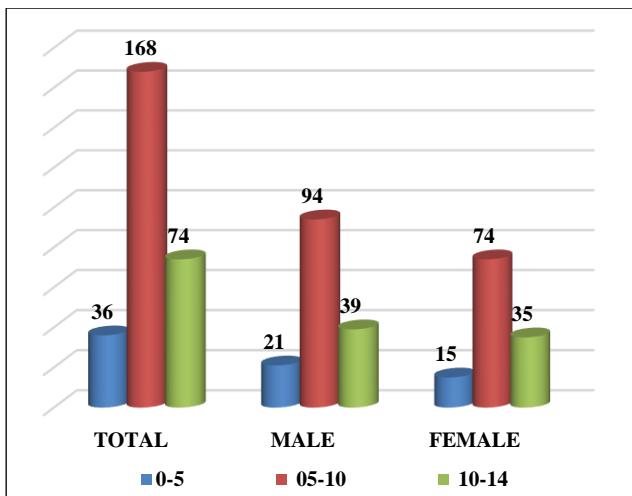


Figure 1: Age distribution of cases in the study (years).

Of the 278 cases, vivax malaria accounted for 102 (36.69%), falciparum malaria in 152 (54.68%) and mixed in 24 cases (8.63%) (Figure 2).

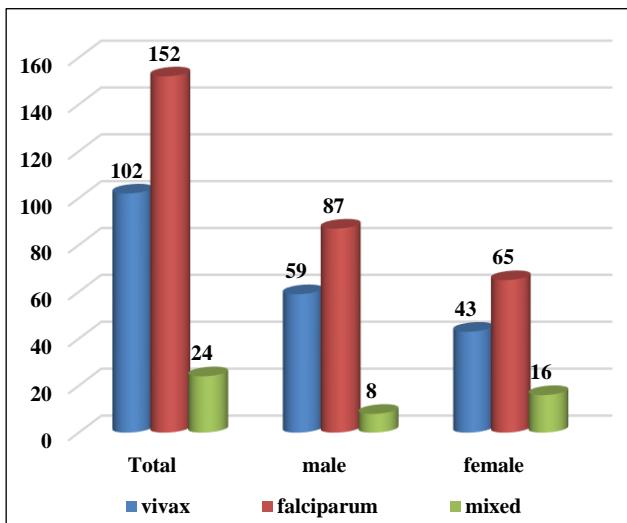


Figure 2: Species distribution of cases in study.

P. falciparum malaria infection was predominant in the study and most common in the age group of 5-10 years whereas vivax malaria in 0-5 years and mixed infection in 10-14 years. Falciparum malaria and vivax malaria were more common in males (*P. falciparum*: 87 cases; *P. vivax*: 59 cases) and mixed infection in females (16 cases). In the study, majority of the subjects were from rural areas (68%) and regarding distribution of plasmodium species, vivax infections were more common in rural areas (83 cases), falciparum infections (98 cases) and mixed infections (16 cases) from urban areas. This pattern of distribution clearly explains the severity of falciparum infections in cases admitted from urban areas. Clinical features of all the subjects in the study are summarized in Table 2.

Table 2: Clinical features and findings in subjects of the study.

Clinical feature	No. (%)	PV	PF	Mixed
Fever	278 (100)	102	152	24
Vomiting	144 (51.80)	78	55	11
Pallor	235 (84.53)	84	135	16
Headache	168 (60.43)	70	84	14
Hepatomegaly	108 (38.85)	45	55	8
Splenomegaly	210 (75.54)	75	124	11
Oliguria	98 (35.25)	28	58	12
Cerebral malaria	28 (10.07)	8	18	2
Severe anaemia	198 (71.22)	71	116	11
Hyperparasitemia	28 (10.07)	8	18	2
Hyperbilirubinemia	48 (17.27)	18	28	2
Circulatory failure	18 (6.47)	6	11	1
Hemolysis	6 (2.16)	2	3	1
DIC*	14 (5.04)	5	8	1
Sepsis	4 (1.44)	1	3	0

*DIC: Disseminated intravascular coagulation

Fever was the most common in all the groups (100%) of the study. 84.53% of cases identified with pallor with majority in falciparum infections (135/278), Splenomegaly was observed in 75.54% of subjects with 124 cases in falciparum infections, 71.22% of cases with severe anemia and 116 cases in falciparum infections, 11 cases of mixed infections and 71 cases of vivax infections. Cerebral malaria was diagnosed in 28 cases (10.07%) with 18 cases in falciparum infections, 8 cases of vivax and 2 cases of mixed infections. Hyper parasitemia was identified in same proportion of cases with cerebral malaria. Complications of malaria with DIC was observed in 5.04 % of cases with 8 cases of falciparum, 5 in vivax and one case of mixed infections. Circulatory collapse in 18 cases and four cases of sepsis were observed in subjects of the study. Renal involvement was specially observed in the subjects of present study.

Renal involvement

Oliguria was observed in 98 cases (35.25%) of cases with 58 cases of falciparum infections, 28 cases of vivax and 12 cases of mixed infections. Renal involvement was observed in 38.16% of falciparum infections and 27.45% of vivax infections. Renal complications were significantly higher in falciparum infections than cases of vivax. 50% of mixed infections had renal involvement.

Of the 98 cases identified with oliguria, 68 cases developed acute renal failure as a severe complication and associated with increased S. creatinine (>3 mg/ml) and urine output <12 ml/kg/24 hours despite adequate fluid replacement.

Urine dipstick analysis identified hematuria in 84 cases (30.22%) with 54 cases of falciparum infections

(35.53%), 28 cases of vivax (27.45%) and 2 cases (8.33%) of mixed infections (Figure 3).

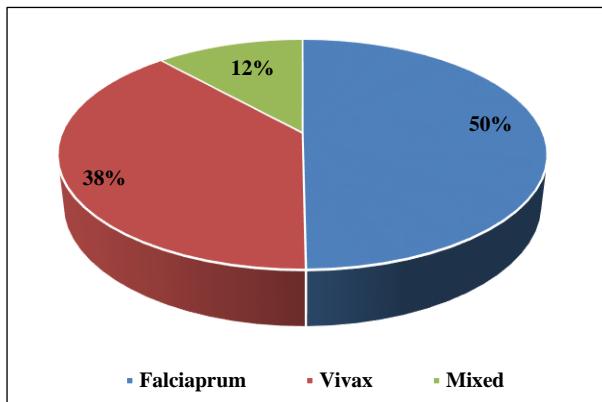


Figure 3: Subjects with hematuria in the study.

Blood urea levels were >40 mg/dl in 72 cases and between 20-40 mg/dl in 22 cases of present study. The mean blood urea levels in the cases was 44.29 ± 30 , S. creatinine was 0.957 ± 0.34 and demonstrated a statistically significant association between raised blood urea, S. creatinine and development of renal failure (p value <0.01) in present study. Mean blood urea and serum creatinine increases as the severity of malaria increases.

DISCUSSION

Malaria regained as a parasitic disease of major public health importance with increasing number of cases reported universally. However, the numbers of cases are more in tropical countries with clinical profiles showing marked variability. Cases with renal involvement are increasingly being reported. Renal involvement displays the full spectrum of interaction between red cell abnormalities and TH1 and TH2 activation. The spectrum of renal abnormalities ranges from mild immune mediated glomerulonephritis to acute tubular necrosis leading finally to renal failure.

The present study showed an increased surge in number of cases of malaria among children when compared with previous studies with an incidence of 22.8% among all febrile cases attending the pediatric outpatient and in emergency. This clearly explains an increase of pediatric cases of malaria when compared with the total incidence of all cases of malaria among all age groups. As mentioned in many studies in India and globally, male predominance was observed in present study also with 55.4% and females with 44.6%, these findings were in lieu with findings of Yadav D et al, and Patel U et al, who reported the same figures in their studies.^{5,6} High male predominance was attributed to higher health seeking behavior for male children and more outdoor activity of male children may be an contributory factor. In present study the most common age group affected was 5-10 years which is on par with the findings in the

study of Jasani JH et al and Marsh K et al.^{7,8} This can be explained by increased exposure to mosquito bites than in other age group children and lesser protective wear in this age. Falciparum malaria was predominant in present study with 54.68% and vivax with 36.69%. Results of present study were on par with findings of Shetty G et al, with Falciparum reported to 61.2% in his study, whereas some of the studies reported a higher incidence of vivax cases in their studies.⁹ Faseela TS et al, reported an increased incidence of mixed infection, which was attributed to endemicity for malaria in that area.¹⁰ The incidence of particular species differs from region to region and is based on the endemicity of the species distribution. The place of present study is endemic to falciparum and hence an increase of falciparum cases has been reported in present study.

The clinical symptoms of present study were clearly on par with the findings of Muddaiah M et al.¹¹ Fever was the most common presenting complaint in present study and was similar to many studies. Percentage of children having vomiting, headache and pain abdomen in present study was less compared to studies done by Sownumi A et al, and Rasheed A et al.^{12,13} Pallor was identified in 86% of cases in present study and most of the cases were with falciparum malaria. These findings were similar to reports of Herris VK et al.¹⁴ Splenomegaly was seen in 75% of the patients in present study. Similar rate was observed in study by Taha K et al, was 76%.¹⁵ Hepatomegaly was noted in 38% of the patients in the present study which is contrary to the findings in the study of Singh RK et al.¹⁶ Some of the studies reported that spleenomegaly and hepatomegaly are common in falciparum infections than vivax which is similar to our findings. There was no statistically significant difference in clinical presentation of various types of malaria. 71% of the cases in the study had severe anemia which is contrary to the findings of Trampuz A et al, who reported 52% in his study. The causes for anemia in malaria are multifactorial.¹⁷ Following are possible causes for anemia in malaria, extra-vascular clearance and/or intravascular destruction of infected RBCs, Clearance of uninfected RBC and activation of the monocyte/macrophage system with suppression of erythropoiesis along with dyserythropoiesis. Cerebral malaria was reported in 10% of cases in present study which is similar to the findings of Sanklecha MU et al, who reported 12% of cases in his study.¹⁸ DIC as the major complication was reported in 5% of cases with majority of due to falciparum malaria as par with the findings of Price RN et al.¹⁹

In present study renal involvement was observed in 35.25% of cases with majority (38.16%) observed in falciparum infections. Findings of this present study was on par with the findings of Abdul Manan J et al, who reported an incidence of 38% renal involvement in malaria cases in his study.²⁰ A few studies reported higher cases of renal involvement in mixed infections than falciparum and vivax cases. This variation is due to multiple factors like differences in endemicity of species,

immune mechanisms involved in the subjects of the study and management strategies involved like more usage of quinine in resistant cases of malaria. The hemodynamic changes are more malignant in case of falciparum malaria as the RBC parasitization rate and micro-vascular obstruction was maximum among falciparum malaria. Acute renal failure was observed in 68 cases in present study which coincides with the findings of Prakash J et al, who reported 22% of cases in his study progressing to renal failure in his study, however few studies reported lesser involvement in their studies.²¹

CONCLUSION

To conclude, the present study states that male children are more vulnerable to malaria and more common in 5-10 years age group. Falciparum infections were more common and also involved with severe complications than vivax malaria. Renal involvement is more in falciparum and mixed infections than vivax malaria. Early diagnosis and prompt treatment help in early recovery of cases and halts to progression to renal failure. There is an urgent need for a biomarker for early identification of renal involvement in malaria before biochemical involvement is detected.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kumar TR, Tenali SRLA. Clinical profile and renal complications among cases of malaria in children attending a tertiary care hospital of south India. *Int J Contemp Pediatr* 2019;6:1445-9.