Original Article

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A Comparative Study of Clinical Profiles of Vivax and *Falciparum Malaria* in Children at a Tertiary Care Centre in Uttarakhand

Paediatrics Section

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ABSTRACT

Background: *Falciparum malaria* has been constantly associated with high morbidity and mortality for a long time. *Vivax malaria*, which was once thought to be a relatively benign condition, is appearing in its more malignant form, with severity gradually becoming a serious concern.

Aim: This study is aimed to find out and compare the clinical and pathological manifestations of vivax and *falciparum malaria* in pediatric age group in Uttarakhand.

Setting and Design: A prospective study was carried out at a tertiary care hospital of a medical college in Uttarakhand, India.

Material and Methods: This study was done for a period of 2 years, from December 2010 to November 2012. Patients of 18 years age or below from Uttarakhand and nearby regions, who were smear positive or antigen positive were included in the study.

Statistical Analysis: p value was calculated using Pearson Chi-square with Yates correction by DAG stat software.

Result: Eighty Five patients were found to be suffering from malaria. 61 (71.8%) had *vivax malaria*, while 24 (28.2%) patients suffered from falciparum. Larger majority of malaria patients in both the groups happened to be males. The detailed study of morbidity profile clearly establishes that the complication related severity, earlier attributed to only falciparum is equally seen in vivax. Thrombocytopenia was the commonest finding in both. Other complications seen in both groups were those of cerebral malaria, severe anemia, ARDS, renal failure, malarial hepatitis, leucocytopenia, pancytopenia, shock with multiorgan dysfunction and hemoglobinuria. Even the mortality in the two groups was of the same order as p value calculated for the difference between the two species was well above 0.05.

Conclusion: *Vivax malaria* is an important cause of mortality and morbidity. The severity of illness is almost similar in both vivax and *falciparum malaria*.

Key words: Severe malaria, *Vivax malaria*, *Falciparum malaria*

INTRODUCTION

Malaria is endemic in the tropics and subtropics with highest prevalence in Africa followed by Southeast Asia. India contributes 80% of Southeast Asia malaria burden (24 million cases per year) [1]. While *P. falciparum* is prevalent infection in Africa, *P. vivax* causes majority of burden in India [2]. The proportion of *P. vivax* and *P. falciparum* varies in different parts of India [2]. Most of Indo Gangetic plains and northern hilly states, north western India and southern Tamil Nadu have less than 10% *P. falciparum*. In the forested area inhabited by ethnic tribes, *P. falciparum* is recorded as much as 30% - 90%, while in the remaining area it ranges from 10% - 30% [2]. However much of the research and publications are focused on *P. falciparum* and much less on *P. vivax* infection [3,4].

Vivax Malaria has long been considered to have a benign course with multiple relapses. The typical complications seen in *falciparum malaria* are not usually found in vivax mono-infections. However, during the past few years, the trend in the clinical manifestations of *vivax malaria* has been changing [5]. Several isolated studies from India, Indonesia and Papua New Guinea have reported severe complicated cases of *vivax malaria* [6-9]. *P. vivax* is now also getting recognized as a major cause of severe and fatal malaria despite its low parasite biomass, increased deformability of infected RBC & an apparent paucity of parasite sequestration [10]. Cases of malaria, as seen round the year, peak during monsoons from July to October [11].

This study was carried out to analyze the trends in clinical features and severity of disease in both *P. falciparum* and *P. vivax* infections in our hospital, which is a tertiary care center which caters to patients from Uttarakhand and some parts of Uttar Pradesh and Himachal Pradesh, India. During the last two years, total 85 cases of malaria required admission. Even though scattered throughout the year these cases were mostly confined to the monsoon season.

MATERIAL AND METHODS

A prospective study was planned during the period from December 2010 to November 2012. This study included consenting patients of age 18 years and below with either a smear positive for plasmodium species or malarial antigen positive by RDT (rapid diagnostic test). Categorization of severe malaria and treatment was carried out according to WHO guidelines [12]. The study plan was approved by hospital research committee.

Diagnostic methods used were conventional Thick & thin Peripheral smear stained with Leishman stain, examined under oil immersion. The slide was considered negative when there were no parasites in 100 HPF. Rapid diagnostic tests were based on detection of specific plasmodium antigen, LDH (optimal test) for vivax & HRP2 for falciparum.

Apart from peripheral blood film & rapid diagnostic test other lab investigations were undertaken like hemoglobin, total leucocyte count, platelet count, bleeding time, clotting time, blood sugar, blood urea, S. creatinine, total Serum Bilirubin (Direct and Indirect), SGPT, SGOT. Other appropriate blood test & CSF examination were done wherever needed.

RESULTS

Total 85 cases of malaria were detected by either malaria antigen

study and/or through peripheral blood smear. Out of these, 61 (71.8%) patients were found to have *P. vivax* while 24 (28.2%) had *P. falciparum*. Only one case which had mixed infection was excluded from the study.

Male to female patient ratio recorded in our study turned out to be 17:7 in falciparum and 42:19 in vivax. Median age in both vivax and falciparum was 12 years [Table/Fig-1].

It may be noted that the patients of both the plasmodium species had severe as well as non severe malaria (severe being categorized according to the WHO classification) [12]. In falciparum 18 (75.0%) cases were of severe malaria while only 6 (25.0%) were non severe. In vivax group 38 (62.3%) patients suffered from severe malaria and rest 23 (37.7%) were non severe. When these results were compared statistically the p value was found to be 0.3 signifying no statistical difference between the falciparum and vivax [Table/Fig-1].

Severe malaria was noted in both species. 38 (62.3%) patients of vivax and 18 (75%) patients of falciparum species were having severe malaria [Table/Fig-1]. 18 (29.5%) vivax cases and 9 (37.5%) of falciparum case were having severe thrombocytopenia (<50,000 Platelets). Many of these were associated with clinical bleed in the form of epistaxis, petechias, GI hemorrhage (malena or hematemesis). Leucopenia (TLC < 4,000) was found in 12/61 (31.5%) cases of vivax and 4/24 (16.7%) cases of falciparum [Table/Fig-2].

Severe anemia was recorded in 6/61 (9.8%) cases of vivax & 6/24 (25%) cases of falciparum. Pancytopenia was found in 31(50.8 %) of vivax and 14 (58.0%) of falciparum cases.

Among vivax cases 10 (16.4%) patients had CNS involvement in the form of multiple seizures, coma, or raised intracranial tension. In falciparum, 8 (33.3%) patients had CNS involvement [Table/Fig-2]. Among the cases with CNS manifestations, falciparum had multi system involvement in all; while 50% presented with multisystem involvement in vivax. The other 50% had isolated CNS involvement.

Studies were also pursued with liver and renal function. Liver involvment or malarial hepatitis was seen in only 4/61 (6.6%) in vivax group and 5/24 (20.8%) in falciparum group. Renal functions were deranged in 5/61 (8.2%) in vivax group and 5/24 (20.8%) in falciparum group. In falciparum group of renal failure patients, 3 improved on conservative treatment and 2 expired while in vivax group only 1 patient survived while the other 3 expired. Due to multisystem involvement and shock, even dialysis could not take place before the patients expired.

In vivax group, 5/61 (8.2%) patients had hemoglobinuria. In falciparum group 2/24 (8.3%) patients suffered from this complication [Table/Fig-2].

The number of patients suffering from hypoglycemic complications was 4/61 (6.6%) in vivax group and 2/24 (8.3%) in falciparum.

Shock, requiring ionotropic support was found in 4/61(6.6%) in vivax group and 3/24 (12.5%) in falciparum group.

Age group	*P. vivax* n= 61 (71.8%)				*P. falciparum* n=24 (28.2%)			
	Severe n=38 (62.3%)		Non-severe n=23 (37.7%)		Severe n=18 (75.0%)		Non-severe n=6 (25.0%)	
	Male	Female	Male	Female	Male	Female	Male	Female
0-5	8 (13.1%)	0 (0.0%)	6 (9.8%)	2 (3.27%)	4 (16.6%)	1 (4.16%)	1 (4.16%)	2 (8.33%)
5-10	5 (8.1%)	3 (4.9%)	3 (4.9%)	1 (1.63%)	3 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
>10	13 (21.3%)	9 (14.75%)	7 (11.4%)	4 (6.55%)	7 (29.1%)	3 (12.5%)	2 (8.33%)	1 (4.16%)
Total	26 (68.4%)	12 (31.6%)	16 (69.6%)	7 (30.4%)	14 (77.8%)	4 (22.2%)	3 (50.0%)	3 (50.0%)

[Table/Fig-1]: Age and sex wise distribution of malaria cases

Morbidity	Total	*P. vivax*	*P. falciparum*	p value
All Patients	85	61(100%)	24(100%)	
Severe malaria	56	38(62.3%)	18(75.0%)	0.3
S. Anemia (Hb<5)	12	6(9.8%)	6(25.0%)	0.14
Thrombocytopenia <1 lakh	55	41(67.2%)	14(58.3%)	0.6
Thrombocytopenia <50,000	27	18(29.5%)	9(37.5%)	0.6
Leucoytopenia	16	12(19.6%)	4(16.7%)	0.9
Pancytopenia	45	31(50.8%)	14(58.0%)	0.7
CNS manifestations	18	10(26.3%)	8(33.3)	0.1
ARDS	7	5(8.2%)	2(8.3%)	0.6
Deranged LFT	9	4(6.6%)	5(20.8%)	0.1
Deranged RFT	10	5(8.2%)	5(20.8%)	0.2
Hypoglycemia	6	4(6.6%)	2(8.3%)	0.8
Shock	7	4(6.6%)	3(12.5%)	0.6
Hemoglobinuria	7	5(8.2%)	2(8.3%)	0.6

[Table/Fig-2]: Morbidity profile: comparison between vivax and falciparum

Age group	*P. vivax*	*P. falciparum*	p value
0-5	0(0.0%)	3(12.5%)	0.05
5-10	2(3.3%)	0(0.0%)	0.82
>10	3(4.9%)	1(4.1%)	0.81
Total	5(8.2%)	4(16.7%)	

[Table/Fig-3]: Mortality profile: comparison between vivax and falciparum

Of all the severe malaria cases, 5/61 (8.2%) patients developed ARDS in vivax group and 2/24 (8.3%) in falciparum.

A comparison of morbidity profile between vivax and falciparum shows there was no statistically significant difference regardless of the complication involved [Table/Fig-2].

There were 5 (8.2%) deaths in *vivax malaria* while 4(16.7%) in falciparum. Comparison of the two outcomes shows no significant statistical difference between the two species of malaria [Table/Fig-3].

DISCUSSION

According to WHO report 2010, out of all malaria cases in South East Asia region more than 50% cases are of vivax [1]. The status of *P. vivax* as a major threat affecting the world's most populous region is gaining attention. The belief that *vivax malaria* is rarely threatening and relatively benign is increasingly being challenged [13-18].

Out of total malaria cases 72% cases were of vivax while only 28% cases were of falciparum. The study showed that incidence of severe vivax infection is more than twice as likely as that of severe falciparum. A statistical comparison of cases of severe malaria showed no significant difference between the two species.

The study also brings out that male children hospitalized due to malaria are more than twice the number of female children. Correspondingly the ratio of male to female in severe malaria also shows the same trend. This finding may be due to the increased probability of boys having an outdoor exposure, although a genetic basis cannot be ruled out.

Like other studies by Kochar [6], Sharma and Khanduri [19], Makkar [20], Antinori [21], Narang [22], thrombocytopenia was the most common presentation in both the species. The lowest platelet count here was 5000 cells which was in falciparum but there are many cases of platelets below 20000 even in vivax group. Some of the possible mechanisms for thrombocytopenia in vivax can be attributed to its lytic effect, immunological reactions, sequestration and oxidative stress [23-25]. Many of these patients had clinical bleed in the form of epistaxis and GI bleed.

The other hematological morbidity associated with malaria includes severe anemia and leukocytopenia [26]. Incidence of severe anemia was found to be 9.8% in vivax and 25.0% in falciparum [Table/Fig-2]. Severe anemia may cause significant morbidity and indirect mortality alongwith other co- morbidities. Leukocytopenia was observed in 19.6% cases of vivax and 16.7% cases of falciparum. Pancytopenia was also significantly observed in our study compounding the effect of anemia. Leukocytopenia was a transient finding which resolved with treatment.

Next most common presentation was found to be cerebral malaria. Cerebral Malaria is the most lethal entity of severe malaria and children are more prone than other susceptible group [12]. 10 (16.4%) case from vivax and 8 (33.3%) case from falciparum group showed CNS manifestations. All the patients in falciparum group had multisystem involvement. The corresponding figure for vivax was 50% while the other 50% had isolated Cerebral Malaria. This study thus further reinforces the findings in Bikaner study by Kochar [27].

Respiratory complications in *P. vivax malaria* have been less frequently reported. Acute respiratory distress syndrome (ARDS), acute pulmonary injury (ALI), and interstitial pneumonia are some of its reported complications [28-30]. Small airway obstruction, gas exchange alteration, increased phagocytic activity and accumulation of pulmonary monocytes are the possible mechanisms [19,28-30]. In our study ARDS was seen in both the species and was one of the presentations in three out of five vivax deaths. Most of these patients developed the respiratory distress after the treatment for severe malaria was started. Anstey et al., [28,29] demonstrated an additional role of sequestration of vivax infected erythrocytes in pulmonary microvasculature. They also demonstrated progressive alveolar, capillary dysfunction after treatment of *vivax malaria*, suggesting a greater inflammatory response to the given parasite burden in vivax than in *falciparum malaria*.

There have been studies of acute renal failure and malarial hepatits in *vivax malaria* [31-38]. Acute tubular necrosis due to renal ischemia is the predominant mechanism of renal failure. Hemolysis, cholestasis and hepatocellular injury are important factors leading to jaundice. In this study renal failure was present in 5(8.2%) patients of vivax and 5(20.8%) of falciparum group. Kute et al., [33] showed similar trends. Hepatits was present in 4(6.6%) patients of vivax and 5(20.8%) of falciparum. Out of these 2 patients had encephalopathy, of which 1 was in stage 3 who was falciparum positive, and the other in stage 1 was vivax positive. Some rarely reported manifestations seen in our patients were those of shock and hemoglobinuria.

In all these complications interesting fact was that there was no statistical difference between the two groups i.e. vivax and falciparum. The detailed study of morbidity profile clearly establishes that the complication related severity, earlier attributed to only falciparum is equally dominant in vivax [Table/Fig-2].

Mortality in severe vivax 5(8.2%)was found to be comparable to falciparum mortality 4(16.7%) in the present study. It is interesting to note that not even a single case of mortality was observed in 0-5 years of age group in vivax. Here infact the mortality showed a rising trend with advancement of age. On the other hand, in falciparum the minimum mortality was found to be in 5-10 age groups, while the maximum was in 0-5 year's age group unlike vivax [Table/Fig-3].

The difference between the age specific mortality between vivax and falciparum were found that to be statistically insignificant. In 0-5 year age group p value is 0.05 suggesting a trend of severe falciparum presenting early towards mortality while in vivax the mortality is greater in older age group.

CONCLUSION

The study shows vivax as an important cause of morbidity and mortality from malaria among children in Uttarakhand and nearby places. The prevalence of vivax is much higher than that of falciparum. The present study shows vivax as quite an important cause of severe malaria. In fact a comparison of severe malaria cases shows no significant difference in severity vivax and falciparum.

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