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Original Research Article

Spectral presentation of *Plasmodium vivax* malaria in Central Rural India

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Abstract

Aims and Objectives: To assess the clinical course, complications, their response to antimalarial and outcome in patients with *Plasmodium vivax malaria* infection.
Method: This observational study included 201 patients admitted to medical wards of Kasturba Hospital, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, India from December 2014 to November 2015. The diagnosis of *P. vivax* malaria was established by peripheral smears and rapid diagnostic test (RDT). Of 201 patients with malaria, 45 had *vivax* malaria. Clinical features, biochemistry, course during stay, response to treatment and outcome were recorded in all the study patients.
Results: Forty five indoor patients positive with *vivax* malaria were included in the study, among them majority of patients were young with male predominance. Fever was most common presenting symptom. Complications observed were thrombocytopenia, jaundice, cerebral malaria, anaemia, acute renal failure respiratory distress, algid malaria, metabolic acidosis and hypoglycaemia. Total 42 (93.33%) cases of *P. vivax* malaria were responded to chloroquine while 6.67% of patients were found to be resistance to the treatment and they were treated with ACT. All patients (100%) were discharge after successful treatment on *vivax* malaria.
Conclusion: Thrombocytopenia and respiratory distress was more common complications observed with *Vivax* malaria. All patients responded to treatment and no death observed in our study, this shows that *vivax* positive population in central rural India still sensitive to chloroquine.
Keywords: *Plasmodium vivax*, Peripheral Smears, Antimalarial, Biochemistry Cerebral malaria, Algid malaria.

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1. Introduction

Plasmodium vivax is the second important parasite of human malaria widely perceived as causing mild and self-limited illness. Unlike *P. falciparum*, it has wider geographical distribution with an at risk population of 2.5 billion persons. Although the exact burden of disease caused by *P. vivax* infection is still a matter of debate, this parasite causes approximately 100–300 million clinical cases each year [1]. *Vivax* malaria is long considered to have a benign course. It is known for multiple relapses; but the typical complications seen with falciparum malaria are not found with *vivax* mono infection, [2].

P. vivax causes an acute febrile illness with no complications or death. However, in recent years

complications due to *P. vivax* are being increasingly reported from different parts of the world [3,4]. The reason for appearance of severe *vivax* malaria in many parts of the world may be linked with declining efficacy of chloroquine, global warming, and lack of primaquine alternative due to its long course of treatment (14 days) for liver stage clearance of infection [1]. Further it is only in 1990s that clinical laboratory parameters of severe malaria (severe anaemia and RD) other than coma is defined [5-7]. Severe anaemia and RD are commonly found in *P. vivax* malaria. A molecular tool like PCR is now widely used in malaria research. Moreover, large-scale disease surveillance system in different epidemiological settings has also improved the ability to capture unexpected trends. The present prospective study was undertaken to observe the clinical course, more common complications of *vivax* malaria and their outcomes.

2. Materials and Method

This was a single center, prospective, observational study in which 201 patients admitted to a tertiary care center of Central Rural India, from December 2014 to November 2015 with complaints of fever and having clinical features of severe malaria were included. Before starting the study, ethical clearance was obtained from Institutional Ethics Committee and written informed consent taken from the participants. Subjects who were not willing to participate were excluded from the study. All the patients were screened for a possible malaria infection using a peripheral smears and rapid diagnostic test (RDT). Out of total patients, 45 cases were positive for *vivax* malaria. Detailed demographic and clinical evaluation was done. Baseline investigation on admission had done as compete blood count, serum creatinine, urea, serum bilirubin and liver enzymes and urine protein was recorded. Patient had been started on standard treatment of malaria as per the treating physician. Over the period in hospital he/she had been reviewed for any complication developing and response to the treatment. Investigations had repeated after three days, if any complication was seen on the baseline investigation. Course of the disease in hospital and response to the antimalarial had been noted. The statistical analysis was done using SPSS statistical software version 15 and p value of< 0.05 was taken as significant.

3. Observations and Results

Forty five indoor patients positive with *vivax* malaria were included in the study, among them majority of patients were young (12-30 years) with male predominance (male-25 and female-20). Peripheral smear examination was found positive in 28 (62.22%) patients, RDT test were found positive in 44 (97.77%) patients. Fever was most common presenting symptom while most of the patients were afebrile during admission were of the elderly age group, presented with altered behaviour, loose stool, rash and weakness.

Complications like thrombocytopenia, respiratory distress, anaemia and jaundice were more common in *vivax* malaria. Cerebral malaria, acute renal failure and metabolic acidosis were observed in only one patient of each complication. There was no any patient with algid malaria and hypoglycaemia, (Table 1).

Table 1: Distribution of patients according to complications

Complications	No. of patients	%
Anaemia	3	6.67
Thrombocytopenia	24	53.33
Severe Thrombocytopenia	6	13.33
Respiratory Distress	3	6.67
Cerebral Malaria	1	2.22
Acute renal Failure	1	2.22
Jaundice	3	6.67
Algid Malaria	0	0.0
Metabolic Acidosis	1	2.22
Hypoglycaemia	0	0.0

Figure 1 shows the distribution of severity of anemia according to hemoglobin concentration while figure 2 shows the distribution of severity of severe thrombocytopenia according to platelets counts. In case of *vivax* malaria range of hemoglobin was 3.6 to 5.5 mmHg. In most of the cases (66.67%) platelets counts were 21000 to 30000.

Figure 1: Distribution of Severity of anemia according to Hemoglobin concentration

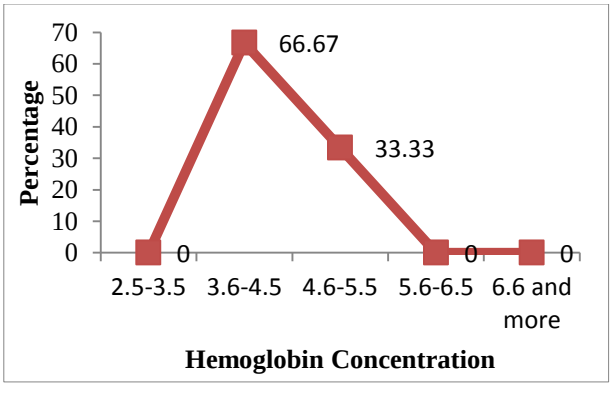
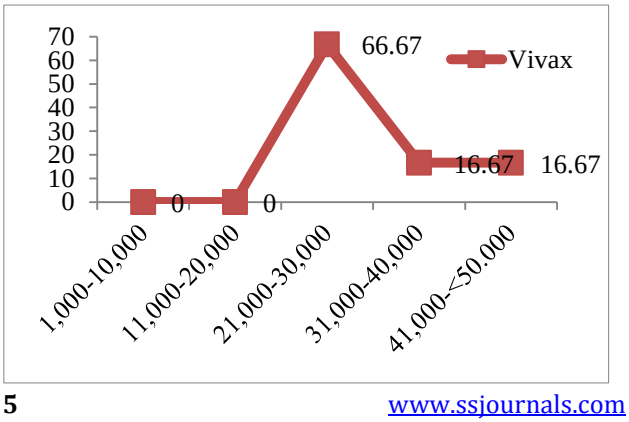


Figure 2: Distribution of severity of severe thrombocytopenia according to platelets counts



Total 42 (93.33%) patients were treated with chloroquine. As quantitative peripheral smear was not available so keeping respond to fever as criteria for resistance, though no reference was available, we observed 3 patients were resistant to chloroquine and they were treated with ACT. All patients were discharge after successful treatment and there was no any mortality observed with *vivax* malaria (Table 2).

Table 2: Show treatment response and treatment outcome of patient

Treatment Response	*vivax* Malaria	
	No. of patients	Percentage
Response	42	93.33%
Resistance	3	6.66%
Treatment Outcome		
Discharged	45	100%
Death	0	0.0%

4. Discussion

Severe and complicated malaria is usually caused by *P. falciparum* but it has been increasingly observed that *P. vivax* malaria, which was otherwise considered to be benign malaria, with a low case-fatality ratio, can also occasionally result in severe disease as with *P. falciparum* malaria [1]. However in the past few years many cases of severe *vivax* malaria were seen and some cases resulted in death. Hence this study was done to find out various complications of *vivax* malaria and their outcomes. The exact causes of changes in the clinical profile of *vivax* malaria are uncertain. They may include genetic alterations of the parasite or change in vector and its biting habits or chloroquine resistance or increasing use of ACTs. Further research is needed to answer these questions [2].

It was previously presumed that the severe disease with *vivax* infection is actually caused by coinfection of vivax and falciparum species. With application of the recently developed tests of malarial antigen and the nucleic acid amplification technique it has become evident that *vivax* monoinfection can be a cause of severe malaria and death [8]. The mechanisms of organ involvement in *vivax* malaria are debatable. Enhanced inflammatory responses as well as the sequestration of parasitized red cells in microcirculation were thought to be the possible mechanisms [9]. The inflammatory and immunological response plays a significant role in pathophysiology of severe *vivax* malaria. In the study by Andrade et al in Brazil the patients with severe *vivax* malaria were younger, had lived in the endemic area for shorter time and had less previous episodes of malaria [10].

Microscopy of thick and thin stained blood smears is considered to be the gold standard for malaria diagnosis [11]. Thick smears are used to detect infections whereas thin smears are important for species identification and quantification of parasitaemia. The diagnostic accuracy of microscopy mainly relies on the quality of blood smears and experience of the laboratory personnel preparing and reading the blood slides [12]. On the other hand Rapid diagnostic tests are simple to perform, easy to interpret. This test detect malaria antigen in a small amount of blood (5 – 15 µl) [13]. Given the fact that microscopy is likely to miss very low parasite densities [14] the use of RDTs can be a useful diagnostic alternative in diagnosing [15]. We used microscopy as a gold standard and RDT as bedside test for diagnosis. Patient positive with either one test considered as a positive for malaria. In present study out of 45 patients, 44 patients were positive by RDT comparing with microscopy in which only 28 were positive. This may be due to subjectivity of the microscopic test. This shows the need to train laboratory workers and microbiologist. Our observation was similar to study of Chandramohan [16] et al and Daumba et al [17].

The most common complications observed were thrombocytopenia and respiratory distress, which was similar to previous studies [18-20]. Anaemia and jaundice were the second most common complication, observed in the study. Cerebral malaria was observed in one patients; this has also been reported in one patient in Pakistan and in three patients in Bikaner, India [21,22]. It was not commonest presentation in our study but was most dreaded complication, leading to death. So any degree of impaired consciousness and any other signs of cerebral dysfunction should be treated with utmost urgency as cerebral malaria. Previous studies [19,20] reported different percentage of cerebral malaria, this difference over years may be due to newer drugs, newer diagnostic methods and improvement in the health sector. Renal failure and metabolic acidosis were observed in only one patient of each complication. Renal failure was significantly less in compare to earlier studies done in both *vivax* and *falciparum* malaria. Saini et al [20] observed ARF in 11.76 % patients while Limaye et al [2] observed ARF in 3.5 % patients of *vivax* malaria. In our study, we found no patient with algid malaria and hypoglycaemia.

If malaria cases were not properly managed, either due to missed or delayed diagnoses, malaria may progress from mild through complicated to severe disease. As a result of widespread drug resistance, many malaria endemic regions have shifted to artemisin in combined therapy. Antibiotics such as tetracycline and its derivatives (doxycycline) can also be used for treatment and prophylaxis of malaria [23]. In our setting we used chloroquine for *vivax* malaria and ACT with doxycycline for resistant *vivax* malaria. Resistance to an antimalarial drug is defined as the ability of a parasite to survive and/or multiply despite the administration and absorption of a given drug in doses equal or higher than those usually recommended but within tolerance of the subject [24]. But in our study we did not do the parasite counts, we consider the patients resistant to

treatment in whom fever was persistent on day three. Out of 45 patients 42 were responded to treatment which they received, while 3 patients were resistant. In chloroquine resistant *vivax* patients, we shifted the patients on Artemisin in combined therapy result of which was outstanding. No death observed in our study.

5. Conclusion

In current study, thrombocytopenia and respiratory distress was more common complications observed with *Vivax* malaria. All the patients were treated with antimalarial therapy and no death observed in our study, this shows that *vivax* positive population in central rural India still sensitive to chloroquine.

A further large-scale study is required to determine the underlining pathogenesis of severe disease and the degree to which it is related to multidrug resistance of *P. vivax* infection. There is also an urgent need to re-examine the clinical spectrum and burden of *P. vivax* malaria so that adequate control measures can be implemented against this emerging but neglected disease.

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