Original Research Article

# Study of neurological manifestations in plasmodium vivax malaria

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## Abstract

**Background:** Cerebral malaria is the most dreaded and a potentially life-threatening complication of malaria. The percentage of neurological manifestations of vivax malaria cases is on the increasing trend. **Aim:** To highlight the increasing incidence of neurological manifestations of vivax malaria. **Material and Methods:** Total number of indoor patients of *P. vivax* malaria in our hospital was 339 out of them 48 patients had neurological manifestations.Presence of malarial parasite on thick and thin smear and/or positive p-LDH based rapid malaria antigen test was considered diagnostic of malaria. Neurological manifestations of *P. vivax* malaria by definition refers to involvement of signs such as high grade fever with altered sensorium, generalized tonic-clonic or partial convulsion. **Results:** The highest incidence of neurological manifestations of vivax malaria was seen in the age group of 21-30 years; males predominated the study with 66.7%. Altered sensorium (77.1%) followed by convulsion (58.3%) was common finding in neurological manifestations. Mortality was higher (62.5%) in patients of neurological manifestations of vivax malaria with premorbid conditions. Association of altered sensorium and parasite index which was statistically significant. **Conclusion:** *Plasmodium vivax*is no longer a benign species and is causing presentations akin to *P. falciparum.* It is imperative that clinicians are aware and are ready to handle the complications caused by *P. vivax.*

**Key Words:** *Plasmodium vivax,* altered sensorium, parasitic index, mortality.

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## INTRODUCTION

Malaria, a disease of antiquity, has proved to be a formidable deterrent to the cultural and socioeconomic progress of man in the tropical, sub-tropical and monsoon prone zones of the world. Although *Plasmodium vivax* type of malaria has an enormous burden of disease, research is grossly inadequate because this malaria supposedly causes only benign tertian fever and has an uncomplicated course of illness. However, with implementation of molecular diagnosis, it has become evident that *P. vivax* monoinfection could also be involved in multiple organ dysfunction and severe life-threatening disease as seen in *P. falciparum* infection.[1,2] Reported severe manifestations with *P. vivax* monoinfection are similar to those of severe *P. falciparum* infection and include cerebral malaria with generalized convulsions and status epilepticus.[3,4] Neurological manifestations of malaria by convention refers to falciparum malaria, but vivax malaria being more common, the percentage of neurological manifestations of vivax malaria cases is on the increasing trend.Cerebral malaria is the most dreaded and a potentially life-threatening complication of malaria. Cerebellar ataxia, extrapyramidal rigidity and various psychiatric symptoms have been described either as the early manifestations of cerebral malaria or as a part of the post malaria neurological syndrome.[5] This study intended to highlight the increasing incidence of neurological manifestations of vivax malaria and hence of the urgency of diagnosing and treating vivax malaria and not treating it as a benign disease.

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## MATERIAL AND METHODS

This prospective observational study was performed among patients admitted with severe malaria at a tertiary care referral hospital. Total number of indoor patients of *P. vivax* malaria in our hospital was 339 out of them 48 patients had neurological manifestations. Demographic profile including the name, age, gender, and residential address were collected. Information was recorded pertaining to clinical symptoms at presentation, examination findings, biochemical and hematological investigation, and treatment outcome. Presence of malarial parasite on thick and thin smears and/or positive parasite lactate dehydrogenase (p-LDH) based rapid malaria antigen test was considered diagnostic of 'malaria'.To exclude confounding factors, we did not recruit any patient with mixed infection (*P. falciparum* plus *P. vivax*). Every patient with peripheral smear positive for *P. vivax* underwent optimal malarial antigen test to exclude co-infection with *P. falciparum*. Neurological manifestations of *P. vivax* malaria by definition refers to involvement of signs such as high grade fever with altered sensorium, generalized tonic-clonic or partial convulsion when other metabolic and structural causes have been ruled out, cranial nerve palsy or demyelination, ataxia, psychosis, hemiplegia and altered consciousness with evidence of disseminated intravascular coagulopathy. Venous blood of patient was collected in an EDTA-containing vacutainer. A thin and a thick peripheral blood smear for malarial parasites were prepared and stained with Geimsa stain. Each slide was examined by light microscopy for a minimum of 100 high power fields or for a duration of at least 15 minutes. Simultaneously, a drop of blood was placed on the rapid malarial antigen detection kit [parasite lactate dehydrogenase (p-LDH) based immune-chromatographic antigen detection assay]. Presence of malarial parasite on thick and thin smear and/or positive p-LDH based rapid malaria antigen test was considered diagnostic of malaria.

## RESULTS

A total of 339 indoor patients had*P. vivax* malaria during the study period. Out of them 48 patients had neurological manifestations. The neurological manifestations were common in 21-30 years (44%) followed by less than 20 years and more than 50 years (17% each). The manifestations were common in male (67%) (Table 1).

**Table 1:** Demographic profile

| Patient characteristics | Frequency | Percentage |
|---|---|---|
| Age (years) | | |
| < 20 | 8 | 16.7% |
| 21-30 | 21 | 43.8% |
| 31-40 | 5 | 10.4% |
| 41-50 | 6 | 12.5% |
| >50 | 8 | 16.7% |
| Sex | | |
| Male | 32 | 66.7% |
| Female | 16 | 33.3% |

Maximum cases of neurological manifestations were found in the month of September (37.5%) followed by October (20.8%). Altered sensorium (77.1%) followed by convulsion (58.3%) was common finding in neurological manifestations of *P. vivax* malaria but focal neurological deficit, Bell's palsy, ataxia, psychosis was also seen.

**Table 2:** Various neurological manifestations in *P. vivax* malaria

| Type of Presentation | Frequency | Percentage |
|---|---|---|
| Altered Sensorium | 37 | 77.1 |
| Convulsion | 28 | 58.3 |
| Focal Neurological Deficit | 7 | 14.6 |
| Bell's palsy | 1 | 2.1 |
| Ataxia | 2 | 4.2 |
| Psychosis | 1 | 2.1 |

Association of isolated neurological manifestations of vivax malaria and that of with other system involvements including hepatic, renal, hepatorenal, pulmonary involvement was statistically significant ($p<0.005$). Mortality was high (87.5%) if neurological manifestations of vivax malaria associated with other system involvement.

**Table 3:** Association among Parasite index and Sensorium

| Parasite Index | | Sensorium | | | | | Total |
|---|---|---|---|---|---|---|---|
| | | Coma | Conscious | Delirium | Drowsy | Stupors | |
| Less than 5% | Count | 0 | 11 | 3 | 1 | 21 | 36 |
| | Percent | 0% | 30.55% | 8.33% | 2.77% | 58.33% | 100% |
| 5 to 10% | Count | 0 | 0 | 0 | 0 | 6 | 6 |
| | Percent | 0% | 0% | 0% | 0% | 100% | 100% |
| More than 10% | Count | 3 | 0 | 0 | 0 | 3 | 6 |
| | Percent | 50% | 0% | 0% | 0% | 50% | 100% |
| **Total** | **Count** | **3** | **11** | **3** | **1** | **30** | **48** |
| | **Percent** | **6.25%** | **22.91%** | **6.25%** | **2.08%** | **62.5%** | **100%** |

Chi-Square test Value df p value, Association, Pearson Chi-Square 27.610 8 0.0005 Significant

Association between parasite index and altered sensorium was statistically significant. Thus, high parasite index associated with higher grade of sensorium.

**Table 4:** Association among Parasite index and convulsion

| Parasite index | | Convulsion | | Total |
|---|---|---|---|---|
| | | Present | Absent | |
| Less than 5% | Count | 22 | 14 | 36 |
| | Percent | 61.11% | 38.88% | 100% |
| 5 to 10% | Count | 2 | 4 | 6 |
| | Percent | 33.3% | 66.7% | 100% |
| More than 10% | Count | 4 | 2 | 6 |
| | Percent | 66.7% | 33.3% | 100% |
| **Total** | **Count** | **28** | **20** | **48** |
| | **Percent** | **58.33%** | **41.66%** | **100%** |

Chi-Square test Value df p value Association, Pearson Chi-Square 1.829 20.2004 Not Significant

There was no association between parasite index and convulsion and focal neurological deficit.

**Table 5:** Association among Parasite index and focal neurological deficit

| Parasite index | | Focal neurological deficit | | | | Total |
|---|---|---|---|---|---|---|
| | | Hemiplegia | Paraplegia | Quadriplegia | Others | |
| Less than 5% | Count | 0 | 1 | 4 | 31 | 36 |
| | Percent | 0.0% | 2.77% | 11.11% | 86.11% | 100% |
| 5 to 10% | Count | 1 | 0 | 0 | 5 | 6 |
| | Percent | 16.7% | 0.0% | 0.0% | 83.3% | 100% |
| More than 10% | Count | 1 | 0 | 0 | 5 | 6 |
| | Percent | 16.7% | 0.0% | 0.0% | 83.3% | 100% |
| **Total** | **Count** | **2** | **1** | **4** | **41** | **48** |
| | **Percent** | **4.16%** | **2.08%** | **8.33%** | **85.41%** | **100%** |

Chi-Square test Value df p value Association, Pearson Chi-Square 7.102 6 0.262 Not Significant

## DISCUSSION

Neurological manifestations of malaria are usually caused by *P. falciparum* but it has been observed that *P. vivax* malaria, which was otherwise considered to be benign malaria, with a low case-fatality ratio, is now increasingly associated with severe disease as with *P. falciparum* malaria. The reported neurological manifestations in vivax malaria include cerebral malaria, hemiplegia, Bell's palsy, psychosis, cerebellar ataxia, status epilepsy, etc. The objective of our study was to note the incidence and demographic, clinical profile with neurological manifestations of *P. vivax* malaria. Till date,a similar study of neurological manifestations of vivax malaria in adult population has not been found but various case reports of same are available. All our recruited patients were admitted as per our hospital policy, hence there were no OPD recruitments. The age profile of patients admitted with neurological manifestations of vivax malaria in our study depicts that most of the admitted patients (43.8%) were in the age group of 21- 30 years. The findings observed in our study match with those observed in a retrospective study done in South Canara aimed at studying the demographic profile of malaria. Many of the patients were between the age group of 15 and 40 years, with high incidence between the age group of 21 and 30 years.[6] The factors responsible for the age pattern include outdoor work for young adult males and outdoor sleeping habits which then are more prone to get mosquito bites. Additionally, city laborers from outstation stay in shanties with high vector population. The pattern observed in vivax malarial deaths was different as compared to those who survived. In areas with moderate transmission, cerebral malaria in young children is the most common presentation. In areas with low transmission, such as South and Southeast Asia, severe malaria occurs in all age groups, but young adults are the most affected.[7] This matches with the age pattern of neurological manifestations of vivax malaria observed in our study with peak in the age group of 21-30 years. Males outnumbered females in number of admissions. The findings in our study are supported by a similar finding highlighting the burden of malaria in India.[8,9] The reason for male dominance is that male subjects have more outdoor work and more prone to vector bite. Alterd sensorium 37 cases (77.1%) followed by convulsion 28 cases (58.3%) were common manifestations and focal neurological deficit 7 cases (14.5%), ataxia 2 cases (4.2%), Bell's palsy 1 case (2.1%), psychosis 1 case (2.1%) was also found.Three cases of *Plasmodium vivax* malaria (all adult male patients) complicated by seizures and symptoms of diffuse meningoencephalitis were reported rather recently by Sarkar *et al.*[10] Two patients had predominantly meningeal signs, while in the third patient the features were purely of encephalitis. All cases were treated with artesunate. Published reports by various authors have found presentations ranging from seizures,

decreased level of consciousness, aphasia, hemiparesis, delirium, coma, stupor, psychosis associated with *Plasmodium vivax*.[3,10-12]Tilluckdharry*etal* reported a 44-year-old Trinidadian male who presented with fever and psychotic episodes in association with vivax malaria.[13]Kochar*et al* reported 11 cases of severe *Plasmodium vivax* malaria in Bikaner (western India). Table 3 depicts association of altered sensorium and parasite index which is statistically significant ($p< 0.005$), that means higher parasite index associated with high grade of altered sensorium, while association between parasite index and convulsion or focal neurological deficit is statistically not significant (Table 4 and 5). Thus, *Plasmodium vivax*, as has been traditionally believed is no longer a benign species and is causing presentations akin to *P. falciparum*. It is imperative that clinicians are aware and are ready to handle the complications caused by *Plasmodium vivax* which have been traditionally associated with *P. falciparum* malaria.

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