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TO STUDY THE CLINICAL PROFILE OF *PLASMODIUM VIVAX* AND *PLASMODIUM FALCIPARUM* MALARIA IN A TERTIARY CARE CENTER.

Medicine

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ABSTRACT

Malaria has been the one of the oldest known infections to the mankind. This study was designed to observe and compare the clinical features and complications among the patients suffering from vivax and falciparum malaria. **Design-** It was a comparative, prospective and observational study done over a period of 18 months. **Results-** The most common haematological complication was thrombocytopenia observed in 72% patients while anaemia was present in 49% patients. Thrombocytopenia was common in patients of both *P.vivax* (72%) and *P.falciparum* group (73%). Renal dysfunction (7% vs 22%), hepatic dysfunction (21% vs 49%), cerebral malaria, dyselectrolemia and pulmonary complications were observed in both the groups with higher number of patients with these complications in falciparum group with statistically significant difference observed in renal and hepatic complications between the two groups.

KEYWORDS

INTRODUCTION

Malaria is a disease of tropical and subtropical areas and in India 95% of population resides in malaria endemic areas. In India 60 - 65% of infections are due to Plasmodium vivax *P.vivax* and 35% due to Plasmodium falciparum (*P.falciparum*).

The perception of malaria as an infection which affects relatively few people, causing a benign course of disease and being treatable with widely available therapies largely explains almost complete neglect of this important infection. The clinical manifestations of severe malaria are several and occur in different anatomical sites. Both parasite and host-related factors contribute to the pathogenicity of the severe forms of the disease. Currently, this infection is endemic in many countries of Asia, South Pacific, North Africa, Middle East and South and Central America. [1,4]

This study was carried out to analyze and compare the trends in clinical features, severity and complications of the disease in both *P.falciparum* and *P. vivax* infections at a tertiary care hospital.

AIMS AND OBJECTIVES

- To study the clinical manifestations of *P. vivax* malaria.
- To study the clinical manifestations of *P. falciparum* malaria.
- To compare the profile of various complications of vivax and falciparum malaria.

MATERIAL AND METHODS

Study design-

It was a Comparative, Prospective, observational study.

Sample size-

A minimum of 121 patients diagnosed with malaria who attended the outpatient or inpatient Department of Medicine were recruited for the study.

Patients suffering from vivax infection were kept under vivax group and patients suffering from falciparum infections were kept under falciparum group.

Establishment of diagnosis of malaria by:

1. Detection of asexual forms of *P.vivax* and *P.falciparum* from peripheral blood smears –

The diagnosis of malaria rests on the demonstration of asexual forms of the parasite in stained peripheral-blood smears. Both thin and thick blood smears were examined. The thin blood smear was prepared using the Leishman's stain.

2. Rapid diagnostic test (antigen detection).

Malaria antigen detection tests were done by rapid immunochromatographic assay utilizing monoclonal antibodies against histidine rich protein II which is a water soluble protein produced by trophozoites and gametocytes of *P.falciparum* and Plasmodium Lactate Dehydrogenase (LDH) specific for *P.vivax.*

OBSERVATION AND RESULTS

A total of 121 patients suffering from malaria were enrolled for the study. 84 patients had vivax malaria and 37 had falciparum malaria. A comparison of the clinical features (signs and symptoms) and complications between the two types of malaria was done.

CLINICAL FEATURES (symptoms and signs)

Most of the patients commonly presented with symptoms like fever, headache, vomiting and pain abdomen. Fever was seen in 96% patients and fever associated with chills and rigors was seen in 86% patients. Headache, vomiting and pain abdomen were the presenting complaints in 39%, 43% and 28% of the patients respectively. Other symptoms noted were decreased appetite, breathlessness, diarrhoea, petechial rashes, epistaxis, altered sensorium, seizures, decreased urine output.

Table1: Comparison of Symptoms among Vivax & Falciparum Groups

SYMPTOMS	TOTAL (%)	P.vivax (%)	P.falciparum (%)
Fever	118 (98%)	81 (97%)	37 (100%)
Fever with chills and rigors	110 (91%)	78 (93%)	32(87%)
Headache	45 (37%)	29 (34%)	16 (43%)
Vomiting/Nausea	68(56%)	52 (61%)	16 (43%)
Pain Abdomen	28 (41%)	13 (22%)	15 (11%)
Diarrhoea	15 (12%)	9 (11%)	6 (16%)
Bodyaches/Myalgia	31 (26%)	22 (26%)	9 (24%)
Decreased appetite	6 (5%)	2 (2%)	4 (11%)
Breathlessness	5 (4%)	2 (2%)	3 (8%)
Petechial Rashes	5 (4%)	2 (2%)	3 (8%)
Epistaxis	3 (2%)	1 (1%)	2 (5%)
Altered sensorium	9 (7%)	3 (4%)	6(16%)
Seizures	3 (2%)	1 (1%)	2 (5%)
Decreased urine output	6 (5%)	2 (2%)	4 (11%)

Table2: Comparison of Clinical Signs among Vivax & Falciparum Groups.

SIGNS	TOTAL	P.vivax	P.falciparum
Pallor	38 (31%)	23 (27%)	15 (40%)
Icterus	31(26%)	17 (20%)	14 (37%)
Pedal edema	5 (4%)	3 (4%)	2 (5%)
Crepts in chest	5 (4%)	2 (3%)	3 (8%)
Tachycardia	18 (15%)	10 (12%)	8 (22%)
Tachypnea	5 (4%)	3 (4%)	2 (6%)
Spleenomegaly	23 (19%)	17 (20%)	6 (16%)
Hepatomegaly	19 (14%)	11(12%)	7 (16%)
Hepatosplenomegaly	7(6%)	4(5%)	3(8%)
Shock	7 (6%)	5 (6%)	2 (5%)

Pallor and icterus were seen more in patients with P.falciparum malaria than in patients suffering from P.vivax malaria. Rest of the clinical signs in patients with vivax and falciparum malaria were comparable.

COMPLICATIONS-

Table3: Comparative Profile of Complications among Vivax & Falciparum Groups.

COMPLICATIONS	TOTAL (n=121)	P.vivax (n=84)	P.falciparum (n=37)
Anaemia	59(49%)	36(43%)	23(62%)
Thrombocytopenia	87(72%)	60(72%)	27(73%)
Leukopenia	25(21%)	18(21%)	7(19%)
Leukocytosis	6(5%)	3(4%)	3(8%)
Deranged coagulation	5(4%)	2(2%)	3(8%)
Liver dysfunction	36(30%)	18(21%)	18(49%)
Renal failure	14(12%)	6(7%)	8(22%)
Hyponatremia	24(20%)	14(17%)	10(27%)
Hypokalemia	16(13%)	8(10%)	8(22%)
Hypoglycemia	9(7%)	6(7%)	3(8%)
Cerebral malaria	3(2%)	1(1%)	2(5%)

DISCUSSION

Clinical profile of patients suffering from *P.vivax* malaria

In this study, fever was the most common presenting complaint seen in 81(97%) patients of vivax infection. Fever was not observed in 3 patients as they had taken anti malarial treatment before admission. This was followed by vomiting which was present in 52(61%) patients and headache in 29(34%) patients. Various clinical signs commonly observed were; pallor in 23(27%), icterus in 17(20%), spleenomegaly in 17(20%), hepatomegaly in 11(13%) and shock in 5 (6%) patients.

Singh et al, in a study conducted in 2013on 90 patients of P.vivax, observed that fever was seen in 100% patients followed by vomiting in 17.8% and headache in 15.6% patients. They also observed pallor in 73.3%, icterus in 23.3%, spleenomegaly in 31.1%, hepatomegaly in 32.2% and shock in 7.8% patients. [2]

Clinical profile of patients suffering from *P. falciparum* malaria

Fever was again the most common presenting complaint in the falciparum group of this study. It was present in 37(100%) of patients followed by headache in 16(43%), vomiting in 16(43%), pain abdomen in 15(40%) and myalgia in 9(24%) patients.

Clinical signs observed were pallor in 15(40%), icterus in 14(37%), spleenomegaly in 6(16%), hepatomegaly in 7 (18%), altered sensorium in 6(16%) and shock in 2(5%) patients.

In a study by Wasnik et al in 2012 clinical manifestations observed in 80 patients of P. falciparum were fever in 100%, pallor in 65%, icterus in 35%, spleenomegaly in 30%, hepatomegaly in 28.7%, hepatosplenomegaly in 28.7%, impaired consciousness in 17.5% and shock in 1.25% of patients. Comparable results were obtained in another study by Singh et al where all 49 patients of P.falciparum malaria had fever while 77.6% patients had pallor. [2, 3]

Complications of P. vivax and P. falciparum

In this study hepatic dysfunction was present in 18(21%) cases of *P.vivax* and 18(49%) cases of *P.falciparum*. Difference was statistically significant with $p<0.05$.The maximum level of S. bilirubin observed in *P.vivax* group was 12.3 mg/dl and in *P.falciparum* group was 11.2mg/dl. Hyperbilirubinemia was observed in 21(25%) patients of vivax and 20(54%) patients of falciparum group. The maximum level of SGPT observed in P.vivax group was 266 IU/L while in P. falciparum group it was 210 IU/L. SGPT levels of more than 3 times the upper normal limit were observed in 2 patients among vivax group and 4 patients among falciparum group. Of 11 patients with *P.vivax* infection in which PT/INR was done, 2 patients had an INR of > 1.5 and of 10 patients with *P.falciparum* infection, 3 patients had INR of > 1.5. None of the patients in the study had hepatic encephalopathy.

In a study by Nadkar et al in 2012; the observed incidence of hepatic involvement was 19.46% in vivax malaria and 36.32% in falciparum malaria. Wasnik et al observed hyperbilirubenemia in 28(35%) patients. [4, 3]

Hyperbilirubinemia in malaria results from intravascular haemolysis of parasitized RBCs, hepatic dysfunction and an element of microangiopathic haemolysis due to DIC. [3]

Limaye et al observed that the incidence of high bilirubin was significantly higher ($p<0.01$) in falciparum malaria 46 (22.33%) than vivax malaria 18 (5.32%). [5]

A serum bilirubin level of 4.31 ± 3.52 mg/dl predominantly conjugated (maximum = 16.2 mg /dl) was seen in 57.5% of patients in P.vivax malaria in a study by Kochar et al. The AST, ALT and Alkaline Phosphatase levels were111.25 ± 97.47 IU/L (maximum = 426 IU/L), 151.78 ± 123.76 IU/L (maximum = 529 IU/L) and 290.83 ± 218.41 IU/L (maximum = 866 IU/L) respectively. [6]

Renal dysfunction was present in 6 (7%) patients in *P.vivax* group and 8(22%) in *P.falciparum* group in this study. Difference was statistically significant with $p<0.05$. The mean serum creatinine level in vivax group was 1.54±1.37 mg/dl and 2.24 ± 2.12 mg/dl in falciparum group. Hemodialysis was required in 2(3%) patients of vivax and 6(16%) patients of falciparum infection. Limaye et al in 2012 reported that Acute renal failure (creatinine>3mg/dL) was significantly ($p=0.001$) more common in falciparum 40 (19.42%) and mixed infection 18 (13.23%) than vivax infection 12 (3.55%). Four patients of vivax malaria required Hemodialysis whereas 26 patients of falciparum (12.62%) and 14 patients of mixed malaria (10.29%) were dialysed. [5]

Kochar et al reported renal dysfunction in 45% patients in their study. The levels of Blood urea and serum creatinine were 116.26 ± 103.23 mg/dl (maximum = 252 mg/dl) and 3.85 ± 3.24 mg/dl (maximum = 12.6 mg/dl) respectively. Hemodialysis (2–8 dialysis in a patient) was required in six patients. [6]

Nadkar et al reported the frequency of renal failure as 32% in severe vivax malaria and 55% in severe falciparum malaria. In a case series of 8 patients of P. vivax with ARF by Amitabh et al, HD requirement was reported in two patients. Kute et al in 2012 reported Acute kidney Injury in 25 patients suffering from *P.vivax* malaria who subsequently required Hemodialysis. Shiddhapur et al also reported a case of *P.vivax* associated Acute Renal Failure. [4, 7, 8, 9]

Andrade et al found a strong linear trend between increased levels of C-reactive protein, Tumor necrosis factor alpha (TNF-α), Interferon gamma (IFN-γ), IFN gamma/ Interleukin (IL)-10 ratio and the disease severity of vivax malaria. [10]

Studies have shown that *P. vivax* can cause both sequestration-related complications such as cerebral malaria, renal dysfunction, hepatic dysfunction, and ARDS and non-sequestration-related complications such as anaemia and thrombocytopenia. [6]

Pulmonary complications like ARDS were seen in 2 patients from each group in this study. One patient from vivax group had pleural effusion. 5 patients had Tachypnea on presentation. Development of ARDS in malaria infection has been reported in many other studies also. There was one death in the *P. vivax* group in this study in a patient who developed ARDS. Pulmonary syndromes associated with P.vivax malaria include acute non-cardiogenic pulmonary edema, ARDS, acute pulmonary injury and interstitial pneumonia.

Limaye et al in their study reported ARDS in 10 (3%) of vivax, 16

(7.7%) of falciparum and 12 (8.8%) cases of mixed malaria. Nadkar et al reported 8 patients with vivax malaria with ALI/ARDS, out of which 5 succumbed. [5, 4]

Kochar et al reported 4 patients with ARDS of which two died of this complication. Singh et al in their study reported ARDS in both the falciparum and vivax groups and it was the cause of death in 2 patients. [6, 2]

In this study altered sensorium was seen in 3 patients of vivax group and 6 patients of falciparum group. Cerebral malaria with GCS ≤ 9 was seen in 2 patients of falciparum and 1 patient of vivax group. Seizure was reported in 1 patient of falciparum group. Kochar et al reported Cerebral malaria in 5 patients, of which 2 had associated seizures. A study in Mumbai in 2011 by Nadkar et al reported cerebral involvement in 8.19% of patients with severe vivax malaria. Out of 40 patients with cerebral vivax malaria, 2 died. Cerebral malaria was seen in all age groups but maximum patients were in the 2nd and 7th decade of their lives. They reported status epilepticus in two patients. Limaye et al from Mumbai in 2012 reported 14 patients with impaired consciousness, of which 3 patients had unarousable coma (cerebral malaria). Lampah et al from Papua Indonesia reported 6 (25%) patients with cerebral malaria who had vivax mono infection and no apparent alternative cause, with a median GCS of 9. [6, 4, 5, 11]

Anaemia was seen in 36(43%) patients of vivax group and 23(62%) patients in falciparum group. The mean Hb. level in vivax group was 10.73±2.8 g/dl and in falciparum group was 9.73±2.5g/dl with a statistically significant difference, $p<0.05$.

A study by Singh et al in 2014 reported anaemia in 73.3% in vivax group and 77.6% in falciparum group. Wasnik et al form Mumbai reported severe anaemia of Hb. < 5g/dl in 7.5% of patients and pallor in 65% patients. [2, 3]

Thrombocytopenia was seen in 60(72%) patients in vivax group and 27 (73%) patients in falciparum group in this study with no statistically significant difference between the two groups, $p>0.05$.

Nadkar et al reported Thrombocytopenia in 435 (89.13%) of vivax patients and in 178 (79.82%) of falciparum patients. A study from Bikaner Rajasthan by Kochar et al in 2010 reported that incidence of thrombocytopenia in P.vivax mono infection (31.09% [143/460]) was greater as compared to *P.falciparum* mono infection (16.19% [85/525]). The occurrence of severe thrombocytopenia was also higher in P.vivax mono infection (18.18% [26/143]) in comparison to P.falciparum mono infection (10.59% [9/85]). [4,12]

CONCLUSION

The most common haematological complication was thrombocytopenia that was observed in 72% patients of this study while anaemia was present in 49% patients. Thrombocytopenia was common in patients of both *P.vivax* (72%) and *P. falciparum* group (73%). Renal dysfunction, hepatic dysfunction, cerebral malaria, dyselectrolemia, and pulmonary complications were observed in both the groups with higher number of patients with these complications in falciparum group with statistically significant difference observed in renal and hepatic complications between the two groups.

Malaria is an important public health problem in India causing significant morbidity and mortality. Falciparum malaria has always been a cause of more severe form of infection but vivax malaria also presents with increased severity and complications. So the patients of vivax malaria should be adequately monitored for occurrence of different complications as their early detection and treatment or referral to a higher centre can be life saving.

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