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# To study clinical, biochemical and hematological profile in severe Plasmodium vivax malaria at tertiary care center of Agra

**Sanjay Singh[1], Rameshwar Dayal[2], Nisha Chaudhary[3], Mohd Javed[4]**

**1-Assistant Professor department of medicine F.H. Medical college Agra**

**2-Associate Professor department of medicine F.H. Medical college Agra/corresponding**

**3-Assistant professor department of Microbiology Autonomous Medical college Firozabad**

**4-Assistant professor department of medicine F.H. Medical College Agra**

## Abstract

**Objectives:** The objectives were to study the clinical, biochemical and hematological profile in Plasmodium vivax malaria in F.H. Medical college Ethmadpur Agra.

## Results

From the total patients of 240 severe disease present in 106 cases 78% of cases were having malaria for the first time. Fever present in 100% of patients, headache in 46%, jaundice present in 39%, nausea/vomiting in37.5%, pain in abdomen in 14.5%, oliguria present in 18.5% patients,4.5% patients were had petechiae/bleeding. 19.5 % patients were had parasitaemia between 25000-150000. Thrombocytopenia was most common haematological complication present almost in 75% patients which were normalised after treatment. TLC was low (<4000/cm$^2$) in 45 cases which was increased to normal after treatment. Severe anaemia (Hb<7%) present in 38 patients out of which 24 patients was female. 63 patients were had serum creatinine ≥3mg/dl (30 male and 33 females), High bilirubin (>3mg/dl) was present in 74 patients out of which 24 were females and 50 males. The bilirubin level >10mg/dl was present in 8 patient out which 3 were male and 5 female.

## Conclusion

Malaria due to Plasmodium vivax can cause severe disease with renal, cerebral, hepatic, involvement occurs with increasing frequency anaemia and thrombocytopenia is very common in vivax malaria so vivax malaria no longer is benign condition.

**Key words** P. vivax malaria; thrombocytopenia; severe anemia.

## Introduction

Malaria is the most prevalent parasitosis in the world. The most recent WHO report estimates that in 2019, there were 228 million cases and approximately 405,000 deaths worldwide (WHO, 2019)[1]. The maximum cases were reported in the WHO from African region at 93%

(213 million), followed by the South-East Asian region (in which India falls) at 3.4%. India is responsible for the large majority of cases in South East Asia with 6.7 million cases.

Thrombocytopenia is the most frequent reported complication in India followed by anaemia[2]. Respiratory distress or pulmonary compromise has been reported in P. vivax mono-infections in different post mortem studies in India[3]. Cerebral malaria reported infrequently by P. vivax malaria with manifestations of coma, seizures, altered consciousness caused by this species confirmed by microscopy[4].

The pathophysiological mechanism of clinical manifestations by P. vivax malaria is poorly understood. There is some different mechanism than those described for P. falciparum as P. vivax parasite load is low during infection and restricted invasion in young red blood cells. The exacerbated production of pro inflammatory cytokines, the activation and expression of endothelial adhesion molecule and autoimmune mechanism are some of the mechanisms that can cause clinical complications by the P. vivax[5].

As there are no separate complication criteria for P. vivax malaria so we use the same criteria as for falciparum.

## Material and methods

### Study area and period

The study was conducted at F.H. Medical College Ethmadpur Agra. The study was conducted from January 2020 to December 2020.

### Study design

An institutional based cross-sectional study was employed

### Source population

All acute febrile with suspicion of malaria attending F.H. hospital during the study period.

### Study population

Patients with positive on blood smear and satisfy inclusion criteria was studied.

**Inclusion criteria:** Patients older than 14 years of age either sex and p. vivax positive by thick and thin smear.

**Exclusion criteria:** Patients who already took antimalarial treatment within 14 days and having mixed malarial infection.

### Sample collection and processing

As the diagnosis is based on peripheral blood smear, both thin and thick blood smear was prepared and examined by microbiologist and the blood film smear was taken as gold standard for diagnosis of infection and to identify the species.

To determine the density of malaria parasite experienced microbiologist counted asexual stage P vivax parasites on a slide against 200 WBCs in thick blood film Parasites per microlitre blood were calculated by formula

$$\text{Parasite/}\mu\text{L} = \frac{\text{Parasite counted}}{200} \times \text{Total WBC count}$$

Blood samples were taken from each patient by EDTA and dry tube venipuncture, samples were taken before the start of antimalarial treatment. The following analysis were carried out: automated hemogram, thick drop, peripheral blood smear, serum glucose quantification, creatinine, total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase and species confirmation by thin smear.

## Results

### Sociodemographic characteristics of study

Total 240 patients were studied out of which 112 male 128 females, 196 from rural area and 46 lives in urban area. The rural population neither use any mosquito repellent nor use wire mosquito nets wired window in the house, surprisingly only 18 % urban population use mosquito repellent products.

### Clinical profile

From the total patients of 240 severe disease present in 106 cases 78% of cases were having malaria for the first time. Fever present in 100% of patients, headache in 46%, jaundice present in 39%, nausea/vomiting in37.5%, pain in abdomen in 14.5%, oliguria present in 18.5% patients,4.5% patients were had petechiae/bleeding. 19.5 % patients were had parasitaemia between 25000-150000.

**Haematological characteristics** Thrombocytopenia was most common haematological complication present almost in 75% patients which were normalised after treatment. TLC was low (<4000/cm$^2$) in 45 cases which was increased to normal after treatment. Severe anaemia (Hb<7%) present in 38 patients out of which 24 patients was female.

### Biochemical characteristics

63 patients were had serum creatinine ≥3mg/dl (30 male and 33 females), High bilirubin (>3mg/dl) was present in 74 patients out of which 24 were females and 50 males. The bilirubin level >10mg/dl was present in 8 patient out which 3 were male and 5 female.

**Table 1**

**Classification criteria for severe P. vivax malaria patients**.

Classification criteria

| | |
|---|---|
| Platelet count | ≤50,000/uL |
| Hypoglycaemia | ≤60 mg/dL |
| Metabolic acidosis | plasma bicarbonate <15 mmol/l |
| Serum creatinine | ≥1.5 mg/dL |
| Hyperlactatemia | lactate >5 mmol/l |
| Indirect Bilirubin | ≥1.5 mg/dL |
| Total Bilirubin | ≥1.5 mg/dL |
| Transaminases | ≥40 U.I. |
| Haemoglobin | ≤7 g/dL |
| Parasite count | ≥50.000 parasites/μL |
| Coma status | |
| Seizures | |
| Altered state of consciousness | |
| Breathing difficulty | |
| Pulmonary oedema | |
| Haemoglobinuria | |

Table 2

Demographic characteristics

| Descriptions | rural | urban |
|---|---|---|
| Gender | | |
| Female | 74 | 18 |
| Male | 62 | 26 |
| Use of wire net for window | 0 | 5 |
| Insecticide use | 0 | 8 |
| Use of repellents | 0 | 10 |
| Use of mosquito bed nets | 0 | 5 |

Table 3

Patient distribution according to age and sex

| Age | Male | Female | Total |
|---|---|---|---|
| 15-30 | 50 | 66 | 114(63.3%) |
| 31-45 | 21 | 15 | 36(20%) |

| | | | |
|---|---|---|---|
| 46-60 | 10 | 11 | 21(11.5%) |
| >60 | 5 | 4 | 9(5%) |
| Total | 86 | 94 | 180 |

Table 4

Hematological and biochemical profile

| | Male | female |
|---|---|---|
| **Parasite counts** | | |
| <100 | 3 | 3 |
| >100-1000 | 24 | 27 |
| >1000-10000 | 58 | 64 |
| >10000-100000 | 26 | 32 |
| >100000 | 1 | 2 |
| **TLC** | | |
| <4000 | 20 | 25 |
| 4000-11000 | 88 | 92 |
| >11000 | 4 | 11 |
| **Platelets counts/µl** | | |
| | Male | Female |
| ≤10000 | 11 | 0 |
| 10000-50000 | 53 | 68 |
| 50000-150000 | 23 | 26 |
| >150000 | 25 | 34 |
| Hemoglobin | | |
| | Male | Female |
| ≤7 | 14 | 24 |
| 7.1-12 | 79 | 84 |
| >12 | 19 | 10 |
| **Creatinine mg/dl** | | |
| | Male | Female |
| >3 | 30 | 33 |
| **Total bilirubin mg/dl** | | |
| | Male | Female |
| >3-10 | 50 | 24 |
| >10 | 3 | 5 |

Table 4

Clinical features in severe P. vivax malaria

| Clinical features | Present Study | Song et al33 | Echeverri et al32 | Sarkar et al21 |
|---|---|---|---|---|
| Fever | 100 % | 100% | 99% | |
| Headache | 38.5% | 29.5% | 99% | |
| Jaundice | 36% | | 15% | 66% |
| Nausea/ Vomiting | 37.5% | 34% | 39% | |
| Pain in abdomen | 14.5% | 34% | 34% | |
| Convulsions | | | | 14% |
| Altered sensorium | | | | 56% |
| Oliguria (<400ml) | 18.5% | | | 30% |
| Petechial/ bleeding | 4.5% | | | 2% |
| Splenomegaly | 37% | | | |
| Hepatomegaly | 28% | | | |

**Discussion**

Previously P. vivax malaria was known as benign disease but now several studies shows that P. vivax can cause severe malaria[6] at present there is no separate criteria for severe malaria caused by P. vivax WHO indicates to use same criteria as P. falciparum despite different biological and epidemiological behavior. Our study shows that rural population not used any measure to avoid mosquito bites as bed net, repellent, spray. There is only 18% population in urban area use any measure to avoid mosquito bite.

Thrombocytopenia was most common complication present in 75% patients The inconsistent degree of reduction in circulating platelet count are consistently reported in the different types of malaria. Severe thrombocytopenia is quite rare in P. vivax malaria. 11 patients from our suffer from severe thrombocytopenia. Thrombocytopenia is consistent with

finding of Robinsons et al[7] (71%) and is slightly higher than that reported by other investigators Rodriguez et al[8] (58.97%) and Bashwari et al[9] (53%).

The mechanism of thrombocytopenia is poorly understood the hypothesis of thrombocytopenia include that the platelets sequestrated by spleen during the removal of parasite cells, another hypothesis states that acute malaria infection platelets are found to be hypersensitive and there is increased concentrations of platelet-specific proteins such as beta thromboglobulin (BTG), platelet factor 4 (PF4). Production of thromboxane A2 and prostacyclin also increased. It has also been postulated that these hypersensitive (hyperactive) platelets will enhance haemostatic responses, and may be this is why bleeding episodes are rare in acute malarial infections, despite the significant thrombocytopenia.

Anaemia was the second most haematological complication present in our study severe malaria was present in 38 of patients out of which 24 were females. Pathogenesis of anaemia in malaria is particularly complex multifactorial and incompletely understood it is thought to result from a combination of haemolysis of parasitized RBCs accelerated removal of both parasitized and innocently un parasitized RBCs depressed as well as ineffective erythropoiesis with dyserythropoitic changes and anaemia of chronic disease or other factors causative to anaemia in malaria include decreased RBC deformability, splenic phagocytosis and/or pooling so they have an increase rate of clearance from circulation. 9 TNF alpha has also been implicated and may cause ineffective erythropoiesis. 8 Anaemia develop because of direct parasitization of RBC by plasmodium resulting in lysis of infected cells certain immunological factors also play a major role in development of anemia[10]. Normocytic normochromic pattern was observed as pre-dominant type of anaemia and it correlate with the degree of parasitemia. Reticulocytes reflects the increase activity in marrow which is due to compensatory erythroid hyperplasia.

Hypoglycemia was also commonly present in severe P. vivax malaria[11] in our study 16% of patients was having sugar level less than 70 the use of quinine effects glucose metabolism by stimulating insulin production.

A total of 240 plasmodium vivax malaria cases were studied of which 79 (33%) patients developed AKI which is about to similar to the study of Kuashik R et al[12] . Several hypothesis including mechanical obstruction caused by cytoadherence and sequestration of infected erythrocytes, immune mediated glomerular pathology, release of cytokines, reactive oxygen intermediates and nitric oxide by activated mononuclear cells, and alterations in the renal and systemic hemodynamics have been proposed as the mechanisms for renal failure in falciparum malaria.

Jaundice was seen in 34%. Jaundice in malaria is multifactorial hepatic dysfunction due to microvascular sequestration of parasitized red cells causes significant rise in serum bilirubin. The finding was reported among 15% of the patients by Echeverri et al[13] at Columbia but Sarkaret al[14] reported jaundice in 66% of cases.

Hepatomegaly present in 20% of cases and splenomegaly were noted in 34.5% of cases. It was seen in 17% and 10% of the cases respectively in the study done by Echeverri et al[13] at Columbia.

Neurological involvement in the form of seizures and altered sensorium were observed among 9.5% of the patients which is in contrast to the results of Kocher et al and Sarkar et al with a finding of 12.5% and 70% respectively.

## Conclusion

Malaria due to Plasmodium vivax can cause severe disease with renal, cerebral, hepatic, involvement occurs with increasing frequency anaemia and thrombocytopenia is very common in vivax malaria so vivax malaria no longer is benign condition.

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