

# Multiorgan Dysfunction in *Plasmodium vivax* Malaria: A Prospective Study

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## Abstract

**Background:** *Plasmodium vivax* is the most widely distributed human malarial parasite with an at risk population of 2.5 billion persons. With an implementation of molecular diagnosis, it has become evident that *P. vivax* mono infection could also result in multiorgan dysfunction and severe life threatening disease as seen in *Plasmodium falciparum* infection.

**Aims and Objectives:** (1) To study, the clinical profile of *P. vivax* malaria, (2) to study, multiorgan dysfunction in *P. vivax* malaria.

**Materials and Methods:** A total of 102 patients of documentary *P. vivax* infected patients and fulfilling the criteria for severe malaria according to WHO during study period from September 2012 to September 2014 were taken for this study. Detailed history and examination along with investigations were noted in all patients.

**Results:** In the present study, maximum patients with severe vivax malaria belonged to 21-30 years followed by 41-50 years. About 62.7% patients are males and 37.3% patients are females with severe *P. vivax* malaria with organ dysfunction. In our study, out of 102 patients of severe *P. vivax* malaria, 44 patients (43.1%) are having multiorgan dysfunction, while 58 patients (56.9%) are having single organ dysfunction. Hematological dysfunction was the most common dysfunction either alone or in combination, presents in 89.2%. Followed renal dysfunction was present in 34.3% and jaundice in 21.6%. 7.8% patients had central nervous system manifestation while respiratory dysfunction (acute respiratory distress syndrome [ARDS]) was seen in only 2%. Most of the patients (56.9%) had presented with single organ dysfunction. 33.3% had two organ dysfunction, whereas 7.8% had three organ dysfunction. Four organ dysfunction were observed in only 2% patients. In our study, 93.1% patients survived and 6.9% patients expired due to severe *P. vivax* malaria with multiorgan dysfunction.

**Conclusion:** In the present study, similar to severe falciparum malaria as mentioned in past studies multiorgan dysfunction and associated mortality though less common and less severe is seen in severe vivax malaria.

**Key words:** Falciparum, Malaria, Severe, Thrombocytopenia, Vivax

## INTRODUCTION

*Plasmodium vivax* is the most widely distributed human malarial parasite with an at risk population of 2.5 billion persons. With an implementation of molecular diagnosis, it has become evident that *P. vivax* mono infection could also result in multiorgan dysfunction and severe life threatening disease as seen in *Plasmodium falciparum* infection.<sup>1</sup>

*P. vivax* can cause both sequestration related and non-sequestration related complications of severe malaria as defined by WHO, including cerebral malaria (coma persisting for more than 30 min after generalized convulsions), renal failure (24 h urine output <400 ml in adults and serum creatinine level >3 mg/dl), circulatory collapse (systolic blood pressure <80 mm of hg in adults), severe anemia (hemoglobin [Hb] level <5 g/dl), haemoglobinuria (not associated with effects of G6PD deficiency), abnormal bleeding (significant and/or evidence of disseminated intravascular coagulation), acute respiratory distress syndrome (ARDS) (non-cardiogenic pulmonary edema), jaundice (serum bilirubin level >3 mg/dl), and acidosis (arterial pH <7.25 or plasma bicarbonate level <15 mmol/l).<sup>2</sup>

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In such situation assessment of multiorgan dysfunction is required for risk of stratification, prognostication and planning of treatment to prevent the progress of disease and hence morbidity and mortality.

## MATERIALS AND METHODS

This prospective study was conducted on patients, who were admitted at our Medical College Hospital to the medicine ward and intensive care unit under medicine department. Clearance was obtained from the Ethical Committee for the study. Patients of age 18 or above with documentation of *P. vivax* infection were included in study. All patients with age <18 years, HIV positive individuals, patients with diseases, such as chronic renal failure, diabetes mellitus with micro vascular and macro vascular complications, rheumatic heart disease, coronary artery disease, and sickle cell anemia, and all patients other than *P. vivax* malaria were excluded from study. The study was carried out on 102 severe vivax malaria patients out of 460 vivax positive patients, admitted during the period of 24 months from September 2012 to September 2014. Peripheral blood smear for malarial parasite (MPQBC) and/or rapid malarial antigen test was done by chromatographic immunoassay for quantitative determination of malaria parasite infection in human blood and to confirm mono infection. Patients were further investigated if they fit the category of severe and complicated malaria as per WHO criteria.

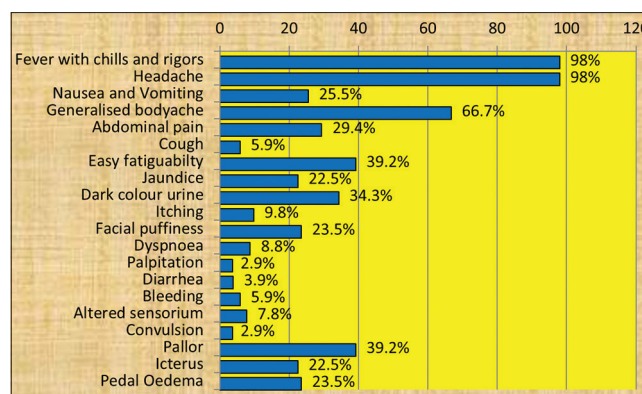
### Statistical Analysis

Data were analyzed by statistical product and service solution V-16 (SPSS 16) statistical software. Data were presented in frequency and percent distribution form. Association in between the parameters was tested using Pearson's Chi-square test or Fishers exact test. The significance level was set at  $P < 0.05$ .  $P < 0.05$  was considered as significant.

## RESULTS

Out of 460 vivax positive patients 102 (22.1%) were having severe malaria as per WHO criteria. In the 102 cases of severe, *P. vivax* cases 62.75% were male and 37.25% were female. In the 102 cases of severe, *P. vivax* malaria, 11.76% were up to 20 years of age, 23.53% were 21-30 years, and 17.65% were 31-40 years of age group. 20.59% cases were 41-50 years of age and 10.78% were 51-60 years old. Furthermore, 15.69% cases were found above 60 years. Maximum number of patients was in the age group of 21-30 years. Mean age was  $39.75 \pm 15.66$ .

Graph 1 shows commonest presenting symptom in severe *P. vivax* malaria was fever with chills and rigors along with headache present in 98% of cases.



**Graph 1: The most common presenting symptom in severe *Plasmodium vivax* malaria was fever with chills and rigors along with headache present in 98% of cases**

The most common presenting symptom in severe *P. vivax* malaria was fever with chills and rigors along with headache present in 98% of cases. Generalized body ache was the following most frequent symptom. Dry cough was present only in 5.9%, while vomiting was present in 25.5% and abdominal pain was in 29.4%. 22.5% patients had history of jaundice. Dark color urine was present in 34.3% and facial puffiness and pedal edema were present in 23.5%. Patients presented with altered sensorium were only 4.9% and those who were having convulsions were 2.9%. Most of the patients (66.7%) had presented with acute illness of 2-7 days duration of fever, 25.5% the fever was of 8-14 days duration and 5.9% it was >14 days.

Severe anemia with Hb <5 g% was present in 2.8% patients and lowest Hb observed was 3.5 g%. 67.6% patients had normal complete blood count (CBC) value. Majority (83.3%) patients had platelet count in range of 40000-1.5 lacks. 5.9% had platelet count below 40000. Serum bilirubin was raised above 3 in 22.5% patients and highest bilirubin value noted was 7.6. Prothrombin time deranged above 16 was observed in 6.9% patients while acidosis was present in only 6.9%. Serum creatinine raised above 1.5 was seen in 34.8%. Majority (41.2%) of severe vivax malaria patients had Grade 1 (low) parasitemia, while heavy, Grade 4 parasitemia was observed in 10.8%. Splenomegaly was most common finding present, either alone or in combination in 84.3% patients, while hepatomegaly either alone or in combination was present in 62.7%. Isolated splenomegaly was present in 29.4% and isolated hepatomegaly was seen in 7.8%. 54.9% patients had both hepatosplenomegaly.

In the present study out of 102 severe *P. vivax* malaria cases 43.14% had multiorgan dysfunction and 56.86% had single organ dysfunction.

Graph 2 shows, in present study, most of the patients (56.9%) had presented with single organ dysfunction.



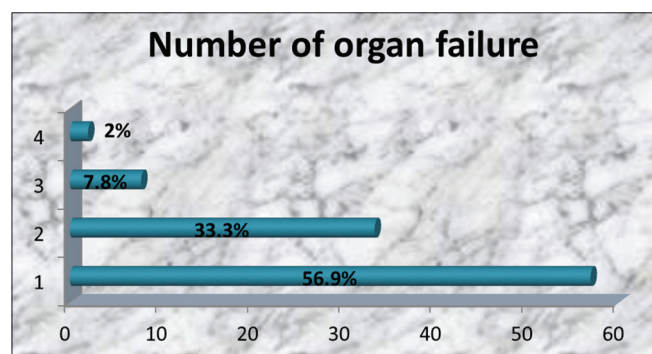
33.3% had two organ dysfunction while 7.8% had three organ dysfunction. Four organ dysfunction were observed in only 2% patients.

Graph 3 shows incidence of organ dysfunction present in vivax malaria.

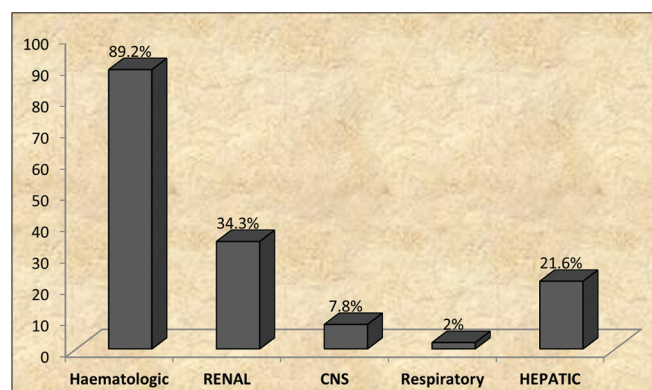
Hematological dysfunction was the most common dysfunction either alone or in combination, presents in 89.2%. Followed renal dysfunction was present in 34.3% and jaundice in 21.6%. 7.8% patients had CNS manifestation while respiratory dysfunction (ARDS) was seen in only 2%.

Hematological dysfunction was the most common dysfunction either alone or in combination, presents in 89.2%. Followed renal dysfunction was present in 34.3% and jaundice in 21.6%. 7.8% patients had central nervous system (CNS) manifestation while respiratory dysfunction (ARDS) was seen in only 2%.

In 2 organ dysfunction hematological along with renal was commonest presentation, seen in 18.6% followed by hematological with hepatic dysfunction present in 10.8%.



**Graph 2:** In present study, most of the patients (56.9%) had presented with single organ dysfunction. 33.3% had two organ dysfunction while 7.8% had three organ dysfunction. Four organ dysfunction was observed in only 2% patients



**Graph 3:** Incidence of organ dysfunction present in vivax malaria

Hematologic dysfunction and cerebral vivax malaria in combination was seen in 3.9%.

Hematological dysfunction along with hepatic and renal dysfunction was commonest three organ dysfunction seen in 3.9%.

Four organ dysfunction were observed in only two patients, one had hematological, renal, CNS and hepatic dysfunction and other had hematologic, renal, respiratory and hepatic dysfunction.

In single organ dysfunction, *P. vivax* malaria maximum patients were having lower age groups (below 50 years) while in multiple organ dysfunction patients having *P. vivax* malaria maximum patients were having higher age groups (above 40 years). There was statistically significant ( $P < 0.001$ ) difference with higher percentage patients having multiple organ dysfunction in higher age groups with *P. vivax* malaria.

In multiple organ dysfunction patients 27.3% had 2 plus parasitemia grade, 47.7% had 3 plus grade and 25% had 4 plus parasitemia grade. In single organ dysfunction *P. vivax* malaria patients 72.4% had 1 plus parasitemia and 27.6% had 2 plus. There was statistically significant ( $P < 0.001$ ) that higher parasitemia grade is seen in multiple organ dysfunction patients than in single organ dysfunction patients.

It was found that 6.9% had expired of *P. vivax* malaria patients. Of those *P. vivax* malaria patients up to 60 years ago 95.3% survived and 4.7% expired while those more than 60 years old 18.8% had expired. There was statistically significant ( $P < 0.05$ ) difference of the outcome of *P. vivax* malaria patients at 60 years age difference.

All 7 patients expired had 4 plus parasitemia grade and in 4 plus parasitemia grade 63.6% *P. vivax* malaria patients expired, while all in Grade 3 and lower had survived.

In single organ dysfunction, all patients survived while in multiple organ dysfunction 15.9% expired and 84.1% survived. There was statistical significant ( $P < 0.01$ ) difference of outcome of patients according to organ dysfunction in *P. vivax* patients.

In hematological organ dysfunction 7.7% expired, in CNS dysfunction 25% expired, 20% with renal dysfunction and 100% with respiratory dysfunction expired. All 2 patients with 4 organ dysfunction expired, 50% with 3 and 2.9% with 2 organ dysfunction had expired. No mortality is seen in single organ dysfunction.



15.9% of multi organ dysfunction plasmodium malaria needed Quinine, while it was none in single organ dysfunction patients. While, artesunate was needed in 74.1% and chloroquine in 25.9% of single and 84.1% and none of multiple organ dysfunction patients, respectively.

In *P. vivax* malaria patients with multiple organ dysfunction 22.7% needed hemodialysis and it was needed only in 1.7% with single organ dysfunction patients. In multiple organ failure patients 15.9% needed ventilator support. Of 11 patients needing hemodialysis, 18.2% expired and 81.8% survived. Of *P. vivax* malaria patients all 7 patients needing ventilator support had expired.

## DISCUSSION

Out of 460 vivax mono infection, 102 admissions of severe vivax malaria fulfilling WHO criteria of severe malaria were included in our study. Incidence of severe vivax malaria found to be lower (22.2%) as compared to falciparum (30.9%) and mixed infection (35.3%). Limaye *et al.*<sup>3</sup> in their study noticed similar that incidence of severe malaria in vivax, falciparum and mixed infection were 14.8%, 31.1%, and 35.3% respectively.

In our study, the incidence of *P. vivax* malaria is more in younger age group and maximum, i.e., 23.5% in age group of 21-30 years which is comparable to 23.15%, 37.5%, and 25.9% of studies conducted by Nadkar *et al.*,<sup>1</sup> O'Brien *et al.*,<sup>4</sup> and Bansal *et al.*,<sup>5</sup> respectively. The factors responsible for age pattern include outdoor work for young adult males and outdoor sleeping habits which are more prone to get mosquito bites.

In our study, the percentage of males is 62.37% and females is 37.3% which is comparable to males - 71.9% and females - 28.1% in a study conducted by Nadkar *et al.*<sup>1</sup> and males - 57% and females - 43% in a study conducted by Apte *et al.*<sup>6</sup> and males 52.5% and females - 47.5% in a study conducted by Bansal *et al.*<sup>5</sup>

In our study incidence of fever with chills and rigors is 98% which is comparable to 99% in a study done by Apte *et al.*<sup>6</sup> and Echeverri *et al.*<sup>7</sup> and to 100% in a study done by O'Brien *et al.*<sup>4</sup> In our study 66.7% patients have acute illness of fever up to 7 days, 25.5% have fever of 8-14 days duration and 5.9% more than 14 days which is comparable to 78 up to 7-8 days, 18% between 8 and 14 days and 4% more than 14 days in study conducted by Sarkar *et al.*<sup>8</sup> Apte *et al.*<sup>6</sup> found that 94% had fever up to 8 days while 6% had more than 8 days.

We observed 84.3% patients with splenomegaly and 62% with hepatomegaly, while Apte *et al.*<sup>6</sup> in their study shows

splenomegaly in 54% and hepatomegaly in 43%. We observed that all the studies from Indian subcontinent show high percentage of splenomegaly as compared to other international studies, this might be due to most of the subjects in this region are from malaria endemic area.

Incidence of multiorgan dysfunction in our study is 43.1% of patients. This is in concordance with the studies done by Nadkar *et al.*,<sup>1</sup> Sarkar *et al.*,<sup>8</sup> Kochar *et al.*<sup>2</sup> and Bansal *et al.*<sup>5</sup> which were 42.8%, 46%, 47.5% and 39.9% respectively.

In present study in hematological investigations, we found thrombocytopenia as commonest finding in 89.2% either mild or severe which is comparable to 86.4% in a study conducted by Singh *et al.*<sup>9</sup> and to 89.7% in a study conducted by Bansal *et al.*,<sup>5</sup> to 89.3% in a study conducted by Nadkar *et al.*<sup>1</sup> Bleeding tendency is seen in 5.9% in severe thrombocytopenia which also had deranged PT >16. All these patients required platelet transfusion. But we had no fatality due to bleeding complication.

Anemia was present in 39.1% while severe anemia according to WHO definition (Hb <5 g%) found in only 2.9% which required whole blood or PCV transfusion. It is comparable to studies conducted by Apte *et al.*<sup>6</sup> and SP Singh *et al.*<sup>9</sup> who found severe anemia in 4% and 7.9% respectively. Limaye *et al.*<sup>3</sup> observed that severe anemia (Hb <5 g/dL) was significantly less common in vivax infection (2.96%). the need for packed red cell transfusion was less in vivax malaria (2.37%).

Anaemia in vivax malaria is due to hemolysis and bone marrow dyserythropoiesis. The cause of hemolysis is increased fragility of both parasitized as well as non-parasitized red blood cells.

In our study most patients 67.6% have CBC in normal range (5000-10000), while leucopenia was observed in 20.6% and increased CBC in 11.8%. In a study conducted by Echeverri *et al.*<sup>7</sup> the white cell count was abnormal in 34% of the patients: 29% leucopenia and 5% leukocytosis. 21% patients in a study conducted by Apte *et al.*<sup>6</sup> had leucopenia, (11%) had leukocytosis and (68%) had normal count.

Table 1 shows comparison of CBC profile in vivax malaria with other studies.

In present study 41.2%, 27.5%, 20.6%, and 10.8% severe vivax malaria patients have 1+, 2+, 3+, and 4+ grade of parasitemia respectively. This is in concordance with a study conducted by Apte *et al.*,<sup>6</sup> they found out of 140 patients 39% had +1 parasitemia, 26% had +2 parasitemia, 22% had +3 parasitemia, and 13% had +4 parasitemia. While



**Table 1: Comparison of CBC profile in vivax malaria with other studies**

Parameter	Present study (%)	Apte <i>et al.</i> <sup>6</sup> (%)	Singh <i>et al.</i> <sup>9</sup> (%)	Limaye <i>et al.</i> <sup>3</sup> (%)	Echeverri <i>et al.</i> <sup>7</sup> (%)	Nadkar <i>et al.</i> <sup>1</sup> (%)	Bansal <i>et al.</i> <sup>5</sup> (%)
Thrombocytopenia (%)	89.2		86.4			89.7	89.3
Severe anemia (Hb<5 g)	2.9	4	7.9	2.96			
Normal CBC	67.6	68			66		
Leucopenia	20.6	21			29		
Leukocytosis	11.8	11			5		

CBC: Complete blood count, Hb: Hemoglobin

Arthi *et al.*<sup>10</sup> found 84.7% having 1+ parasitemia 11.5% having 2+ parasitemia and 3.8% having 3+ parasitemia but no patients having 4+ parasitemia. In our study, all patients with multiorgan dysfunction had 2+ or more than 2+ grade of parasitemia.

This is similar to a study conducted by Arthi *et al.*<sup>10</sup> who observed that parasitic index can be correlated well with severity and course of malarial disease.

In present study of 102 severe vivax malaria patients organ dysfunction observed were hematologic, renal, hepatic, CNS and respiratory. Hematologic dysfunction, including thrombocytopenia and severe anemia was the most common organ dysfunction, found in 89.2% patients which is in concordance to 89.1% and 89.7% in a studies conducted by Nadkar *et al.*<sup>1</sup> and Bansal *et al.*<sup>5</sup> respectively.

In present study next common organ dysfunction observed was renal present in 34.3%, followed by hepatic dysfunction, present in 21.6%. Nadkar *et al.*<sup>1</sup> also mentioned renal dysfunction as 2<sup>nd</sup> most common complication presented in 31.9% followed by hepatic dysfunction presented in 19.5%. Apte *et al.*<sup>6</sup> in their study, found hepatic dysfunction 2<sup>nd</sup> common dysfunction in 40% next to thrombocytopenia (68%). Singh *et al.*<sup>9</sup> observed renal dysfunction only in 6.4%.

In our study, CNS dysfunction was observed in 7.8% which was in concordance with 6.4%, 8.1% and 3.5% in a studies conducted by Bansal *et al.*<sup>5</sup> Nadkar *et al.*<sup>1</sup> and Limaye *et al.*<sup>3</sup> respectively.

In present study ARDS as respiratory dysfunction found in only 2 cases (2%). This is in concordance with 1.4%, 1.6%, 3%, and 2.1% in studies conducted by Bansal *et al.*<sup>5</sup> Nadkar *et al.*<sup>1</sup> Limaye *et al.*<sup>3</sup> and Singh *et al.*<sup>9</sup> respectively. Apte *et al.*<sup>6</sup> found slightly more incidence of ARDS, i.e., in 12%.

Table 2 shows comparison of incidence of multiorgan dysfunction in severe malaria with different studies.

Incidence of multiorgan dysfunction in our study is 43.1% of patients while that in studies done by Nadkar *et al.*<sup>1</sup>

Sarkar *et al.*<sup>8</sup> Kochar *et al.*<sup>2</sup> and Bansal *et al.*<sup>5</sup> which were 42.8%, 46%, 47.5%, and 39.9%, respectively.

In present study 33.3% had presented with 2 organ dysfunction while 3 organ and 4 organ dysfunction were presented in 7.8% and 2% patients. This is in concordance with studies done by Nadkar *et al.*<sup>1</sup> and Bansal *et al.*<sup>5</sup> Nadkar *et al.*<sup>1</sup> observed 2, 3, 4 organ dysfunction in 33.8%, 8.8%, 0.2%, respectively while Bansal *et al.*<sup>5</sup> observed that in 29.1% and 10.7%. They didn't find four organ involvements.

In our study, in 2 organ dysfunction hematological along with renal was commonest presentation, seen in 18.6% followed by hematological with hepatic dysfunction present in 10.8%. Hematologic dysfunction and cerebral vivax malaria in combination was seen in 3.9%. This is similar to a study conducted by Nadkar *et al.*<sup>1</sup> in which the commonest organ combination observed was thrombocytopenia with renal involvement. While Sarkar *et al.*<sup>8</sup> mentioned renal failure with jaundice (12/44, 27%) was the most common combination in their study.

In our study hematological dysfunction along with hepatic and renal dysfunction was commonest three organ dysfunction seen in 3.9%. This finding is consistent with previous studies. Sarkar *et al.*<sup>8</sup> in their study mentioned that out of 92 multiorgan complication patients 39.1% had three organ dysfunction in which jaundice, renal failure and anemia was commonest combination followed by cerebral malaria, jaundice and anemia. Kochar *et al.*<sup>2</sup> in their study observed three organ dysfunctions in 9 patients (22.5%) in which, renal failure, jaundice and thrombocytopenia was commonest combination.

We observed four organ dysfunction in only two patients, one had hematological, renal, CNS and hepatic dysfunction and other had hematologic, renal, respiratory and hepatic dysfunction. This is comparable with previous studies. Kochar *et al.*<sup>2</sup> in their study of 40 severe vivax infections, only 2 had 4 organ involvement. That were with cerebral malaria, renal failure, severe anemia, thrombocytopenia and ARDS, jaundice, renal failure and severe anemia. Nadkar *et al.*<sup>1</sup> in his study observed 4 organ complications were seen in 1 (0.20%) patient.



**Table 2: Comparison of incidence of multiorgan dysfunction in severe malaria with different studies**

Organ dysfunction	Present study (%)	Nadkar <i>et al.</i> <sup>1</sup> (%)	Bansal <i>et al.</i> <sup>5</sup> (%)	Limaye <i>et al.</i> <sup>3</sup> (%)	Singh <i>et al.</i> <sup>9</sup> (%)	Apte <i>et al.</i> <sup>6</sup> (%)
Hematological	89.2	89.1	89.7	68	86.4	68
Renal	34.3	31.9	11.6	3.5	6.4	17
Hepatic	21.6	19.4	19.8	5.3		40
CNS	7.8	8.1	6.4	3.5	19.3	10
Respiratory	2	1.6	1.4	3	2.1	12

CNS: Central nervous system

In present study, it is found that Incidence of multiorgan involvement increases with increasing age. Maximum multiorgan dysfunction patients (34.1%) were in age group >60 years. While in younger age group majority patients had single organ involvement. Dondorp *et al.* in a large multicenter treatment trial conducted in Asia concluded that presenting syndromes in severe malaria depend on age.<sup>11</sup>

In present study, we found that mortality associated with severe vivax malaria was 6.9% which is concordance with 9%, 6.9% in studies conducted by Nadkar *et al.*,<sup>1</sup> and Bansal *et al.*<sup>5</sup> respectively. This is discordance with studies conducted by Limaye *et al.*<sup>3</sup> who found lower mortality 1.7% and by Sarkar *et al.*<sup>8</sup> who found 20% mortality.

In our study statistically significant difference ( $P < 0.05$ ) was observed of outcome in patients more than 60 years compared to younger patients. Maximum mortality of 18.8% was found in patients more than 60 years. This is comparable with studies conducted by Nadkar *et al.*,<sup>1</sup> and Bansal *et al.*,<sup>5</sup> they found 17.5% and 29.4% mortality in patients more than 60 years, respectively.

None of the patients with single organ dysfunction expired. However, mortality in multiorgan dysfunction was 15.9%. Nadkar *et al.*<sup>1</sup> observed similar in their study that mortality in single organ dysfunction was 6.9% but it rose to 27% in multiorgan dysfunction.

In our study, all 7 patients expired had 4 plus parasitemia grade and in total 11 of 4+ parasitemia grade 63.6% severe *P. vivax* patients expired. Thus, we observed statistically significant difference of outcome of patients according to severity of parasitemia. Aarthi *et al.*<sup>10</sup> in their study also noticed only one patients having heavy parasitemia expired while 25 severe vivax patients having low parasitemia recovered.

### Hematologic Dysfunction

In hematologic dysfunction thrombocytopenia was most common finding present in 89.2%. Platelet count was below 40000 in 5.9% patients. All these patients suffered from abnormal bleeding in the form of petechiae, ecchymoses,

malena, mild hematemesis, hematuria, all necessitating platelet transfusion. Bleeding due to thrombocytopenia was not fatal.

46.1% patients had thrombocytopenia as only single organ patients. None of the patients among them expired. But mortality found to be increasing when increasing associated organ involvements This is comparable to findings of a studies conducted by Nadkar *et al.*<sup>1</sup> and Bansal *et al.*<sup>5</sup>

### Renal Dysfunction

In present study renal dysfunction, as acute renal failure (ARF) according to WHO criteria found in 34.3% in severe vivax malaria. Majority patients were treated conservatively with fluids and diuretic. 31.4% (11/35) required renal replacement therapy in the form of hemodialysis. Maximum creatinine observed was 9.5%. This is in concordance with studies conducted by Nadkar *et al.*<sup>1</sup> and Bansal *et al.*<sup>5</sup>

There were no death observed when patients presented with renal dysfunction as a single organ dysfunction but mortality rose to 5.3% when associated with thrombocytopenia. Mortality increased when there was increased in associated organ involvements.

### Hepatic Dysfunction

In present study, Incidence of hepatic involvement was found in 21.6% which is in concordance with 19.5% in a study conducted by Nadkar *et al.*<sup>1</sup> Maximum bilirubin seen was 7.6 mg%. None of the patients had signs of hepatic encephalopathy or DIC.

No mortality was found when presented as single organ dysfunction or associated with thrombocytopenia but mortality increased when associated with 3 or 4 organ dysfunctions along with renal or respiratory dysfunction.

### ARDS

We found two patients with respiratory distress syndrome both were associated with other organ dysfunction and developed ARDS after admission. Both of these patients required ventilator support. Both patients died because of ARDS. Nadkar *et al.*<sup>1</sup> found 62.5% mortality in ARDS patients.



### Cerebral Malaria

In our study incidence of cerebral malaria was 7.8%. All patients with CNS involvement were having associated organ involvement. In other words in single organ involvement no patient had cerebral malaria. All 7.8% patients having cerebral malaria was having altered sensorium with Glasgow coma scale <13 at the time of presentation. All patients of cerebral malaria along with hepatic or hematologic dysfunction survived. Mortality was 100% in patients with renal dysfunction along with hematologic and hepatic dysfunction.

Table 3 shows comparison of outcome associated with different organ involvement which is 100% if associated with ARDS and lowest with thrombocytopenia.

Table 4 shows none of the patients with single organ dysfunction expired. But mortality in multiorgan dysfunction was 15.9%. Nadkar *et al.*<sup>1</sup> observed similar in their study that mortality in single organ dysfunction was 6.9% but it rose to 27% in multiorgan dysfunction.

Table 5 shows in present study we reported different organ dysfunctions (thrombocytopenia-89.2%, ARF-34.3%,

**Table 3: Outcome according to organ dysfunction**

Organ dysfunction	Present study (%)	Nadkar <i>et al.</i> <sup>1</sup> (%)	Bhansal <i>et al.</i> <sup>5</sup> (%)	Singh <i>et al.</i> <sup>9</sup> (%)	Aarthi <i>et al.</i> <sup>10</sup> (%)
Hematologic	7.7				
Renal	20				50
Hepatic	18.2				
CNS	25	5		18.51	
Respiratory	100	62.5	60	66.7	

CNS: Central nervous system

**Table 4: Number of organ dysfunction and mortality**

Author	One organ (%)	Two organ (%)	Three organ (%)	Four organ (%)
Present study	0	2.9	50	100
Nadkar <i>et al.</i> <sup>1</sup>	6.9	13.9	6.9	100
Bansal <i>et al.</i> <sup>5</sup>	8.3	33.3	58.3	

**Table 5: Comparison between severe vivax and severe falciparum infection**

Parameter	Nadkar <i>et al.</i> <sup>1</sup> (%)	Bansal <i>et al.</i> <sup>5</sup> (%)	Limaye <i>et al.</i> <sup>3</sup> (%)	Aarthi <i>et al.</i> <sup>10</sup> (%)	Singh <i>et al.</i> <sup>9</sup> (%)	Present study (%)
Thrombocytopenia						
Vivax	89.1	89.8	68		86.4	89.2
Falciparum	79.8	82.3	73			
Severe anemia						
Vivax			2.9		7.9	2.9
Falciparum			12.6			
ARF						
Vivax	31.9	11.6	3.5	7.4	6.4	34.3
Falciparum	55.1	49.7	19.4	31.2		
Jaundice						
Vivax	19.5	19.8	5.3	3.7	12.1	21.6
Falciparum	36.3	35.7	22.3	25		
Cerebral malaria						
Vivax	8.2	6.4	3.5	-	19.3	7.8
Falciparum	14.4	31.8	13.2	31.2		
ARDS						
Vivax	1.6	1.4	3	3.7	2.1	2
Falciparum	2.2	2.5	7.7	25		
Mortality						
Vivax	9	6.9	1.8	3.7	6.4	6.9
Falciparum	16.1	15.3	9.7	25		
Age group having max. mortality						
Vivax	>60 years	>60 years			>70 years	>60 years
Falciparum	41-50 years	31-50 years				

ARDS: Acute respiratory distress syndrome, ARF: Acute renal failure



jaundice-21.6%, and cerebral malaria-7.8% ARDS-2%) and associated mortality 6.9% in severe vivax infection which is comparable with those observed in previous studies as mentioned in above studies. In present study incidence of different organ dysfunctions and mortality is found to be less in severe vivax infection compare to severe falciparum malaria as observed in above mentioned studies.

## CONCLUSION

In our study single organ dysfunction is present in 55.9% of severe vivax infection which is more common than multiorgan dysfunction in severe vivax malaria present in 43.1%.

In our study common age group of patients with severe vivax malaria is 21-30 years age group, but maximum incidence of multiorgan dysfunction is in >60 years age group. Increased mortality is seen in patients with age >60 years. Males (62.75%) are more common affected than females (37.25%).

In our study fever with chills along with headache is common presentation and majority of multiorgan dysfunction patients have duration of fever >14 days.

Thrombocytopenia (89.2%) is most common single organ dysfunction followed by ARF (34.3%). Jaundice is seen in 22.5% followed by cerebral malaria (7.8%) and ARDS 2%.

Two organ dysfunction are seen in (33.3%) and thrombocytopenia with ARF is most common 2 organ dysfunction, while ARF Jaundice and thrombocytopenia is most common three organ dysfunction. Three organ dysfunction are seen in 7.8%. Four organ dysfunction are less common seen in only 2 patients.

Outcome is better in single organ dysfunction but it rises to 15.9% in patients with multiorgan dysfunction ( $P < 0.01$ ).

In our study, we noted that ARF if present as single organ dysfunction doesn't have any mortality, but mortality increases if associated with other complications. 80% patients with ARF survived and 11 required hemodialysis out of which 2 died. ARF in severe vivax infection has favorable outcome if treated promptly. In our study it is found that ARDS is associated with poor outcome. Ventilator requirement is more in multiorgan dysfunction and outcome is poor in patients with ventilator requirement.

In present study, similar to severe falciparum malaria as mentioned in past studies multiorgan dysfunction and associated mortality though less common and less severe is seen in severe vivax malaria.

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