Malaria is a vector-borne disease that is endemic in 91 countries. South East Asia is the second most affected region in the world, with India carrying the highest burden of the disease. Four species of *Plasmodium* are known to cause malaria in humans. *Plasmodium vivax* and *Plasmodium falciparum* are the most common species found in India, but *Plasmodium malariae* have also been reported. Severe complications of malaria have been more commonly seen in *P. falciparum* infections, and those caused by *P. vivax* have been considered benign. However, the literature has alarming reports of complicated malaria seen in vivax infections in recent times. This article reports three such cases of *P. vivax* infection with severe manifestations of malaria such as are found in *P. falciparum*. This recent evidence indicates that it is important to suspect complicated malaria in *P. vivax* infection and initiate the appropriate treatment as early as possible to avoid morbidity and mortality.

**Key words:** Complicated malaria, *Plasmodium vivax*, severe manifestations

### INTRODUCTION

According to the latest WHO estimates, there were about 219 million cases of malaria in 2010 and 660,000 deaths. The highest malaria mortality rates are seen in countries that have the highest rates of extreme poverty. In South East Asia, the second most affected region in the world, India has the highest incidence of malaria (with an estimated 24 million cases per year), followed by Indonesia and Myanmar (WHO 2012 malaria report). In India, *Plasmodium vivax* (*P. vivax*) infection accounts for 60–65% of malaria and *Plasmodium falciparum* for 35%. *P. vivax* previously considered as a benign infection is now recognized as a cause of severe and fatal malaria. Severe manifestations with *P. vivax* monoinfection are similar to those of severe *Plasmodium falciparum*. Here, we report three cases of *P. vivax* infection that presented with severe manifestations of malaria.

### CASE REPORTS

**Case 1**

A 25-year-old male presented to the Emergency Department with complaints of a high-grade fever with chills and rigors, extreme weakness, and reduced urine output for 3 days. On examination, he was febrile, dehydrated, icteric, no edema. Blood pressure was 80/50 mm Hg, and pulse rate was 110/min. His blood sugar was 50 mg/dl, hemoglobin of 9 g/dl, platelet of 70,000 cells/mm$^3$, erythrocyte sedimentation rate (ESR) - 6/14 mm, total count of 6000 cells/mm$^3$, total bilirubin - 3.5 mg/dl, serum glutamic oxaloacetic transaminase - 250 U/L, serum glutamic-pyruvic transaminase - 196 U/L, Amylase - 20U/L, serum creatinine was 3.0 mg/dl. Rapid card test for malaria was positive, so he was provisionally diagnosed as complicated malaria and admitted into Intensive Care Unit and started on intravenous fluids, intravenous artesunate.

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smear examination revealed *P. vivax* species. His blood pressure (BP) dropped, and he was started on inotropes. Chloroquine was initiated to cover vivax infection, and artesunate was continued along with other supportive medications. His vitals improved over the next 48 h, and his renal function and liver function normalized in 3 weeks. He was discharged and given oral primaquine for 14 days to prevent a relapse of vivax infection.

**Case 2**

A 32-year-old adult male with a fever for 4 days and altered sensorium since that morning, presented to the Emergency Department and immediately developed generalized tonic-clonic seizures of all 4 limbs. His capillary blood glucose was 20 mg/dl, BP of 90/70 mm Hg and pulse rate of 115/min, dehydrated, and icteric. He was immediately stabilized with intravenous lorazepam and was given 100 ml of 25% dextrose, and was started on a dextrose maintenance infusion. His systemic examination showed hepatosplenomegaly but otherwise normal. His blood investigations showed anemia, thrombocytopenia, impaired liver function, and serum creatinine of 3.4 mg/dl. ESR was normal, total count of 7200 cells/mm³, computed tomography brain was normal. Rapid card test for malaria was positive, and he was admitted into the Intensive Care Unit and started on treatment for complicated malaria as per guidelines, with other supportive medications. Over the next few hours, his BP dropped, and he required inotropic support. Peripheral blood smear examination revealed *P. vivax*. He was started on tablet chloroquine and other treatments were continued. The patient improved symptomatically and his liver and renal function gradually improved over 4 weeks, and he was discharged with 14 days of oral primaquine.

**Case 3**

A 42-year-old female presented to the Emergency Department with a sudden onset of breathlessness since morning and a fever with reduced urine output for 5 days. On examination, she was tachypneic, icteric, BP of 60/40 mm Hg, pulse rate of 126/min, saturation of 85%, capillary blood glucose was 40 mg/dl, and she had extensive fine crepts all over her lung fields. She was diagnosed as acute pulmonary edema and treated immediately with diuretics and other medications as per the guidelines. Her saturation improved, and she did not require intubation. Her blood investigations revealed thrombocytopenia, anemia, liver dysfunction, serum creatinine of 5 mg/dl, total count of 5000 cells/mm³, ESR - 6/15 mm, and rapid card test for malaria was positive. She was admitted to Intensive Care Unit and immediately started on inotropic support and started treatment for complicated malaria. Her peripheral smear showed *P. vivax*, and she was started on chloroquine as other treatment was continued. Over the next 24 h, she had nil urine output, so she underwent urgent dialysis. She required 4 sittings of dialysis in total over a period of 2 weeks. Her vitals and renal function improved slowly over a period of 3 weeks, and her liver function normalized in 4 weeks. She was discharged with oral primaquine for 2 weeks.

**DISCUSSION**

Infection with malaria in India is very high and causes significant morbidity and mortality. *P. vivax* and *P. falciparum* are the commonly found species in India though there are very few reported cases of *Plasmodium malariae* infection. Of all the species of *Plasmodium* causing infection in humans, *P. vivax* is the most widespread in the world. Central and South-East Asia, the Horn of Africa and Latin America are the most commonly reported places with *P. vivax* infection.

It causes significant morbidity and mortality among the people except in African populations who are mostly Duffy negative, which makes them less susceptible to malarial infection. But recent data suggest that for erythrocyte invasion, the parasite may use receptors other than Duffy (Duffy antigen/chemokine receptor).

Although often regarded as a benign tertian infection, the alarming evidence in the literature indicates that the morbidity and mortality of *P. vivax* infection have been underestimated, partly because of the significance given to falciparum as the more dangerous species. This diverts attention from vivax.

The severe manifestations with *P. vivax* malaria are hepatic dysfunction, renal dysfunction, severe anemia, ARDS, multiple organ involvement, and cerebral malaria. The exact pathogenesis, parasite host interactions, and reasons for multi-organ dysfunction due to *P. vivax* is unclear.

Here, we report three cases of vivax malaria, all of whom were previously healthy without any prior confirmed malarial illness, but had severe manifestations similar to infection with falciparum such as extreme weakness, thrombocytopenia, hypoglycemia, liver dysfunction, shock, and renal dysfunction. There were no associated co-morbidities in any of the patients. There was no evidence of mixed infection. Only *P. vivax* species was identified by peripheral smear. There was no subjective error. One of them had convulsions secondary to hypoglycemia, and another one had severe renal dysfunction leading to noncardiogenic pulmonary edema requiring dialysis. None of the three patients had features of cerebral malaria, severe metabolic acidosis that required correction. Despite the low levels of hemoglobin in all three patients, none
needed blood transfusions. This article points out that severe complications of malaria are currently often seen even in *P. vivax* infection as what obtained in falciparum infection. The incidence of complicated vivax infection is rising.

**CONCLUSIONS**

This article highlights the fact that severe manifestations of malaria are more commonly now seen in patients infected with *P. vivax* as it used to be with falciparum infection. Though cerebral malaria and severe acidosis was not present in our cases, the literature shows that it can occur with vivax infection. The common complications encountered are liver dysfunction, renal dysfunction, thrombocytopenia, hypoglycemia, and shock. With the alarming evidence in literature, it is clear that complicated vivax malarial infection may also be very easily encountered, but often under-diagnosed. Early recognition and prompt treatment can significantly reduce morbidity and mortality.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. WHO. World Malaria Report 2012. WHO; 2012.
2. Kochar DK, Das A, Kochar SK, Saxena V, Sirohi P, Garg S, *et al.* Severe *Plasmodium vivax* malaria: A report on serial cases from Bikaner in northwestern India. Am J Trop Med Hyg 2009;80:194-8.
3. Sharma A, Khanduri U. How benign is benign tertian malaria? J Vector Borne Dis 2009;46:141-4.
4. Lacerda MV, Mourão MP, Alexandre MA, Siqueira AM, Magalhães BM, Martinez-Espinosa FE, *et al.* Understanding the clinical spectrum of complicated *Plasmodium vivax* malaria: A systematic review on the contributions of the Brazilian literature. Malar J 2012;11:12.
5. Mendes C, Dias F, Figueiredo J, Mora VG, Cano J, de Sousa B, *et al.* Duffy negative antigen is no longer a barrier to *Plasmodium vivax* – Molecular evidences from the African West Coast (Angola and Equatorial Guinea). PLoS Negl Trop Dis 2011;5:e1192.
6. Mehndiratta S, Rajeshwari K, Dubey AP. Multiple-organ dysfunction in a case of *Plasmodium vivax* malaria. J Vector Borne Dis 2013;50:71-3.