

# Severe Plasmodium Vivax Malaria Complicating Pregnancy: A Daunting Obstetric Challenge

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## ABSTRACT

Pregnant women are more prone to severe malaria and its complications. We present a case of severe malaria in a pregnant patient who improved with artesunate therapy. A 30-year-old G3P2L2, 36-week-pregnant woman presented to our institute with five days of fever, joint pain, night sweats, vomiting, dyspnea, and general discomfort. A peripheral smear performed following the complete blood count revealed *P. vivax* parasitemia with ring forms, schizonts and a parasite index of 6.2%. The patient was admitted to the ICU and given intravenous clindamycin and artesunate. After the fifth artesunate dose, the peripheral smear showed no parasites. A clinic follow-up after discharge showed no new disease or treatment issues. The WHO recommends the use of intravenous artesunate for treating severe malaria in all trimesters. This case study shows the importance of diagnosing malaria in pregnant women and the safe use of artesunate compounds to protect the mother.

**Keywords:** thrombocytopenia in pregnancy, severe malaria, pyrexia in pregnancy, malaria in pregnancy, high risk obstetrics

## INTRODUCTION

Malaria, an ancient and deadly disease, has a complex history dating back to 1897 when Roland Ross demonstrated that mosquitoes could spread the disease. India achieved significant success in the 1950s and 1960s, but the disease burden decreased in 1965, leading to complacency. In the early 1970s, DDT resistance led to a comeback, with a 1975 survey projecting 6.5 million cases. In 2016, malaria had 200 million cases worldwide, making it a pathogen with the greatest impact on human history. The disease is transmitted by female Anopheles mosquitoes, and some people may become infected without exhibiting symptoms. India has made significant progress in malaria reduction over the past 15 years, with the National Vector-Borne Disease Control

effort in 2017 recording 842,095 cases and 104 deaths.<sup>1-3</sup>

*Plasmodium vivax*, *malariae*, and *ovale* have less severe clinical presentations, while *Plasmodium falciparum* causes most human malaria deaths. Pregnant women are more likely to have severe malaria, which can lead to intrauterine growth restriction, poor birth weight, and newborn mortality. Severe malaria patients require parenteral antimalarial medication based on clinical criteria such as reduced consciousness, distributive shock, pulmonary oedema, seizures, and ARDS. Pregnant women are three times more likely to have severe malaria, pulmonary oedema, placental infarction, and hypoglycemia.<sup>3</sup>

### CASE REPORT

A 30-year-old G3P2L2, 36-week gestation who moved from another state three months prior presented to our institute with five days of fever, joint pain, night sweats, vomiting, dyspnea, and general discomfort. The patient's obstetric records show two successful full-term normal vaginal deliveries, one 10 years ago and one 5 years ago. The deliveries produced a healthy male and female infant respectively. The patient had impaired consciousness and incoherent speech at initial assessment. The patient exhibited severe pallor accompanied by significant jaundice. During the physical examination, the patient exhibited symptoms including fever, tachycardia, tachypnoea, hypotension and abdominal tenderness (Table 1). The patient was promptly sent to the obstetric ICU.

Vital signs	Result
Pulse	126/min
Blood pressure	100/60 mmHg
Respiratory Rate	24/min
Pulse oximetry (SpO <sub>2</sub> )	90%
Temperature	38.9°C

Table 1: Vital signs at initial presentation

The initial laboratory findings revealed a hypo-proliferative form of anemia accompanied by elevated levels of bilirubin (Table 2).

Laboratory Test	Result
Hemoglobin	6.6 g/dl
Total WBC count	4800/mm <sup>3</sup>
Platelet	20,000/mm <sup>3</sup>
Random blood sugar	48 mg/dl
BUN	35 mg/dl
Serum creatinine	1.5 mg/dl
Total bilirubin	8.1mg/dl
Direct bilirubin	5.0 mg/dl
Indirect bilirubin	3.1 mg/dl
ALT	112 IU/L
AST	192.6 IU/L
Prothrombin time	22 seconds
INR	1.69
Fibrinogen	314 mg/dl
D-dimer	3209 ng/ml

Table 2: Pertinent laboratory test findings.

An arterial blood gas study revealed metabolic acidosis. Hepatosplenomegaly was seen in an emergency abdominal ultrasonography. The ultrasound showed intra-uterine fetal death with cephalic

presentation and severe oligohydramnios. Fetus weight was measured at 2861 grams and there was no evidence of abruptio placenta. A peripheral smear performed following the complete blood count revealed *P. vivax* parasitemia with ring forms, schizonts, and a parasite index of 6.2% (Figures 1, 2).

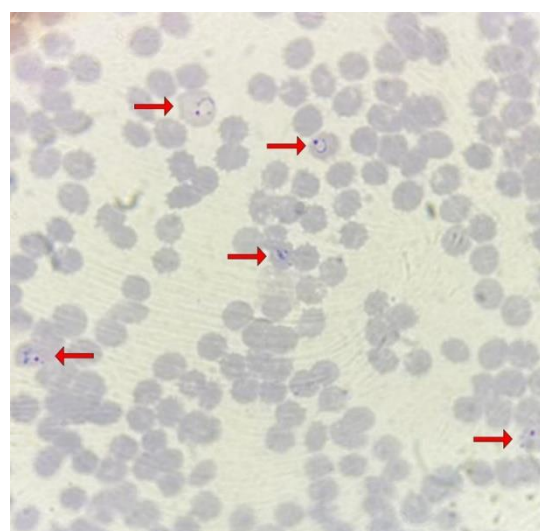


Figure 1: Peripheral blood smear, Leishman stain, 1000x magnification Ring forms of Plasmodium vivax (red arrows)

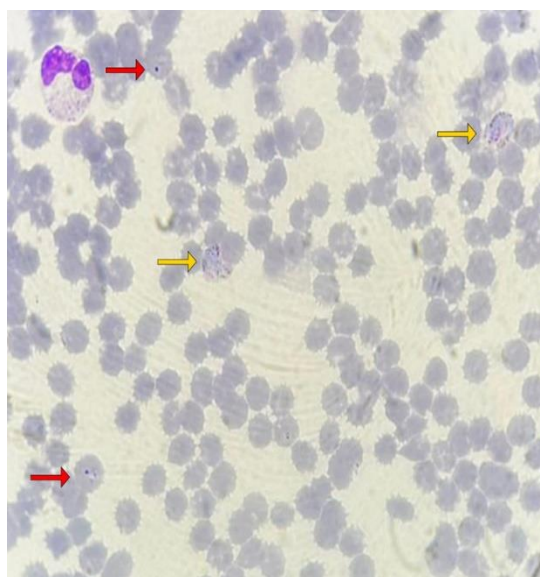


Figure 2: Peripheral blood smear, Leishman stain, 1000x magnification Ring forms of P.vivax (red arrows) and Schizonts of P.vivax (yellow arrows)

The patient was promptly initiated on intravenous (IV) artesunate at a dosage of 120mg and intravenous (IV) clindamycin after the initial resuscitation interventions were performed. The patient was started on a 5% dextrose infusion in order to address her

hypoglycemic condition. The patient was maintained on a non-rebreather mask (NRBM) with an oxygen flow rate of 10 liters per minute and bicarbonate correction was administered. A total of two units of packed red blood cells (PRBC), two units of fresh frozen plasma (FFP), one unit of single donor platelet (SDP) and two units of platelets were arranged. A 2870g male newborn was delivered stillborn following an induction on the second day of hospitalization for a known intrauterine fetal demise. The patient's labor was exacerbated by the presence of hypoglycemia necessitating 5% dextrose infusion. No event related to postpartum hemorrhage was observed. The patient exhibited clinical improvement starting from the fourth day. The patient successfully underwent a course of treatment consisting of five intravenous administrations of artesunate and clindamycin. Following the administration of the fifth dose of artesunate, no presence of blood parasites appeared upon examination of the peripheral smear. During her six days in the intensive care unit (ICU) following delivery, three units of platelets, four units of FFP, one unit of SDP and four units of PRBC were transfused. On the ninth day, the patient was transferred to the High Dependency Unit (HDU). After receiving a tablet of Primaquine 15 mg once daily for 14 days, the patient's anemia and thrombocytopenia improved. Following an 18-day hospital stay, the patient was discharged from the hospital. During the subsequent clinic follow-up, several weeks after the initial visit, the patient did not exhibit any additional difficulties related to her medical condition or the prescribed treatment, as evidenced by the absence of abnormalities in her laboratory test results.

Written informed consent was obtained from the patient and her family for the publication of her information and images.

## DISCUSSION

Maternal morbidity and mortality are dramatically increased by severe malaria, particularly in countries with little

resources.<sup>3</sup> Premature delivery, low birth weight, and intrauterine growth retardation are among the unfavorable pregnancy outcomes linked to malaria caused by the parasite *Plasmodium vivax*. The risk of neonatal death is raised as a result of these outcomes. Furthermore, there is an increased risk of maternal morbidity and mortality in cases of malaria infection.<sup>4</sup>

Preterm delivery is linked to malaria parasitemia, anemia, and elevated TNF $\alpha$  and interleukin 10 levels. Malaria during pregnancy can negatively impact placenta circulation, especially if it obstructs trophoblast invasion-induced remodeling of uterine spiral arteries. Chronic malaria patients often experience fetal growth restriction due to placental insufficiency. Fetal Doppler examinations show alterations in umbilical and brain vascular resistance in pregnant women with symptomatic maternal malaria, suggesting fetal hypoxia and placental dysfunction.<sup>5</sup>

Severe malaria leads to thrombocytopenia and anemia in blood counts. Factors causing malarial anemia include decreased bone marrow function, loss of infected and uninfected red blood cells, pregnancy-related micronutrient deficits, HIV infection, hookworm infection, and chronic inflammation. Anemia can be caused by T cell-mediated parasite removal. Pregnant women with malaria have a higher prevalence of thrombocytopenia than nonpregnant women. Sequestration inside the placenta can result in negative peripheral smears.<sup>4-6</sup> Maternal anemia is linked to pigmented monocytes in the placenta, which can cause inflammatory mediators like TNF and oxidative stress, which can prevent red blood cell formation. These monocytes can also cause thrombocytopenia in malaria, which is caused by platelet activation, sequestration in the spleen, and shortened platelet lifespan. Low interleukin 10 levels can also prevent red blood cell formation.<sup>5,7</sup>

The World Health Organization (WHO) defines severe malaria as a condition characterized by parasitemia and organ failure, which can occur rapidly due to

delayed therapy or treatment failure, and is universally applicable to all patient populations, including pregnant women (Table 3).<sup>8</sup>

Clinical features	Laboratory findings
Impaired consciousness	Hypoglycemia
Generalized weakness	Metabolic acidosis
Failure to feed	Severe normocytic anemia
Convulsions – more than two episodes in 24 hours	Hemoglobinuria
Respiratory distress	Hyperparasitaemia
Shock	Hyperlactatemia
Icterus along with evidence of vital organ dysfunction	Renal impairment
Hemoglobinuria	
Abnormal spontaneous bleeding	
Pulmonary oedema	

Table 3: WHO definition of severe malaria

Preserving the mother's life is the primary goal of treatment for severe malaria. For severe malaria in all trimesters of pregnancy, the World Health Organization (WHO) recommends intravenous artesunate as the

recommended treatment. In India, artemisinin-based combination therapy (ACT) has been found to be one of the most effective ways to treat malaria (Table 4).<sup>1,8</sup>

Type of malaria	First Trimester	Second and third trimester
Plasmodium falciparum	Both IV artesunate and quinine are viable options for treatment.	IV artesunate is recommended.
Plasmodium vivax	Both IV artesunate and quinine are viable options for treatment.	IV artesunate is recommended.
	The administration of chloroquine as a preventive measure till the time of delivery.	The administration of chloroquine as a preventive measure till the time of delivery.
	Following delivery, it is recommended that women be administered with aggressive primaquine therapy.	Following delivery, it is recommended that women be administered with aggressive primaquine therapy.
All severe malaria	It is imperative to avoid any delay in the administration of treatment. Immediate administration is recommended if just one of the medications, namely artesunate, artemether, or quinine, is accessible.	

Table 4: WHO recommendations for the treatment of severe malaria in pregnancy

## CONCLUSION

Severe malaria during pregnancy poses serious risks to both mother and baby. The case report emphasizes the safe use of artesunate compounds during pregnancy, especially in cases of significant parasitemia. Early diagnosis and treatment are crucial, especially for pregnant women from high-prevalence regions, especially those with a distant travel history to malaria-prone areas.

### Declaration by Authors

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