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Delayed Diagnosed of Relapse Malaria Vivax in Pregnancy: Good Outcome After Prompt Therapy

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Abstract

Malaria remains a major global health problem, particularly in endemic regions such as Indonesia, where pregnant women are highly vulnerable to infection and complications. Relapse Plasmodium vivax infection is increasingly recognized as a clinical challenge due to its dormant liver stage and potential for recurrent disease during pregnancy. This study aims to describe the clinical presentation, diagnostic approach, and management outcome of relapse vivax malaria in a third-trimester pregnant patient. A case report design was used based on clinical history, physical examination, laboratory findings, peripheral blood smear, and rapid diagnostic testing. The patient presented with fever, thrombocytopenia, and icteric sclera, and was confirmed positive for Plasmodium vivax with significant parasitemia and received dihydroartemisinin–piperaquine therapy with marked clinical improvement and platelet recovery. Findings emphasize the difficulty of differentiating malaria relapse from other hematologic conditions in pregnancy and the importance of early diagnosis in endemic areas. Early recognition and prompt treatment are essential to improving maternal and fetal outcomes in relapse vivax malaria during pregnancy. Future studies should focus on prevention of relapse, optimization of diagnostic algorithms, and evaluation of safe antimalarial strategies in pregnant populations in endemic regions. This will support better clinical decision-making and maternal health outcomes in practice.

INTRODUCTION

Malaria remains one of the world's most significant public health challenges, particularly in endemic areas such as East Nusa Tenggara. According to WHO data from 2022, the number of malaria cases reached approximately 2.8 million, with 2% occurring in Southeast Asian countries. Among the 11 countries in the Southeast Asia region, only two have been granted malaria-free status by WHO, namely Sri Lanka and the Maldives. Meanwhile, Indonesia and India continue to contribute 65.7% and 22.4%, respectively, of the total malaria burden (Buthelezi et al., 2024). In 2023, East Nusa Tenggara Province ranked as the seventh-largest contributor to malaria cases at the national level.

Malaria in this province is predominantly caused by Plasmodium vivax, followed by Plasmodium falciparum (Arévalo-Herrera *et al.* 2015; File *et al.* 2019; Price *et al.* 2020). Malaria constitutes a complex health issue influenced by various factors, including the infecting Plasmodium species, environmental conditions, climate variability, and the socio-demographic characteristics of the affected region. Malaria can affect all population groups, including pregnant women (Bardoe *et al.* 2024; Villena *et al.* 2024; Zegeye *et al.* 2025). The estimated malaria infection rate among pregnant women in endemic regions of Indonesia is

16.8% (Fitri et al., 2013). Malaria during pregnancy can pose substantial health risks to both the mother and the fetus, including intrauterine fetal death (IUFD), low birth weight, and miscarriage (Hill et al., 2018; Kementerian Kesehatan Republik Indonesia, 2023). The malaria parasite is capable of adhering to placental blood vessels, thereby disrupting maternal–fetal blood flow, which may lead to fetal hypoxia and intrauterine growth restriction. In addition, malaria can induce anemia in pregnant women through mechanisms involving hemolysis and decreased erythrocyte production in the bone marrow (Kementerian Kesehatan Republik Indonesia, 2024).

From a global epidemiological perspective, malaria still accounts for millions of cases annually, with the majority concentrated in Africa and parts of Southeast Asia. World Health Organization reports consistently highlight that while global incidence has declined in some regions, progress remains uneven due to disparities in healthcare infrastructure, vector control implementation, and population mobility. Pregnant women represent a high-risk group because physiological and immunological changes during pregnancy increase susceptibility to infection and severity of complications (Armando *et al.* 2023). These global patterns show that malaria in pregnancy remains a critical maternal health issue requiring continuous attention (Rogerson *et al.* 2018; Minwuyelet *et al.* 2025; Desai dan Cot 2026).

In Indonesia, malaria remains endemic in several provinces, particularly in Eastern Indonesia such as East Nusa Tenggara and Papua. These regions contribute disproportionately to national malaria cases due to environmental, geographic, and socio-economic factors that favor transmission. The clinical case described in the source study highlights that patients with travel history to Papua and prior malaria infection remain at risk of relapse and re-infection, reflecting ongoing transmission dynamics in high-burden areas. This demonstrates that malaria control in Indonesia is still challenged by regional heterogeneity in disease burden.

Previous studies have consistently shown that malaria during pregnancy is associated with adverse maternal and fetal outcomes, including anemia, low birth weight, intrauterine growth restriction, and even maternal and fetal death. Research published in malaria-endemic settings also indicates that Plasmodium vivax, although often considered less severe than P. falciparum, can still cause significant hematological and obstetric complications. These findings reinforce that malaria in pregnancy should not be underestimated, especially in cases with delayed diagnosis or atypical presentation.

Further evidence suggests that relapse infections caused by Plasmodium vivax are linked to the presence of hypnozoites in the liver, which can reactivate weeks to months after initial infection. This biological characteristic creates challenges for long-term disease control, particularly in pregnant women where radical cure options such as primaquine are contraindicated. As shown in the reported clinical case, relapse vivax malaria can occur even after previous treatment and apparent recovery, complicating diagnosis and management strategies in endemic areas.

Despite extensive literature on malaria in pregnancy, there remains a significant gap in understanding relapse patterns of P. vivax in pregnant populations, particularly in resource-limited settings. Many studies focus on acute infection outcomes, while limited attention is given to recurrence mechanisms, diagnostic delays, and clinical misclassification with other hematological conditions such as thrombocytopenic disorders. This gap limits the development of more precise screening and follow-up protocols for high-risk pregnant patients in endemic

regions.

The urgency of this research lies in the persistent burden of malaria in pregnancy and its potential for rapid clinical deterioration if not promptly diagnosed and treated. Delayed diagnosis, as illustrated in clinical cases, can lead to severe maternal complications, including thrombocytopenia, jaundice, and obstetric emergencies requiring early delivery. Therefore, strengthening early detection and improving clinical suspicion in endemic areas is critical to reducing preventable maternal and neonatal complications.

The novelty of this study is reflected in its focus on relapse Plasmodium vivax malaria in late pregnancy with complex clinical presentation, including overlapping symptoms with other hematological and obstetric conditions. This case contributes new clinical insight into how malaria relapse may mimic immune thrombocytopenic purpura or other pregnancy-related disorders, potentially leading to diagnostic confusion. It also highlights the importance of integrating travel history and previous infection data into diagnostic reasoning in endemic settings.

The main purpose of this research is to describe and analyze the clinical progression, diagnostic process, and treatment outcomes of relapse vivax malaria in pregnancy, particularly in a resource-limited healthcare setting. In addition, the study aims to emphasize the role of early clinical recognition supported by laboratory confirmation in improving maternal outcomes. The objective is to provide a detailed clinical understanding that can support better diagnostic and therapeutic decision-making in similar cases.

The expected contribution of this study is to strengthen clinical awareness among healthcare professionals regarding the possibility of malaria relapse in pregnant patients with non-specific symptoms and hematological abnormalities. The findings also aim to contribute to the refinement of clinical guidelines for malaria management in pregnancy, particularly in endemic regions. Ultimately, the benefits of this research include improved early detection, reduced misdiagnosis, enhanced maternal–fetal outcomes, and strengthened public health strategies for malaria control in vulnerable populations.

CASE REPORT

A 33-year-old woman, G3P2A0, at 36 weeks of gestation, was referred to the Emergency Department of TC Hillers General Hospital, Maumere, Sikka. She was referred from another hospital in Nagekeo Regency, East Nusa Tenggara, with a history of severe preeclampsia in a previous pregnancy and suspected immune thrombocytopenic purpura (ITP). She presented with a three-day history of intermittent high-grade fever and red spots on her hands and feet, accompanied by dizziness, weakness, and epigastric pain. Other symptoms, including shortness of breath, chest pain, nausea, and vomiting, were denied, although she reported coughing. Her medical history was notable for a previous episode of Plasmodium vivax malaria in December 2024, asthma, and preeclampsia in a prior pregnancy. She had traveled to Papua three months earlier and denied any history of diabetes mellitus, heart disease, or kidney disorders.

The findings of physical examination at the ED revealed a general state that was still weakened but alert and communicative, blood pressure 100/80 mmHg, pulse rate 87×/min, respiratory rate 20×/min, body temperature 37°C, and oxygen saturation 99% on room air. The patient's body weight was 70 kg. Physical examination of the face and neck found that the eyes

had icteric sclera and the neck looked normal; regular single heart sounds (S1 and S2) without murmurs; bilateral vesicular breath sounds without rhonchi or wheezing; distended abdomen caused by pregnancy with normal bowel sounds and no muscular defense; warm extremities without edema; and a capillary refill time of less than 2 seconds. Obstetric examination showed a fundal height of 28 cm, fetal heart rate 146 beats per minute, positive lochia (+), and uterine contractions (+).

Laboratory results from the complete blood test on June 13, 2025, during the first day of admission revealed hemoglobin 12.2 g/dL, leukocytes 7.89 × 10^3 µ/L, thrombocytopenia with platelets at 20,000/mL, creatinine 0.62 mg/dL, serum glutamic oxaloacetic transaminase (SGOT) 21 µ/L, serum glutamic pyruvic transaminase (SGPT) 7 µ/L, and albumin 2.6 g/dL. The results of the Malaria Rapid Diagnostic Test (RDT) were positive for vivax malaria. Urine examination showed bright yellow. On peripheral blood smear examination stained with Giemsa, Plasmodium vivax was observed. Based on the results of anamnesis, physical examination, and supporting examination, the patient was then diagnosed as relapse vivax malaria in pregnancy.

Table 1. Results of Peripheral Blood Smear Examination (13/06/2025)

Indicator	Result
Malaria Test	Positif (+)
Species Identification	*Plasmodium Vivax*
Parasite Count	298/210 WBC

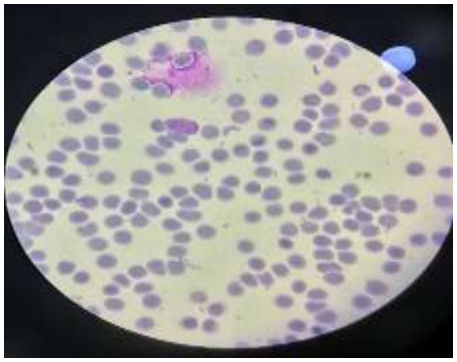


Figure 1. Thick Blood Smear (13/6/2025)

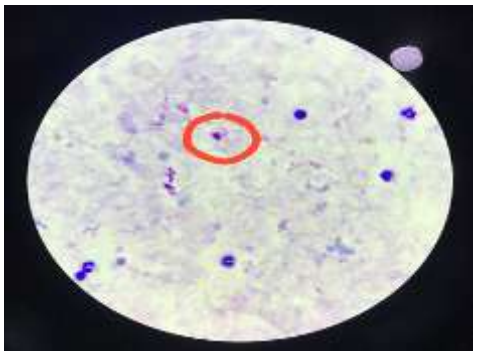


Figure 3. Thick Blood Smear (14/6/2025)

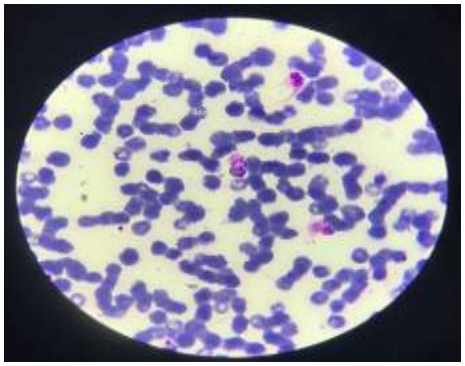


Figure 2. Thick Blood Smear (13/6/2025)

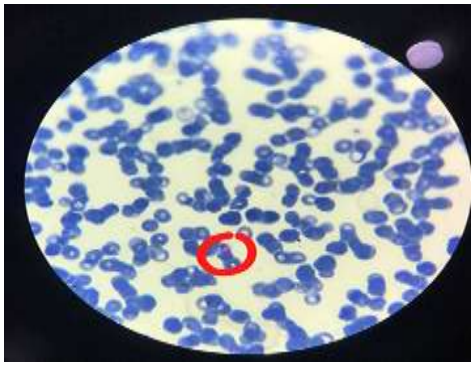


Figure 4. Thick Blood Smear

(14/6/2025)

On the second day of hospitalization (14/06/2025), the patient reported clinical improvement, with the absence of fever and headache. Laboratory investigations on the same day demonstrated a hemoglobin concentration of 10.5 mg/dL, a leukocyte count of 6,920/µL, and a platelet count of 20,000/µL.

Table 2. Results of Peripheral Blood Smear Examination (14/06/2025)

Indicator	Result
Malaria Test	Positif (+)
Species Identification	*Plasmodium Vivax*
Parasite Count	9/502 WBC

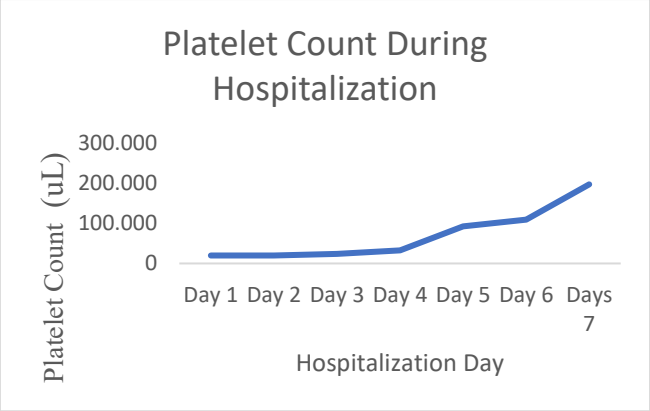
On the third day of hospitalization (15/06/2025), the patient reported being completely asymptomatic. General physical examination was unremarkable. Laboratory investigations revealed a hemoglobin level of 10.5 mg/dL, a leukocyte count of 6,020/µL, and a platelet count of 24,000/µL.

On the fourth day of hospitalization (16/06/2025) Laboratory investigations showed a hemoglobin level of 11.7 mg/dL, a leukocyte count of 6,730/µL, and a platelet count of 33,000/µL. On the fifth day hozpitalization (17/06/2025), the patient experienced abdominal discomfort and uterine contractions and the patient underwent a cesarean delivery performed by the obstetrician, laboratory results indicated a hemoglobin level of 11.7 mg/dL, a leukocyte count of 7,720/µL, and a platelet count of 93,000/µL.

On the sixth day (18/06/2025), laboratory findings showed a hemoglobin level of 11.5 mg/dL, a leukocyte count of 6,650/µL, and a platelet count of 110,000/µL.

On the seventh day (19/06/2025), laboratory results revealed a hemoglobin level of 11.4 mg/dL, a leukocyte count of 11,700/µL, and a platelet count of 198,000/µL.

The patient was treated at our hospital for seven days. During the hospitalization, the patient received symptom-relief therapy, including intravenous paracetamol 1 g when having a fever, and dihydroartemisinin-piperaquine (DHP) at a dose of 4 tablets once daily for three days, from 13/06/2025 to 15/06/2025. The patient was allowed to go home after having no complaints, with stable vital signs and normal general condition after delivery, and showing an increasing trend in platelet count, reaching 198,000/µL before discharge. The patient was advised to have follow-up care at the nearest internal medicine clinic because her home is far from our hospital.



Graphic 1. Platelet count during hospitalization

RESULTS AND DISCUSSION

In this case report, a 33-year-old G3P2A0 woman with a gestational age of 36 weeks presented with complaints of intermittent fever, chills, dizziness, headache, myalgia, and epigastric pain. Based on the anamnesis, the patient is suspected of having malaria, which is characterized by three classic symptoms: intermittent fever every three days accompanied by chills and joint pain. Other possible symptoms include headache, nausea, vomiting, and diarrhea.

The fever associated with malaria has distinct phases: the cold phase (15–60 minutes), during which the patient experiences severe chills; followed by the hot phase, characterized by high fever that can reach 41°C, flushed skin, dry skin, nausea, and vomiting; and finally, the sweating phase, in which the fever suddenly subsides accompanied by excessive sweating and a drop in body temperature. This phase typically lasts 2–4 hours. After completing the final phase, the patient enters the initial phase again, and the cycle repeats. In all types of malaria, fever occurs due to the rupture of mature schizonts. In Plasmodium vivax infections, schizonts mature within three days, giving rise to a characteristic fever pattern known as tertian fever. The patient reported returning from the Papua region approximately three months before hospital admission and had a prior history of malaria caused by Plasmodium vivax in December 2024. According to data from the Indonesian Ministry of Health in 2024, Papua is the area with the highest malaria endemicity, contributing 93% of the total malaria cases in that year. The patient's previous infection with Plasmodium vivax further supports the likelihood of a malaria recurrence. Literature indicates that P. vivax and P. ovale have a higher potential for relapse, as their sporozoites can remain dormant in liver cells as hypnozoites.

On physical examination, icteric sclera was observed. According to the literature, icteric sclera can occur in malaria cases due to both direct and indirect factors. Direct causes include intravascular hemolysis resulting from the destruction of red blood cells infected by the parasite. Indirect factors may involve microangiopathic hemolysis associated with disseminated intravascular coagulation (DIC), G6PD deficiency, reactions to antimalarial drugs, or concurrent hepatitis infection (Nugraha et al., 2020; Santosa & Kurniawan, 2024).

Laboratory tests showed that the patient had thrombocytopenia. According to studies, thrombocytopenia in malaria is more common with Plasmodium falciparum than with Plasmodium vivax. The exact cause of low platelets in P. vivax infection isn't fully understood, but it is thought to result from increased platelet breakdown, shorter platelet lifespan, and

antibody-mediated platelet destruction involving IgG (World Health Organization, 2019). On the first day of hospitalization, the patient's hemoglobin was 12.2 g/dL. Malaria is often linked to anemia, which can happen when the parasite directly invades and destroys red blood cells or when it suppresses red blood cell production in the bone marrow through increased TNF-α. In this case, the patient did not have anemia, which may be due to factors such as the specific Plasmodium species causing the infection, parasite count, the duration of the infection, and the individual's immune status (World Health Organization, 2025). On the peripheral blood smear stained with Giemsa, Plasmodium vivax was observed with a parasite count of 298 per 210 leukocytes, equivalent to approximately 11,370 parasites/μL of blood assuming 8,000 leukocytes/μL. Based on the malaria parasite density classification, this result indicates that the patient falls into the category of severe parasitemia (Yulistiawati & Arfijanto, 2023).

During hospitalization, the patient received symptomatic treatment and was given dihydroartemisinin–piperaquine (DHP) at a dose of 4 tablets once daily for 3 days. This regimen follows the clinical practice guidelines for malaria, based on the patient's body weight of 70 kg. This treatment differs from the regimen used in the general population, which includes primaquine. Primaquine is a hypnozoiticidal agent that targets the hypnozoite stage of Plasmodium vivax and helps prevent relapse; however, it is contraindicated in pregnant and breastfeeding women because it may cause hemolysis in the fetus and newborn (Guntur et al., 2024).

The patient was hospitalized for seven days at TC Hillers Hospital in Maumere. After her postpartum period, the patient's condition improved, her fever resolved, her vital signs became stable, her platelet count increased, and the parasite load decreased significantly following treatment; she was cleared for outpatient care and advised to continue follow-up at the internal medicine clinic of the hospital nearest to her residence.

CONCLUSION

In conclusion, this study highlights that relapse Plasmodium vivax malaria in pregnancy remains a significant clinical challenge, particularly in endemic regions with limited diagnostic resources. The case demonstrates that malaria in pregnancy may present with atypical and overlapping clinical features, including fever, jaundice, and severe thrombocytopenia, which can lead to initial misdiagnosis. The integration of detailed patient history, including prior malaria infection and travel history, alongside rapid diagnostic testing and peripheral blood smear examination, was crucial in establishing an accurate diagnosis. Early initiation of dihydroartemisinin–piperaquine (DHP) therapy contributed to favorable maternal outcomes, including clinical recovery, parasite clearance, and stabilization of hematological parameters. This case reinforces the importance of maintaining high clinical suspicion for malaria relapse in pregnant patients presenting with non-specific systemic symptoms in endemic areas.

For future research, larger-scale studies are recommended to further explore the patterns, risk factors, and recurrence mechanisms of P. vivax malaria in pregnant populations, particularly in high-endemic regions. Prospective cohort studies could provide stronger evidence regarding the relationship between relapse infections and maternal–fetal outcomes, as well as the effectiveness of different treatment protocols in pregnancy. In addition, further investigation is needed into improved diagnostic algorithms that can differentiate malaria from other hematological or obstetric conditions with similar presentations. Future studies should

also evaluate preventive strategies and post-treatment monitoring systems to reduce relapse rates while ensuring maternal and fetal safety.

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