

# A Case Report of Plasmodium Malaria Infection

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## ABSTRACT

**Background:** Malaria is a human infection caused by Plasmodium species. The Indonesia Ministry of Health reported 418,546 positive cases of malaria in Indonesia throughout 2023. Among the five major Plasmodium species, Plasmodium malariae infection is relatively rare and often overlooked by light microscopy due to its low parasitemia.

**Case Report:** A 67-year-old female presented to the emergency room with a fever for almost one week. The fever went down for three days but rose again on the fourth day. The patient had a history of traveling to Papua. Vital signs were normal. Laboratory examinations revealed decreased levels of hemoglobin, erythrocytes, leukocytes, platelets, and hematocrite. The serological examination was positive for malaria, and occult blood examination detected Plasmodium malariae schizont. The patient was subsequently treated with combination drug therapy for malaria and recovered successfully.

**Conclusion:** The symptoms of the patient were attributed to malaria infection. Treatment with artemisinin-based combination therapy is the most effective anti-malarial drug. Early and accurate diagnosis was also crucial delays in appropriate treatment could result in severe complications.

**Keywords:** plasmodium malariae, malaria, tropical infection

## INTRODUCTION

Malaria is a human infection caused by Plasmodium species and transmitted by Anopheles mosquitoes. The World Health Organization (WHO) stated that there were 249 million cases of malaria worldwide in 2022, resulting in 608,000 deaths.<sup>1</sup> This disease is endemic in more than 90 countries, with the highest incidence identified in sub-Saharan Africa. However, Southeast Asian regions, including Indonesia, are also at risk of malaria infection.<sup>2</sup>

The Indonesian Ministry of Health reported 418,546 positive cases of malaria in Indonesia throughout 2023, with 89% of these cases occurring in Papua Province according to the WHO.<sup>3</sup> Five major Plasmodium species can infect human beings: Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, and Plasmodium knowlesi. Among these, P. falciparum and P. vivax are the most common causes of malaria.<sup>2</sup>

Plasmodium malariae infection is relatively rare and can persist in the human host for years due to the recrudescence of blood-stage parasites, which can persist for long periods without causing significant symptoms. Plasmodium malariae parasites are often overlooked by light microscopy due to their low parasite density compared to other Plasmodium species.<sup>2, 4</sup> Although Plasmodium malariae is not the leading cause of death, and occurs less frequently than other Plasmodium species, it can become a significant problem if not immediately

treated. Even with appropriate treatment, inadequate drug levels in the blood can fail to eliminate newly emerging merozoites, extending the prepatent period and causing chronic subclinical infection.<sup>2</sup>

## CASE REPORT

A 67-year-old female presented to the emergency room of Christian University of Indonesia General Hospital, East Jakarta with a fever for almost one week. The fever initially spiked but subsided for three days, only to rise again on the fourth day. She also reported a throbbing headache from the front of her head to the back of her neck along with pain in her bones and joints. The patient mentioned a recent history of traveling to Papua for 10 months, returning to Jakarta in December 2023. The patient had a previous history of malaria infection twice.

Her vital signs were normal, with a temperature of 37.1°C. Physical examination revealed anemic conjunctiva, but other examinations were unremarkable. Laboratory examinations showed decreased levels of hemoglobin (7.9 g/dL), erythrocytes (2.79 million/mL), leukocytes (2.60 thousand/mm<sup>3</sup>), platelets (125 thousand/mm<sup>3</sup>), and hematocrit (23%). Serology examination was positive for malaria, and occult blood examination detected Plasmodium malariae schizonts. Based on these examinations, the 67-year old female patient was diagnosed with Plasmodium malariae infection in the context of a history of malaria and anemia.

Following this, the patient was successfully treated with dihydroartemisinin-piperaquine (DHP), the first-line treatment for uncomplicated malaria in Indonesia, along with additional symptomatic treatment.

## DISCUSSION

Malaria is a severe human infection caused by Plasmodium species and transmitted by female Anopheles mosquitoes.<sup>5</sup> The WHO stated that there were 249 million cases of malaria worldwide in 2022.<sup>1</sup> The Indonesian Ministry of Health reported 418,546 positive cases of malaria in Indonesia throughout

2023, with 89% of these cases occurring in Papua Province according to the WHO.<sup>6</sup> A total of 71 cases of malaria-related deaths reported in 2022. Malaria infection is suspected in patients who are exhibiting the characteristic cyclic fever, especially if they have a history of living or visiting an endemic area, as in the case of the current patient.<sup>2</sup>

Of the 172 Plasmodium species, five major species can infect human being: Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, and Plasmodium knowlesi. Among these, P. falciparum and P. vivax are the most common causes of malaria.<sup>2</sup>

The pathogenesis of malaria results from complex interactions between the parasite, host, and environment. When an infective Anopheles mosquito bites a human, sporozoites from the mosquito's salivary glands enter the bloodstream and within approximately half an hour, migrate to the liver, where they develop into trophozoites.<sup>7, 8</sup> These trophozoites then develop into liver schizonts containing between 10,000 and 30,000 liver merozoites, depending on the species. In the case of P. vivax and P. ovale, some liver trophozoites do not immediately develop into schizonts, but instead become dormant forms known as hypnozoites and remain in liver cells for months to years. These hypnozoites may reactivate when immunity decreases, leading to a relapse of malaria.<sup>9</sup>

Merozoites released from ruptured liver schizonts enter the bloodstream and infect red blood cell, progressing from the trophozoite stage to schizonts. The infected erythrocytes eventually burst, releasing merozoites and infect other red blood cells, causing damage to erythrocytes, and leading to anemia. However, the severity of anemia is not comparable to the level of parasitemia. Some studies suggest that this may be due to the presence of malaria toxins, which disrupt erythrocyte function, and the destruction of erythrocytes by the spleen, which clear the parasites from the bloodstream.<sup>7, 9</sup>

The general symptom of malaria includes the classic triad of cold stage, fever stage, and sweating stage. The acute (paroxysmal) fever typically begins with a cold stage (shivering) followed by high fever and then the profuse sweating stage. The fever believed to be associated with the rupture of merozoites or schizonts, the influence of glycosyl phosphatidylinositol (GPI), and the formation of cytokines or other toxins. 9 In hyperendemic areas, many people with parasitemia may not exhibit any fever or symptoms. Additional symptoms include headaches, nausea, vomiting, diarrhea and muscle or joint pain. These symptoms, combined with a history of visiting or living in an endemic area, receiving a blood transfusion, or previous malaria infection, may suggest a relapse of malaria.10

In some cases, malaria can progress to severe malaria, which is commonly caused by infections of *P. falciparum*, *P. vivax*, or *P. Knowlesi*. 8 However, severe malaria can also be caused by other types of Plasmodium species. Severe malaria is characterized by symptoms such as changes in consciousness, muscle weakness, recurrent seizures within 24 hours, metabolic acidosis, pulmonary edema, circulatory failure or shock, jaundice, abnormal spontaneous bleeding, hypoglycemia, severe anemia, hyperparasitemia, hyperlactatemia, and impaired kidney function. 8, 11 Severe anemia is the most common complication of *P. malariae* infection because of prolonged erythrocyte destruction and bone marrow suppression, even with low parasitaemia level. *P. malariae* infection can also cause nephrotic syndrome, which occurs more frequently in untreated infections with this species than with other Plasmodium species. 11 However, the current patient did not show any signs of severe malaria.

A definite diagnosis of malaria must be made by microscopic examination of blood smears and/ or rapid diagnostic tests (RDTs). RDTs are immunochromatographic tests that detect the presence of parasite antigen and are now recommended by the WHO as the first-line

diagnostic test in all malaria-endemic areas worldwide. 12

*P. malariae* has an incubation period of 18 to 40 days, which is considered relatively long. 5 This may explain why the patient first experienced symptoms almost one month after returning to Jakarta. Malaria caused by *P. malariae* is typically chronic and asymptomatic, with a relatively low parasitic load, usually less than 5,000 parasites/ $\mu$ L of blood. 5 The diagnostic method is microscopic examination of blood films and confirmation of parasites. However, this infection can be easily misdiagnosed when relying solely on microscopy. As a result, it is often mistaken as a bacterial infection, leading to delayed treatment and potentially severe complications. 5

One of the significant challenges in treating malaria in Indonesia is the resistance and reduced efficacy of several anti-malarial drugs, including chloroquine. This may be due to the irrational use of anti-malarial drugs in the past. According to the Decree of the Indonesian Minister of Health Number 556 of 2019 concerning the National Guidelines for Malaria Management Medical Services, patients positive for malaria (based on laboratory examination) should be treated using artemisinin-based combination therapy (ACT) such as DHP combined with Primaquin. This combination is currently considered the most effective treatment for killing malaria parasites and with the dose adjusted to the patient's weight or using a fixed dose combination of DHP. 3, 10 For patients with severe malaria, intravenous Artesunate (2,4mg/kg) can be administered three times, followed by oral DHP and primaquine once the patient's general condition improves and can receive oral medication. 10 The current patient was treated with DHP without primaquine considering that the infection was caused by *P. malariae*.

## CONCLUSION

In this case report, the patient's fever and other symptoms were attributed to malaria infection, which cause damaged to organs

including erythrocytes, leading to anemia. The patient was treated with artemisinin-based combination therapy, currently regarded as the most effective anti-malarial treatment. However, Plasmodium malariae parasites are often overlooked by light microscopy due to their low parasite density, which could become a significant problem if not promptly diagnosed and treated.

**Declaration by Authors**

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