

Concurrent Dengue and Malaria Infection: A Case Series

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ABSTRACT

Introduction: Malaria and dengue are endemic in Indonesia, and therefore, may result in the possibility of co-infection. Urban demographic expansion, deforestation, and agricultural settlements in peri-urban areas are known causes of the increase in the probability of concurrent infection of these two diseases. It is reasonable to envisage that the occurrence of concurrent infections would not be rare, mainly during outbreaks of dengue in the rainy season. However, due to non-systematic investigation of both diseases, only a few cases of malaria and dengue co-infection have been reported. These three patients demonstrated co-infection manifestations with good outcomes and prognoses. **Case Illustrations:** Two cases of co-infection of malaria vivax and dengue fever in male patients aged 35 and 43 years. The difference between these two cases is that one patient had experienced a previous episode of malaria with a fever lasting less than 5 days. Meanwhile, one patient who had never suffered from malaria experienced a relatively longer fever episode, up to 14 days. Thrombocytopenia in these two patients was still above 50,000/ μ L and rose quickly after anti-malarial administration. The third case was a 47-year-old woman with co-infection of malaria falciparum and dengue. This woman lived in Papua and had been infected with malaria before. This third case showed platelet numbers reaching levels as low as 38,000/ μ L and hypotension without signs of shock in the critical phase of dengue. The three patients did not show complications from other organs due to malaria or dengue and responded well to antimalarials with good outcomes. These patients were treated with a combination of DHP and primaquine, along with supportive care for fever and fluid management. **Conclusion:** Whenever co-infection is confirmed, we recommend careful monitoring for bleeding and hepatic complications, which may result in a higher chance of severity. Careful and intense monitoring of fluid requirements is necessary to avoid complications of fluid overload.

KEYWORDS:

Malaria, Dengue, Co-infection, Thrombocytopenia, DHP, Primaquine

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INTRODUCTION

Dengue and malaria are two of the most prevalent mosquito-borne diseases in tropical and subtropical regions, causing significant morbidity and mortality worldwide.¹ While both infections share similar clinical presentations, including fever, headache, and muscle pain, they are caused by different pathogens and transmitted by different

mosquito vectors.² Dengue is a viral infection spread by Aedes mosquitoes, while malaria is a parasitic disease transmitted by Anopheles mosquitoes.^{1,2} Due to their overlapping endemic areas and similar symptoms, concurrent infections of dengue and malaria can occur, presenting diagnostic and treatment challenges for healthcare providers.

In Indonesia, the dengue virus (DENV) is the primary arbovirus affecting humans. The four DENV serotypes can cause a spectrum of clinical manifestations, from mild, self-resolving febrile episodes to severe and potentially fatal forms of the disease.³ According to data from the Ministry of Health, as of the 17th week of 2024, there have been 88,593 cases of Dengue Fever (DF) with 621 fatalities in Indonesia. Reports indicate that out of 456 regencies/cities in 34 provinces, deaths due to DF occurred in 174 regencies/cities across 28 provinces. Dengue cases in Indonesia are reported throughout the year, with an increase in incidence at the end of the rainy season leading into the dry season. Currently, the outbreak cycle in some areas has shortened from every 5-10 years to every 2-3 years.⁴ Besides, 372 out of 514 districts in Indonesia (72.4%) had been certified as malaria-free by December 2022. However, in eastern Indonesia, many districts and cities remain highly endemic, accounting for over 90% of the reported malaria cases. The prevalence in these areas ranges from 0.02% to 12.07%. While most provinces experience hypo endemic to mesoendemic malaria, eastern Indonesia continues to face relatively intense transmission.⁵

Indonesia faces endemic malaria and dengue, creating potential for co-infection. Factors like urban expansion, deforestation, and peri-urban agricultural development increase the likelihood of

simultaneous infection with both diseases. Concurrent cases are particularly plausible during dengue outbreaks in rainy seasons. However, due to inconsistent screening practices for both illnesses, only a limited number of malaria-dengue co-infections have been documented, despite the probability that such occurrences may be more frequent than reported.⁶ Herein, we reported three patients demonstrated co-infection manifestations with good outcome and prognosis.

CASE ILLUSTRATIONS

Case 1

A 35-year-old male patient was admitted to the hospital in October 2023, presenting with a four-day history of high fever, nocturnal chills, nausea, and headache. He reported experiencing fatigue and anorexia. Upon clinical examination, his body temperature was recorded at 38.4°C, with no evidence of skin rashes or haemorrhagic symptoms. Hepatomegaly and splenomegaly were noted, classified as Schuffner grade 1. Laboratory tests revealed a total leukocyte count of 5400/ μ L, haemoglobin level of 12.4 g/dL, and a platelet count that had decreased from 105,000/ μ L to 89,000/ μ L. Liver function tests showed SGOT at 16 U/L and SGPT at 18 U/L, with a creatinine level of 1.2 g/dL. The patient had been stationed in Papua since 2021 and had previous episodes of malaria in 2021 and 2022. Blood smear analysis identified the presence of *Plasmodium vivax* trophozoites and gametocytes

(Fig. 1). Additionally, serological tests for dengue fever returned positive results for both IgM and IgG antibodies. The patient was treated with antipyretics, intravenous fluids, dihydroartemisinin-piperaquine (DHP) for three days, and primaquine for 14 days. His symptoms improved, and his platelet count increased to 227,000/ μ L upon discharge on the fifth day of hospitalization.

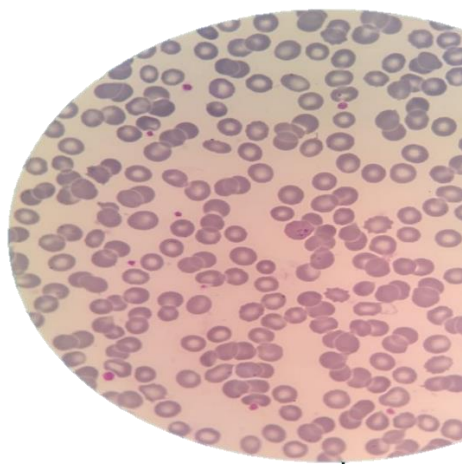


Figure 1. Blood smear analysis of the first patient, showed the presence of *Plasmodium vivax* trophozoites and gametocytes (Magnification 100x)

Case 2

A 43-year-old male patient was admitted to the hospital in December 2023, presenting with a two-week history of fever, chills, and rigors. He had recently returned from a two-month stay in Papua. Over the past two days, his symptoms had worsened, with episodes of vomiting, abdominal pain, and severe headache. Upon admission, his body temperature was recorded at 37.6°C, with no evidence of skin rashes or haemorrhagic manifestations. Hepatomegaly and splenomegaly were not observed. Laboratory tests revealed a haemoglobin level of 13 g/dL, a leukocyte count of 6700/ μ L, and a platelet count of 105,000/ μ L.

Liver function tests showed SGOT at 23 U/L and SGPT at 27 U/L, with a creatinine level of 1.4 g/dL. Blood smear analysis identified the presence of *Plasmodium vivax* trophozoites, schizonts, and gametocytes (Fig. 2). Serological tests for dengue fever returned positive results for IgG antibodies, but negative results for IgM antibodies. The patient was treated with analgesics, antipyretics, antacids, DHP, and primaquine. His platelet counts initially decreased to 65,000/ μ L on the third day of hospitalization but subsequently rose to 97,000/ μ L upon discharge. The patient responded well to treatment and was symptom-free on the sixth day of hospitalization.

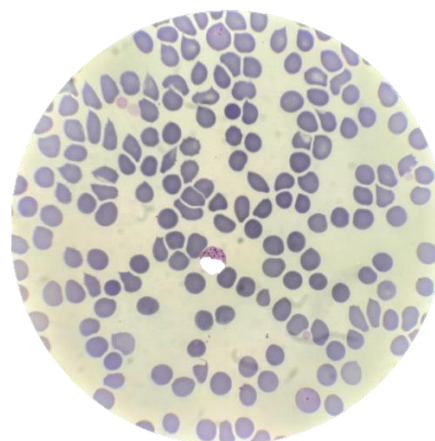
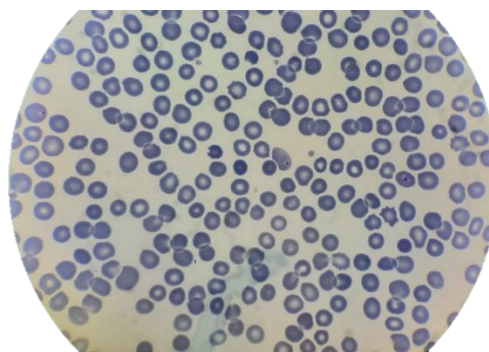


Figure 2. Blood smear analysis of the second patient, showed the presence of *Plasmodium vivax* trophozoites, schizonts, and gametocytes (Magnification 100x)

Case 3

A 47-year-old woman, a resident of Papua for 10 years, presented to the hospital in June 2024 with a four-day history of persistent fever, nausea, vomiting, and nocturnal shivering. She had a previous episode of malaria in 2006. Upon admission, her body temperature was 38.3°C. There were no haemorrhagic manifestations, but slight splenomegaly was noted. The patient exhibited hypotension with a blood pressure reading of 86/54 mmHg, though there were no signs of shock. Laboratory findings included a haemoglobin level of 9.7 g/dL, a leukocyte count of 4270/ μ L, and a platelet count that progressively decreased from 95,000/ μ L to 38,000/ μ L by the seventh day, before rising to 130,000/ μ L upon discharge on the fifth day of hospitalization. Liver function tests showed SGOT at 23 U/L and SGPT at 24 U/L, with a creatinine level of 0.7 g/dL. Serological tests for dengue returned positive results for both IgG and IgM antibodies. A blood smear revealed the presence of *Plasmodium falciparum* gametocytes. The patient was treated with antipyretics, fluid therapy, DHP, and primaquine. Her blood pressure normalized to 110/76 mmHg by the fifth day of hospitalization.

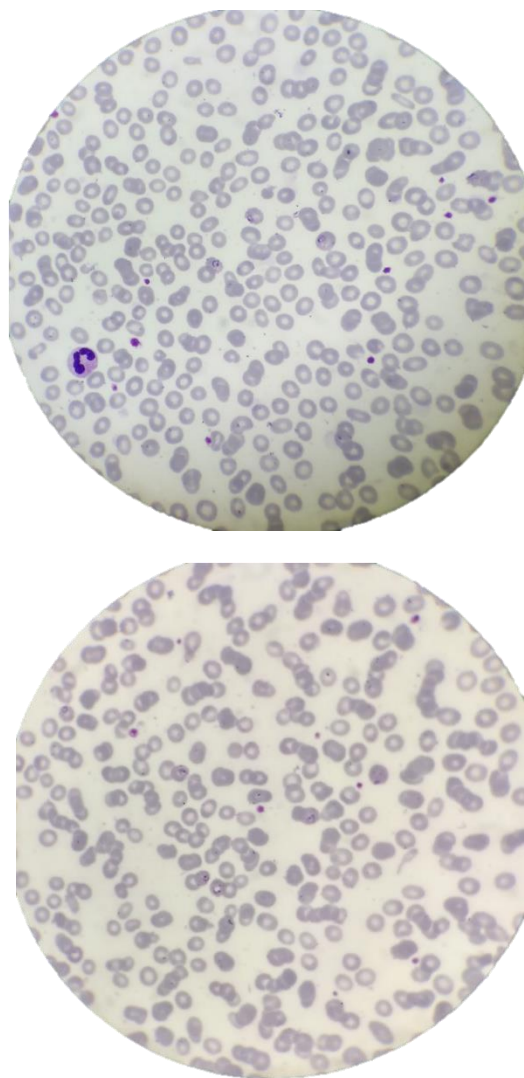


Figure 2. Blood smear analysis of the third patient, showed the presence of *Plasmodium falciparum* gametocytes (Magnification 100x)

DISCUSSION

In an endemic area of dengue fever and malaria, we found a high prevalence of the co-infection. During a dengue outbreak in India, the prevalence of co-infection was 5.8% among all cases of fever (77 of 546). In the French Guiana, the prevalence of co-infection was 7.1% (17 of 238) among patients with dengue, which is similar to our results. In Pakistan, however, the prevalence found was as high as 23.2%. Thus, the prevalence of co-

infection may fluctuate, depending on local endemicity. In these studies, the prevalence was estimated on hospitalized patients, therefore it could not be extrapolated to the community-based level.⁷

However, due to non-systematic investigation of both diseases, only a few cases of malaria and dengue co-infection have been reported. These patients usually demonstrated severe manifestations, in particular hepatic injury. Besides, we observed that the presence of jaundice in dengue patients, and bleeding in malaria patients, are possible indications of co-infection.⁷

A study showed that being co-infected resulted in a much higher chance of presenting deep bleeding as compared to both groups of mono-infected patients, suggesting a possible synergistic pathogenic mechanism, which could be related to both capillary fragility and coagulation disorders, but not the low platelet count. Bleeding is reported as an infrequent finding in malaria, despite common platelet depletion. Conversely, bleeding is the most feared complication of dengue fever, where in addition to platelet depletion, virus-induced endothelial and liver injury concur to the risk of coagulopathy.⁷ Hepatic injury was also a concern in the co-infected group, which, together with bleeding, resulted in a higher chance of dengue severity according to WHO criteria. Jaundice in malaria is mostly a result of cholestasis or

intravascular haemolysis, while in dengue fever it has been associated with fulminant liver failure.⁷

A warning sign commonly used to describe severe dengue is haemoconcentration (increase in the basal haematocrit <20%). However, even with more severe dengue cases, our co-infected patients presented a low mean of haematocrit. An explanation for this fact can be attributed to malaria-induced anaemia, a common complication in vivax malaria. For this reason, the malaria clinical manifestation may be a confounder for health care professionals during the interpretation and application of dengue severity criteria, in areas where both diseases occur. The proper clinical management of co-infected patients may be compromised due to diagnostic delays or misinterpretation, and inappropriate treatment may result in fatal complications.⁶

Dengue warning signs, such as vomiting, abdominal pain and hepatomegaly, were very frequent in the co-infection cases. The cautious detection of these signs is of extreme importance as they characterize potential dengue severity. Dyspnoea was also frequent in all groups, particularly in co-infected patients. Dyspnea is an early clinical feature of plasma leakage and, in dengue, may be the evidence of fluid accumulation of in the pleural cavity. In malaria, dyspnoea may be an evidence of acute lung oedema, which is one of the severity criteria for falciparum malaria. The

clinical management of these cases may be difficult, as the inadequate fluid therapy for dengue treatment may induce fluid overload and large fluid effusion to the lungs⁸.

Co-infected patients presented similar days of fever as compared to malaria patients. That means that a patient with the diagnosis of dengue presenting with prolonged evolution should raise the suspicion of malaria co-infection⁶. No specific dengue serotype was associated to the co-infected patients; however, the number of cases was not big enough to test that hypothesis.⁸

Dengue and malaria are two of the most common arthropod-borne illnesses, and co-infection cases, although rare, have been reported.¹ Our three patients diagnosed with co-infection exhibited stable clinical conditions and rapid clinical improvement after receiving anti-malarial treatment. All three patients had a history of living and traveling in malaria-endemic areas and had previously experienced episodes of malaria infection.

Direct malaria smear examination was performed on the day of hospital admission, enabling prompt diagnosis and treatment initiation. Serological testing for dengue considered the daily fever pattern and platelet count decrease. None of our patients showed significant haematocrit elevation, and fluid maintenance was administered according to the dengue fever algorithm without plasma leakage, except for the third patient who

presented with hypotension and received fluid according to the plasma leakage algorithm, which was adjusted based on clinical improvement to minimize the risk of fluid overload.⁹ First-line treatment for malaria vivax and falciparum was administered to our patients, along with fluid therapy and symptomatic medication, including paracetamol, anti-emetics, and analgesics. Parasite count evaluation was performed on the fourth day, with good results showing no parasites in the blood smear.¹⁰

Concurrent infections of dengue and malaria require prompt diagnosis and treatment to prevent severe complications.¹¹ Chloroquine, an antimalarial agent, has shown some antiviral effects and may be considered in the treatment of dengue-malaria co-infection. However, further studies are necessary to confirm the clinical effects and assess the side effects of chloroquine in dengue patients.^{11,12}

Complications commonly associated with co-infection, such as icterus, bleeding, and hepatic injury, did not occur in our patients. A prolonged fever period was only observed in one patient without a previous history of malaria, lasting 14 days. However, this patient also responded well to therapy and had a good outcome. According to the literature, liver dysfunction is a common complication in patients with co-infection, particularly those with a history of malaria.¹³ In patients with acute liver failure, the development of

jaundice, coagulopathy, and encephalopathy is common.¹⁴ However, in our study, none of the patients developed these complications. It is essential to note that the management of co-infection requires a multidisciplinary approach, including the administration of antimalarial and antiviral therapy, as well as supportive care to prevent complications.

CONCLUSION

Co-infection with malaria and dengue is a relatively frequent occurrence. Given that malaria diagnosis is more straightforward and rapid, it is advisable to systematically test for *Plasmodium* species in cases presenting with acute febrile syndrome in regions where these diseases are endemic. Furthermore, patients diagnosed with malaria who exhibit spontaneous bleeding should be systematically evaluated for dengue. Similarly, in patients with suspected or confirmed dengue who present with jaundice, an investigation for *Plasmodium* species should be conducted. Additionally, in instances where co-infection is confirmed, it is recommended to closely monitor for bleeding and hepatic complications, as these may increase the risk of severe outcomes. Careful and intense monitoring of fluid requirements is important to avoid complications of fluid overload¹⁵.

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