

# Malaria Strikes Beyond the Blood: Acute Hepatic Failure and Multiorgan Dysfunction Syndrome Caused by *Plasmodium falciparum* Infection

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N R Karthik <sup>1</sup>, Rajkumar C <sup>1</sup>, Srihari N <sup>1</sup>, Sriram Balaji <sup>1</sup>, Rachana R <sup>1</sup>, V Mardavada <sup>2</sup>, Sahasya Adalarasan <sup>2</sup>, Krithika S <sup>3</sup>, S Shivamalarvizhi <sup>1</sup>, Janarthanan S <sup>4</sup>, Jayaprakash N <sup>1</sup>, Kapil R. Alex <sup>2</sup>

1. Internal Medicine, Madras Medical College, Chennai, IND 2. Medicine, Madras Medical College, Chennai, IND 3. Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai, IND 4. Internal Medicine, Madras Medical College, Chennai, IND

**Corresponding author:** Sahasya Adalarasan, surgeonsahasya@gmail.com

## Abstract

Malaria is a major public health problem worldwide. Severe malaria can lead to multiorgan dysfunction syndrome (MODS), with manifestations including cerebral malaria, severe anemia, acute kidney injury, and hepatic impairment. In this case, we present a 34-year-old male who presented with jaundice, decreased urine output, and altered sensorium. He had tachycardia and tachypnea with mild hypoxia, suggestive of an underlying compensatory response to severe anemia and metabolic acidosis. Thrombocytopenia, an elevated international normalized ratio, and prolonged activated partial thromboplastin time were consistent with coagulopathy. Significantly elevated serum urea and creatinine levels were indicative of acute kidney injury. Contrast-enhanced CT of the abdomen demonstrated no radiological evidence of chronic liver disease, supporting an acute hepatic process. Furthermore, the peripheral blood smear demonstrated trophozoites and gametocytes of *Plasmodium falciparum*, indicating severe falciparum malaria as the underlying cause of the multiorgan dysfunction. The patient was managed with intravenous artesunate as first-line therapy and subsequently received comprehensive multidisciplinary supportive care for multiorgan dysfunction syndrome. This case highlights the rare occurrence of acute hepatic failure with hepatic encephalopathy as a manifestation of severe *P. falciparum* malaria and emphasizes the importance of early recognition, timely commencement of antimalarial therapy, and multidisciplinary management of malaria-associated multiorgan dysfunction.

**Categories:** Internal Medicine, Infectious Disease

**Keywords:** acute encephalopathy, acute fulminant hepatic failure, acute kidney injury, altered sensorium, coagulopathy, hyperbilirubinemia, malaria, multiorgan dysfunction syndrome (mods), plasmodium falciparum, severe anemia

## Introduction

Malaria continues to be a widespread issue in many parts of the world. An estimated 500 million individuals are affected each year globally, and approximately three million die of *Plasmodium falciparum* malaria [1,2]. This infectious disease is caused by protozoa of the genus *Plasmodium*, transmitted to humans through the bite of infected female Anopheles mosquitoes [3].

Among the *Plasmodium* species infecting humans, *P. falciparum* is most frequently associated with the most severe clinical forms. Its pathogenicity is associated with its ability to invade erythrocytes at all maturation stages, reach high parasitemia levels, and promote endothelial cytoadherence, resulting in profound microvascular occlusion. These mechanisms predispose the patient to severe complications [4]. Severe *P. falciparum* malaria may manifest as multiorgan dysfunction, such as cerebral malaria, severe anemia, acute kidney injury, and hepatic impairment [5].

Fulminant hepatic failure (FHF) is an extremely rare manifestation of severe malaria [6]. Serum levels of hepatic enzymes in malaria-associated FHF may be markedly elevated. Persistent fever, severe anemia, oliguria, and hepatomegaly are suggestive of malarial etiology [7].

Considering the overlap in clinical manifestations of hepatic failure, laboratory investigations are required to confirm malaria as the underlying cause. Repeated smears are required to confirm the diagnosis [8]. Artesunate-based therapy is considered the first-line treatment for all severe malaria cases, irrespective of the *Plasmodium* species involved [7]. In endemic areas, severe malaria should be included in the differential diagnosis of FHF [9].

We present the case of a 34-year-old male patient with FHF secondary to *P. falciparum* malaria, complicated by acute kidney injury, coagulopathy, and hepatic encephalopathy. This case highlights the need for a high degree of suspicion for severe malaria in a patient presenting with fever, hepatic dysfunction, and

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encephalopathy.

Case Presentation

A 34-year-old male patient, a chronic alcoholic for three years before presentation, exhibited yellowish discoloration of the eyes for one week, progressing to yellowish discoloration of the whole body over the preceding day before admission. He also had a fever persisting for four days prior that did not respond to medication, necessitating evaluation at a local primary health care center, where abnormal liver function tests were first detected. He also had an altered sleep pattern for one week prior to presentation. Around this time, he received complementary and alternative medicine (CAM), following which the severity of jaundice increased. He also had decreased urine output for two days and subsequently developed altered sensorium for one day, following which he was referred to a higher center.

On clinical examination, the patient was awake and irritable, afebrile, and not obeying oral commands, suggestive of hepatic encephalopathy. He had pallor, icterus, and pedal edema. Dyspnea, tachycardia (118/min), and tachypnea (22/min), with mild hypoxia (peripheral oxygen saturation (SpO2) 94%), suggested a compensatory response to severe anemia and metabolic acidosis. Abdominal examination revealed tenderness on superficial palpation (Table 1).

| Parameter             | Finding                             |
|-----------------------|-------------------------------------|
| General condition     | Awake and irritable                 |
| Response to commands  | Not obeying oral commands           |
| Temperature           | Afebrile                            |
| Pallor                | Present                             |
| Icterus               | Present                             |
| Pedal edema           | Present                             |
| Dyspnea               | Present                             |
| Pulse rate            | 118/min                             |
| Respiratory rate      | 22/min                              |
| SpO2                  | 94%                                 |
| Abdominal examination | Tenderness on superficial palpation |

TABLE 1: Clinical examination findings at presentation

SpO2: Peripheral oxygen saturation

Laboratory investigations showed decreased hemoglobin (8.3 g/dL), RBC count (2.57 million/cmm), and packed cell volume (PCV) (23.6%), consistent with anemia. The platelet count was significantly decreased to 11,000/cmm, further supported by an elevated international normalized ratio (INR) value (1.58) and prolonged activated partial thromboplastin time (APTT) (36.4 seconds). Elevated levels of direct bilirubin (30.85 mg/dL) and total bilirubin (31.34 mg/dL) were consistent with hepatic/obstructive jaundice, excluding hemolytic jaundice. Liver function tests revealed an elevated aspartate aminotransferase (AST) level of 207 U/L, an elevated alanine aminotransferase (ALT) level of 50 U/L, and alkaline phosphatase (ALP) of 148 U/L within the normal range, excluding obstructive jaundice and suggestive of hepatic jaundice. Total protein and albumin levels were reduced (5 g/dL and 2.3 g/dL, respectively), likely due to impaired hepatic synthetic function. A pH below the reference range (7.30) and reduced bicarbonate level (8 mmol/L) were indicative of metabolic acidosis, likely due to a combination of uremia and lactic acidosis secondary to tissue hypoperfusion. Serum urea (360 mg/dL) and creatinine (7.37 mg/dL) were significantly elevated, suggestive of acute kidney injury, along with elevated serum ammonia (244 μmol/L), reflecting hepatic dysfunction and reduced clearance. Serum sodium was reduced (128 mmol/L), indicating hyponatremia, and serum potassium was elevated (5.7 mmol/L), indicating hyperkalemia, both consistent with the underlying renal impairment (Table 2).

| Parameter        | Patient value    | Reference range     |
|------------------|------------------|---------------------|
| Hemoglobin       | 8.3 g/dL         | 13-17 g/dL          |
| RBC count        | 2.57 million/mm³ | 4.4-5.9 million/mm³ |
| PCV              | 23.6%            | 40-50%              |
| Platelet count   | 11,000/mm³       | 150,000-450,000/mm³ |
| APTT             | 36.4 sec         | 22-34 sec           |
| INR              | 1.58             | 0.8-1.2             |
| Direct bilirubin | 30.85 mg/dL      | <0.3 mg/dL          |
| Total bilirubin  | 31.34 mg/dL      | <1.2 mg/dL          |
| AST              | 207 U/L          | <40 U/L             |
| ALT              | 50 U/L           | <41 U/L             |
| ALP              | 148 U/L          | 44-147 U/L          |
| Total protein    | 5 g/dL           | 6.0-8.5 g/dL        |
| Albumin          | 2.3 g/dL         | 3.5-5.0 g/dL        |
| Arterial pH      | 7.30             | 7.35-7.45           |
| Bicarbonate      | 8 mmol/L         | 22-29 mmol/L        |
| Serum urea       | 360 mg/dL        | 13-43 mg/dL         |
| Serum creatinine | 7.37 mg/dL       | 0.5-1.4 mg/dL       |
| Serum ammonia    | 244 µmol/L       | 15-45 µmol/L        |
| Serum sodium     | 128 mmol/L       | 135-145 mmol/L      |
| Serum potassium  | 5.4 mmol/L       | 3.5-5.0 mmol/L      |

TABLE 2: Laboratory investigations and biochemical parameters at presentation
PCV: Packed cell volume, APTT: Activated partial thromboplastin time, INR: International normalized ratio, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase

A CT of the abdomen demonstrated no hepatomegaly. There was no ascites and no radiological evidence of chronic liver disease, supporting an acute rather than chronic hepatic process. It also revealed that the right kidney was not seen in the right renal fossa and was instead located in the right iliac fossa, with the hilum facing anteriorly. An ectopic and malrotated right kidney reflects a congenital anomaly incidental to the current illness (Figure 1).

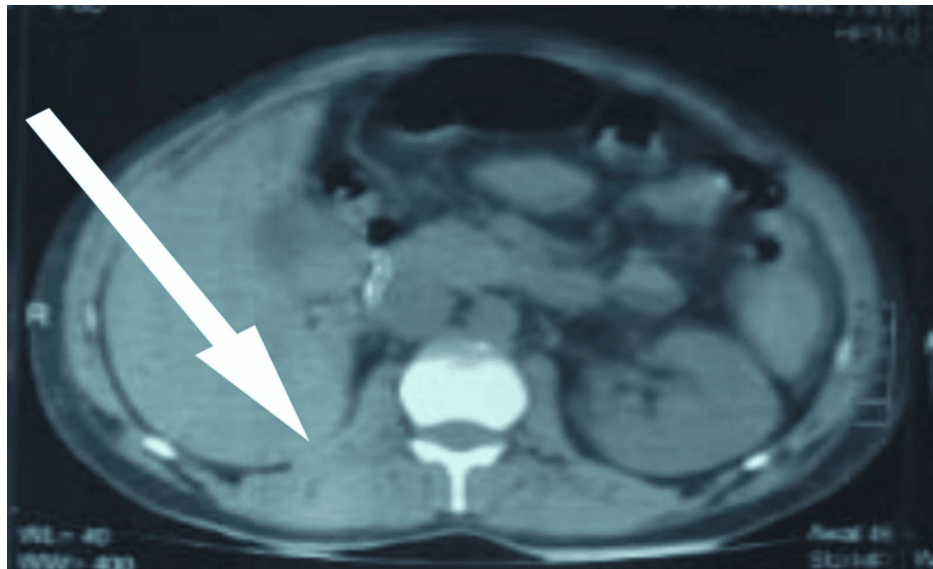


**FIGURE 1: An ectopic and malrotated right kidney (white arrow)**

The combined presentation of fever, jaundice, thrombocytopenia, and multi-organ dysfunction raised suspicion for a possible infective etiology underlying the fulminant hepatic failure, necessitating a peripheral smear examination. Peripheral smear examination demonstrated trophozoite and gametocyte forms of *P. falciparum*, confirming falciparum malaria as the underlying cause of the multiorgan dysfunction (Figure 2).

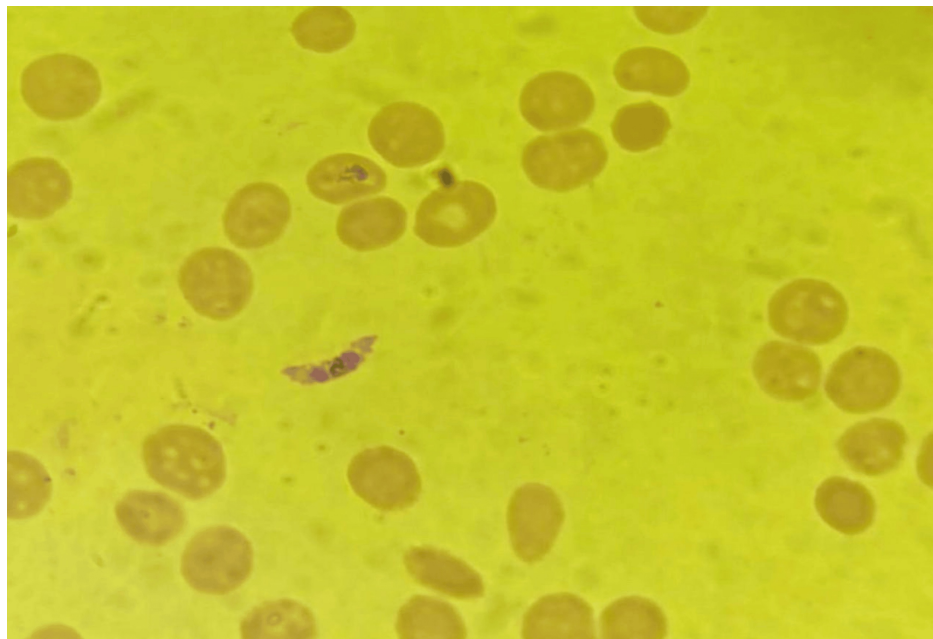


**FIGURE 2: Peripheral smear showing ring-form trophozoite and crescent-shaped gametocyte of *P. falciparum***

Considering the combined findings of clinical, laboratory, radiological, and peripheral smear examinations, the patient was diagnosed with multiorgan dysfunction syndrome (MODS), comprising FHF, hepatic encephalopathy (grade II), acute kidney injury (stage III), coagulopathy, and severe anemia, secondary to *P. falciparum* malaria. The patient was managed with intravenous artesunate (120 mg) as first-line treatment for severe *P. falciparum* malaria, given its effective antiplasmodial activity. He was started on intravenous meropenem (500 mg) and doxycycline (100 mg), each administered twice daily, to provide broad-spectrum antibacterial coverage against possible sepsis/bacterial infection in association with MODS. He was prescribed lactulose syrup (15 mL) three times daily and rifaximin (550 mg) twice daily to manage hepatic

encephalopathy. Intravenous N-acetylcysteine (1 g) was administered to support hepatocyte antioxidant defenses in acute hepatic failure. He was started on intravenous 20% human albumin (100 mL) to address hypoalbuminemia secondary to impaired hepatic synthetic function, along with intravenous vitamin K (10 mg) once daily to support hepatic synthesis of vitamin K-dependent clotting factors. Further supportive care, including head-end elevation at 30°, nasal oxygen supplementation, strict vital signs and intake-output charting, Ryle’s tube feeding, and intravenous fluids (10% dextrose and normal saline), was provided (Table 3).

| Treatment                         | Details                                                                                                          | Purpose                                                                        |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Antiplasmodial therapy            | Intravenous artesunate 120 mg as first-line treatment for severe <i>P. falciparum</i> malaria                    | Treatment of severe <i>P. falciparum</i> malaria                               |
| Antibacterial therapy             | Intravenous meropenem 500 mg twice daily and doxycycline 100 mg twice daily                                      | Coverage against possible sepsis/bacterial infection                           |
| Hepatic encephalopathy management | Lactulose syrup 15 mL three times daily and rifaximin 550 mg twice daily                                         | Management of hepatic encephalopathy                                           |
| Hepatoprotective therapy          | Intravenous N-acetylcysteine 1 g                                                                                 | Support of hepatocyte antioxidant defenses in acute hepatic failure            |
| Albumin replacement               | Intravenous human albumin 20% 100 mL                                                                             | Correction of hypoalbuminemia secondary to impaired hepatic synthetic function |
| Coagulation support               | Intravenous vitamin K 10 mg once daily                                                                           | Support of synthesis of vitamin K-dependent clotting factors                   |
| Supportive care                   | Head-end elevation at 30°, nasal oxygen supplementation, strict vital-sign monitoring and intake-output charting | General supportive management and monitoring                                   |
| Nutritional support               | Ryle's tube feeding                                                                                              | Maintenance of nutritional requirements                                        |
| Fluid management                  | Intravenous 10% dextrose and normal saline                                                                       | Fluid and metabolic support                                                    |

TABLE 3: Therapeutic management and supportive care

Discussion

Malaria is a major public health concern in many developing and tropical countries [1]. Severe *P. falciparum* malaria can rapidly progress to MODS, a life-threatening medical emergency necessitating urgent intensive care [10]. Hepatic dysfunction is frequent in malaria, but progression to acute liver failure is infrequent. Several mechanisms are responsible for liver injury, including microvascular accumulation of parasitized erythrocytes, endothelial dysfunction, decreased hepatic oxygen delivery, hemolysis, cholestasis, and oxidative stress [11].

Batibay et al. reported an adult patient originating from a malaria-endemic region who presented with severe jaundice, azotemia, and altered sensorium, with clinical findings and laboratory markers confirming acute liver failure and hepatic encephalopathy associated with severe *P. falciparum* infection [11]. Consistent with this, the present case features a 34-year-old male with a rare manifestation of acute hepatic failure with jaundice secondary to severe *P. falciparum* malaria. Notably, he demonstrated disproportionately elevated serum bilirubin levels compared with the degree of transaminase elevation.

Taha et al. reported a patient who presented with oliguric acute kidney injury, severe anemia, and markedly elevated serum creatinine and urea, confirming a diagnosis of acute renal insufficiency as a complication of severe *P. falciparum* malaria [12]. Similarly, the patient in the present case had a significantly elevated serum creatinine level of 7.37 mg/dL, urea of 360 mg/dL, oliguria, and metabolic acidosis, consistent with acute kidney injury. Renal involvement is another major component of MODS in this patient.

Jaundice, hepatomegaly, and mildly elevated transaminase levels are reported in 25% to 40% of adults with cerebral malaria and are attributed to hemolysis and localized microvascular congestion [13]. In contrast, the present case represents an extremely unusual manifestation of acute hepatic failure, accompanied by hepatic encephalopathy and altered sensorium, as confirmed by significantly elevated serum transaminase and ammonia levels.

In the present case, alcohol-associated hepatic injury may have impaired hepatic functional capacity.

However, the absence of radiological evidence of established chronic liver disease, together with the acute onset of symptoms and confirmation of *P. falciparum* infection on peripheral smear, supports severe falciparum malaria as a major contributor to the acute worsening of the clinical condition. The coexistence of hepatic, renal, hematological, and neurological dysfunction further supports the diagnosis of malaria-associated multiorgan dysfunction.

Timely recognition and treatment of severe malaria are crucial because untreated *P. falciparum* infection can progress rapidly to life-threatening multiorgan dysfunction. Therefore, intravenous artesunate was initiated as first-line antimalarial therapy. In addition to specific antimalarial therapy, management of this patient required multidisciplinary supportive care targeted at the individual organ dysfunctions, including measures for hepatic encephalopathy, coagulopathy, hypoalbuminemia, metabolic acidosis, anemia, and renal impairment.

Future advancements should focus on the early identification of malaria-associated hepatic dysfunction using reliable biomarkers and prognostic markers. Further research into the underlying mechanisms of hepatic injury may facilitate the development of targeted therapies and improve outcomes in patients progressing to hepatic failure and multiorgan dysfunction.

## Conclusions

This report presents the case of a rare and severe presentation of *P. falciparum* malaria accompanied by acute hepatic failure, coagulopathy, acute kidney injury, severe anemia, and hepatic encephalopathy. The marked hepatic dysfunction and multiorgan involvement highlight the potential for severe falciparum malaria to progress rapidly and result in life-threatening complications. This case emphasizes the significance of early recognition and prompt diagnosis of *P. falciparum* malaria, particularly in patients with a clinical presentation of jaundice and features of multiorgan dysfunction. Early initiation of antimalarial therapy, along with timely multidisciplinary supportive management, is essential to prevent further hepatic injury, advancement of organ dysfunction, and unfavorable outcomes.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Sahasyaa Adalarasan, Srihari N, N R Karthik, Sriram Balaji, V Mardavada, S Shivamalarvizhi, Janarthanan S, Krithika S, Jayaprakash N, Kapil R. Alex, Rachana R, Rajkumar C

**Acquisition, analysis, or interpretation of data:** Sahasyaa Adalarasan, Srihari N, N R Karthik, Sriram Balaji, V Mardavada, S Shivamalarvizhi, Janarthanan S, Krithika S, Jayaprakash N, Kapil R. Alex, Rachana R, Rajkumar C

**Drafting of the manuscript:** Sahasyaa Adalarasan, Srihari N, N R Karthik, Sriram Balaji, V Mardavada, S Shivamalarvizhi, Janarthanan S, Krithika S, Jayaprakash N, Kapil R. Alex, Rachana R, Rajkumar C

**Critical review of the manuscript for important intellectual content:** Sahasyaa Adalarasan, Srihari N, N R Karthik, Sriram Balaji, V Mardavada, S Shivamalarvizhi, Janarthanan S, Krithika S, Jayaprakash N, Kapil R. Alex, Rachana R, Rajkumar C

**Supervision:** Sahasyaa Adalarasan, Srihari N, N R Karthik, Sriram Balaji, V Mardavada, S Shivamalarvizhi, Janarthanan S, Krithika S, Jayaprakash N, Kapil R. Alex, Rachana R, Rajkumar C

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