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Two Cases of Malaria-Associated Acute Respiratory Distress Syndrome and Severe Pulmonary Complications From *Plasmodium falciparum* in Tanzania

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Manuscript Preparation E
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Case series
Patients: Male, 6-year-old • Male, 39-year-old
Final Diagnosis: Malaria ARDS
Symptoms: Difficulty in breathing
Clinical Procedure: —
Specialty: Anesthesiology • Critical Care Medicine • Physiology

Objective: Unusual clinical course

Background: Malaria remains a major cause of morbidity and mortality in tropical regions. Severe *Plasmodium falciparum* malaria can be complicated by malaria-associated acute respiratory distress syndrome (MA-ARDS), which has a high mortality rate, particularly in resource-limited settings where extracorporeal membrane oxygenation (ECMO) is unavailable. Clinicians in this setting must rely on the most readily available conventional methods to benefit patients and optimize treatment outcomes.

Case Reports: We describe 2 patients in Tanzania with severe *Plasmodium falciparum* malaria complicated by life-threatening pulmonary complications. Case 1 was a 6-year-old boy with severe malaria and multiorgan dysfunction who developed acute hypoxemic respiratory failure with diffuse pulmonary infiltrates requiring mechanical ventilation. He received intravenous artesunate, lung-protective ventilation, and prolonged prone positioning (up to 18 hours/day for 3 consecutive days), with gradual improvement and successful extubation on ICU day 6. Case 2 was a 39-year-old man referred after 1 week of treatment for severe malaria who developed MA-ARDS with bilateral pleural effusions, shock requiring norepinephrine, and acute kidney injury requiring hemodialysis; early mechanical ventilation with prone positioning improved oxygenation and supported recovery. These cases describe 2 patients who developed severe *Plasmodium falciparum* malaria resulting in MA-ARDS and were treated with favorable outcomes, regardless of the differences in their ages, by optimizing lung supportive ventilation and prone position, which significantly improved their conditions.

Conclusions: These cases emphasize that early recognition of MA-ARDS and implementation of evidence-based supportive strategies, particularly lung-protective ventilation and prone positioning, may improve outcomes in severe malaria when advanced therapies such as ECMO are not available.

Keywords: Case Reports • Malaria • Prone Position • Pulmonary Edema
Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/951737

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Introduction

Malaria is one of the most prevalent life-threatening parasitic infections worldwide and remains endemic in sub-Saharan Africa [1]. *Plasmodium falciparum* causes the most severe disease and is responsible for most malaria-related deaths [2,3]. A subset of patients with severe malaria develop pulmonary complications, including pulmonary edema, pleural effusion, and malaria-associated acute respiratory distress syndrome (MA-ARDS). Tanzania is among 11 countries with a high malaria burden, and approximately 4.4% of all malaria deaths annually occur in Tanzania [1-3]. Falciparum malaria alone accounts for more than 96% of all malaria cases in Tanzania [4,5]. The literature shows that more than 10% of patients with severe malaria will require intensive care unit (ICU) admission [5,6]. MA-ARDS is challenging to manage and is associated with high mortality, especially in settings where advanced respiratory support, such as extracorporeal membrane oxygenation (ECMO), is not available [7]. In such contexts, optimizing supportive care, including lung-protective ventilation, conservative fluid strategies, and prone positioning, is essential [8,9]. We present 2 cases of severe falciparum malaria complicated by life-threatening pulmonary manifestations managed in a resource-limited ICU.

Case Reports

Case 1

A 6-year-old boy of African descent presented to the outpatient department with a 4-day history of abdominal pain and vomiting. Vomitus was non-projectile and yellowish. He had been treated at a peripheral clinic for malaria and had received 2 doses of intramuscular artemether (34 mg per dose), without clinical improvement. He was unable to tolerate oral intake, and his parents noted facial swelling. Family and social histories were unremarkable.

On examination, he had fever (temperature 39.2°C) and jaundice and was moderately pale, with periorbital edema. His heart rate was 143 beats/min, and oxygen saturation was 94% on room air. Abdominal examination demonstrated right upper quadrant tenderness. He was admitted to the high-dependency unit with a working diagnosis of severe malaria. Laboratory results are summarized in **Table 1**.

Treatment was changed to intravenous artesunate (60 mg per weight-based dosing protocol), clindamycin 150 mg every 8 hours, and paracetamol as needed. A malaria blood film demonstrated a parasite density of 700 parasites per 200 white

Table 1. Laboratory investigations in case 1 from admission to discharge.

Test	Admission	ICU Day 2	ICU Day 4	ICU Day 6
Hemoglobin (11-13.5 g/dL)	7.7	9.2	11.2	15.6
Malaria B/S (parasites/200 WBC)	684/200 WBC	450/200 WBC	36/200 WBC	0/200 WBC
Creatinine (60-120 µmol/L)	124	96	47	67
Urea (2.5-7.8 mmol/L)	18	11	3.1	8
Bilirubin, total (3.4-20.5 µmol/L)	459	450	196	116
Bilirubin, direct (0-5.1 µmol/L)	380	371	171	102
AST (10-40 U/L)	2489	1330	667	220
ALT (7-56 U/L)	914	591	406	190
Albumin (35-54 g/L)	24.3	25.2	30	33
C-reactive protein (<1 mg/dL)	164	105	58	43
Procalcitonin (<0.1 ng/mL)	23	17	9	5
Hepatitis B	Non-reactive	–	–	–
Hepatitis C	Non-reactive	–	–	–
HIV	Negative	–	–	–
Calcium (2.1-2.6 mmol/L)	1.62	1.85	1.97	2.87
Magnesium (0.7-1.05 mmol/L)	0.98	1.13	2.1	3.35
Sodium (135-145 mmol/L)	127	130	132	130
Potassium (3.5-5.5 mmol/L)	5.18	4.8	3.1	3.3
Chloride (96-106 mmol/L)	104	100	98	97

Abbreviations: B/S, blood smear; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

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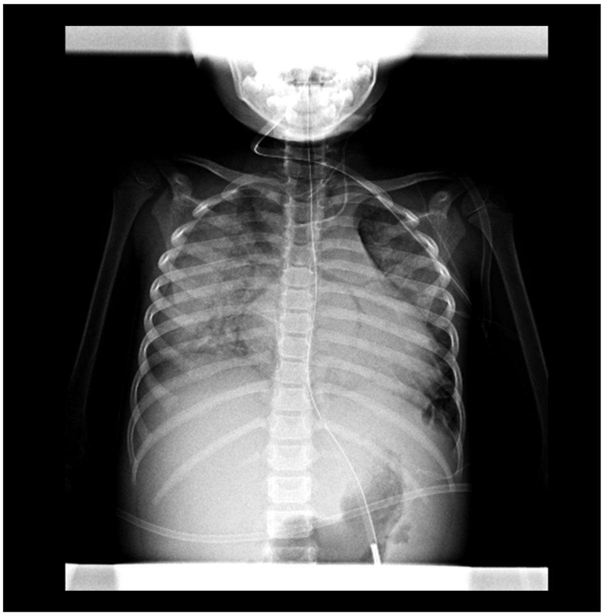

Figure 1. Chest radiograph (anteroposterior view) obtained in case 1 demonstrating diffuse bilateral pulmonary infiltrates consistent with pulmonary edema and acute respiratory distress syndrome.

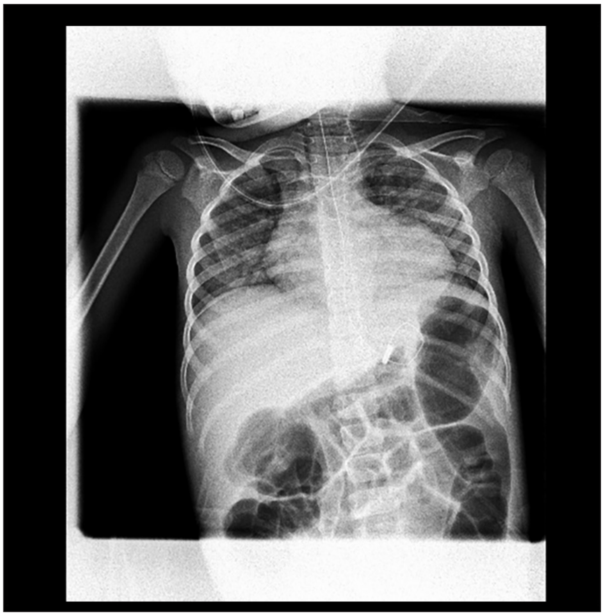

Figure 2. Follow-up chest radiograph in case 1 after extubation demonstrating interval improvement of bilateral pulmonary opacities.

blood cells. Renal function tests showed elevated levels of creatinine (124 µmol/L) and urea (18 mmol/L). Given evidence of multiorgan involvement (acute kidney injury and acute liver injury), he was transferred to the ICU for close monitoring and supportive management.

On ICU day 3, the child developed worsening respiratory distress with tachypnea (respiratory rate 50 cycles/min), increased work of breathing with accessory muscle use, and oxygen desaturation to 78% while receiving 6 L/min oxygen via nasal cannula. Lung auscultation revealed bilateral crackles, and bilateral lower-limb swelling was noted. Continuous positive airway pressure was initiated, but oxygenation did not improve after 12 hours. Chest radiography demonstrated diffuse bilateral pulmonary infiltrates consistent with pulmonary edema (**Figure 1**).

The patient was intubated and mechanically ventilated using pressure-control ventilation, with a fraction of inspired oxygen (FiO_2) of 0.80, inspiratory pressure of 28 cmH_2O, respiratory rate of 40 cycles/min, positive end-expiratory pressure (PEEP) of 10 cmH_2O, and tidal volume of approximately 91 mL. Sedation was initiated with midazolam infusion (0.5 mg/h). On ICU day 5, midazolam was discontinued due to concern for hepatic dysfunction and was replaced with dexmedetomidine infusion (10 µg/h).

Given persistent severe hypoxemia and diffuse infiltrates, prolonged prone positioning was implemented for 18 hours/day, with return to the supine position for the remaining period, for 3 consecutive days. Neuromuscular blockade with atracurium infusion was used on ICU days 1 and 2 because of ventilator asynchrony and was discontinued on ICU day 3. Ventilator settings were gradually weaned as oxygenation improved; FiO_2 was reduced from 0.80 to 0.35 by ICU day 4. The patient was successfully extubated on ICU day 6. A post-extubation chest radiograph showed marked improvement (**Figure 2**).

Case 2

A 39-year-old man of Asian descent presented to the emergency department with a 1-day history of progressive dyspnea. He was referred from peripheral health centers where he had been treated for severe malaria for 1 week. According to his next of kin, symptoms had not improved despite therapy. On arrival, he had fever (temperature 39.3°C) and jaundice. Oxygen saturation was 80% on room air, improving to 92% with 5 L/min oxygen via nasal cannula. His Glasgow Coma Scale score was 12/15 (E4, V2, M6), and he was agitated. Chest auscultation revealed crepitations, and bilateral lower-limb swelling was present.

A focused assessment with sonography for trauma (FAST) examination was performed to evaluate volume status; the inferior vena cava measured 1.2 cm in diameter. Laboratory investigations are summarized in **Table 2**. He was transferred to the ICU with a diagnosis of MA-ARDS, acute liver injury, and malaria-induced acute kidney injury.

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Table 2. Laboratory investigations in case 2 from admission to discharge.

Test	Admission	ICU Day 2	ICU Day 4	ICU Day 6
Hemoglobin	15	14.6	12	12
Malaria B/S (parasites/200 WBC)	320/200 WBC	400/200 WBC	250/200 WBC	80/200 WBC
Creatinine (60-120 µmol/L)	324	620	622	380
Urea (2.5-7.8 mmol/L)	28	26	24	22
Bilirubin, total (3.4-20.5 µmol/L)	300	200	120	28
Bilirubin, direct (0-5.1 µmol/L)	260	180	80	40
AST (10-40 U/L)	120	110	100	80
ALT (7-56 U/L)	280	220	100	60
Albumin (35-54 g/L)	34	32	34	30
C-reactive protein (<1 mg/dL)	100	102	80	32
Procalcitonin (<0.1 ng/mL)	2	2.4	2	1.2
Hepatitis B	Non-reactive	–	–	–
Hepatitis C	Non-reactive	–	–	–
HIV	Negative	–	–	–
Calcium (2.1-2.6 mmol/L)	2.8	2.6	2.4	2.2
Magnesium (0.7-1.05 mmol/L)	1.7	2.21	1.98	2.8
Sodium (135-145 mmol/L)	130	132	1401	128
Potassium (3.5-5.5 mmol/L)	4.8	6.2	5.8	5.2
Chloride (96-106 mmol/L)	1011	1106	110	102

Figure 3. Chest computed tomography (coronal reconstruction) in case 2 demonstrating bilateral pleural effusions with associated parenchymal changes.

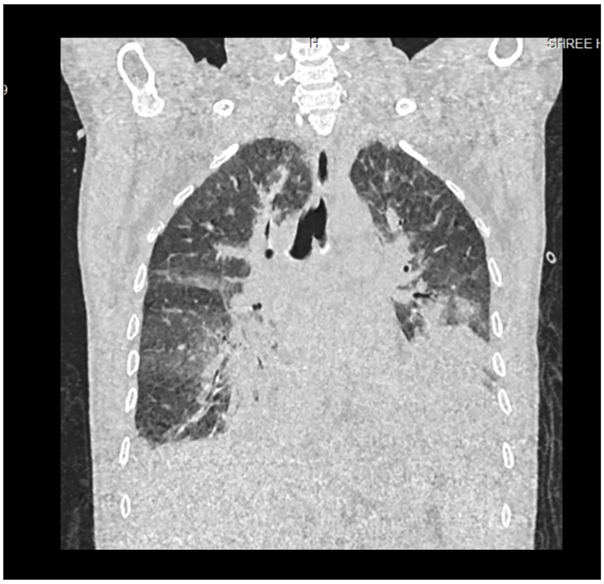

Figure 4. Chest computed tomography (sagittal reconstruction) in case 2 demonstrating more pronounced left-sided pleural effusion.

Table 3. Summary of published case reports of malaria-associated ARDS and reported outcomes.

Author and year	Age (y)	Presentation	Management	Outcomes
Elzein et al, 2017 [7]	29	Fever, flue-like symptoms, dyspnoea	Mechanical ventilation, antibiotics, artesunate-based therapy	Discharged after 21 days in ICU
	23	Fever, headache, nausea	BPAP, artesunate-based therapy	Discharged after 10 days
	29	Confusion, urinary incontinence	Blood transfusion, artesunate-based therapy, High flow nasal canula	Discharged after 10 days
Mohanty and Nandeeshwara 2019 [6]	34	Fever, vomiting, nausea	Mechanical ventilation, artesunate-based therapy, prone positioning	Discharged after 30 days
Monti, 2019 [8]	42	Headache, fever, pleural effusion	Artesunate-based therapy, prednisolone	Discharged after 10 days
Sanclemente-Cardoza et al, 2025 [11]	21	Fever,	Mechanical ventilation, hemodialysis	Death
Hilary et al, 2025 (the present case)	6	Vomiting	Artesunate-based therapy, modified proning	Discharged
	39	Difficulty in breathing	Artesunate-based therapy, haemodialysis, modified proning	Discharged

Abbreviations: ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

Within 2 hours of ICU admission, his condition deteriorated with worsening hypoxemia, desaturating to 60% despite 10 L/min oxygen via non-rebreather mask. Rapid sequence intubation was performed, and mechanical ventilation was initiated using volume-control ventilation, with tidal volume of 380 mL, respiratory rate of 18 cycles/min, and FiO_2 of 0.80. Norepinephrine infusion (0.6 µg/kg/h) was started for persistent hypotension.

On ICU day 2, hemodialysis was initiated because of oliguric acute kidney injury (urine output approximately 200 mL over 48 hours) with persistently elevated creatinine. Chest computed tomography demonstrated diffuse parenchymal changes with marked bilateral pleural effusions, more pronounced on the left (**Figures 3, 4**). Prone positioning was initiated early as an adjunct to lung-protective ventilation, resulting in improved oxygenation and enabling gradual ventilator weaning. A summary of similar published cases and reported outcomes is provided in **Table 3**.

Discussion

These 2 cases illustrate severe falciparum malaria complicated by life-threatening pulmonary involvement: pulmonary edema/ARDS in a child (case 1) and MA-ARDS with marked pleural effusions and multiorgan dysfunction in an adult (case 2). Previous studies have explored the pathophysiology of MA-ARDS, which remains one of the more unpredictable late complications of severe malaria [10].

In both of our patients, deterioration occurred in the setting of severe systemic disease and required escalation to invasive mechanical ventilation. Importantly, prone positioning was applied as a practical, low-cost intervention and was associated with progressive improvement in oxygenation and clinical recovery.

Presentation, Diagnosis, and Clinical Course

Both of our patients presented with fever and evidence of hemolysis and hepatic dysfunction (jaundice), consistent with severe malaria. Diagnosis was supported by malaria blood film microscopy demonstrating *P. falciparum* parasitemia. The patient in case 1 developed delayed respiratory deterioration with diffuse infiltrates consistent with pulmonary edema/ARDS after initial admission, whereas the patient in case 2 presented with established respiratory failure and progressed rapidly to refractory hypoxemia requiring intubation within hours. Both cases required ICU-level supportive care and careful adjustment of ventilator settings, sedation, and hemodynamic support.

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Comparison With Previously Reported Cases

MA-ARDS is an uncommon but well-described complication of severe *P. falciparum* infection and has been reported in both endemic and imported malaria settings. Similar to our experience, published case reports describe the use of lung-protective ventilation and prone positioning as effective adjuncts when hypoxemia is severe and persistent. Mohanty and Nandeeshwara [6] reported successful prone ventilation in severe ARDS due to falciparum malaria, emphasizing early application in conjunction with definitive antimalarial therapy. Other reports and reviews of pulmonary manifestations of falciparum malaria similarly highlight that, in the absence of advanced rescue therapies (eg, ECMO), meticulous supportive care and prone positioning can be lifesaving. Our cases add to this literature by demonstrating feasibility of prolonged proning (18 hours/day) and successful outcomes in both a pediatric and an adult patient treated in a resource-limited setting.

Supportive Management Considerations

Intravenous artesunate remains the first-line therapy for severe malaria [10,11]. Quinine is also used as a second-line treatment, especially when artesunate has failed to achieve the required parasitaemia clearance [12]. In older adult patients and those with significant heart conditions, such as arrhythmia, the administration of quinine has been a challenge in resource-limited settings [13]; therefore, artemisinin-based combination is commonly used in these settings. However, no malaria-specific treatment for ARDS exists, and management follows general ARDS principles. Lung-protective ventilation with lower tidal volumes, limitation of plateau pressures, and individualized PEEP are recommended. Permissive hypercapnia is often avoided in severe malaria when cerebral involvement is suspected, as hypercapnia can increase cerebral blood flow and intracranial pressure. In both of our cases, prone positioning was used to improve ventilation-perfusion matching and recruit dependent lung regions, a strategy supported by broader ARDS evidence and increasingly applied in low-resource ICUs.

Adjunctive Immunomodulation

The data reported on corticosteroid use in MA-ARDS are inconsistent. At least 1 randomized trial did not demonstrate benefit with pulse methylprednisolone and found its continued use was associated with a poor outcome [14]. A 2024 study by Oliveira et al found that use of non-steroidal anti-inflammatory drugs (aspirin) was associated with a large influx of inflammatory monocytes to the lung tissue [15]. Experimental and observational work has explored additional immunomodulators. In our cohort, the Janus kinase inhibitor tofacitinib was administered in the adult case early in the ICU course as an anti-inflammatory adjunct; however, evidence for this practice in MA-ARDS is limited and requires further study. No Janus kinase inhibitor was administered in the pediatric case, due to the absence of robust safety data in this context.

Studies have shown that ARDS caused by malaria is managed similarly to ARDS from other causes, without allowing permissive hypercapnia [16,17], since elevated carbon dioxide increases cerebral blood flow and, in turn, intracranial pressure, particularly in cases suspicious for cerebral malaria [17,18]. Lung protective ventilation should be used with lower tidal volumes (4-8 mL/kg), plateau pressures less than 30 cm of water, and PEEP, which can be adjusted depending on the patient's oxygenation status [19]. Prone positioning is an effective technique used in the ICU to improve oxygenation for patients with ARDS [20]; however, its use depends on the clinician's suspicion index. When applied in a timely manner, studies have shown that prone positioning can reduce ICU length of stay and improve outcomes [19,20]. In our resource-limited setting, where ECMO is unavailable, modified prone positioning was used in these 2 patients, both of whom were managed uneventfully until discharge.

Limitations

Confirmation of *P. falciparum* infection is ideally supported by representative photomicrographs of peripheral blood films. However, these films were accidentally discarded and cannot be retrieved.

Conclusions

MA-ARDS can occur in children and adults with severe falciparum malaria and can progress rapidly to respiratory failure. In resource-limited settings, early recognition and prompt escalation to evidence-based supportive care—particularly lung-protective ventilation and prolonged prone positioning—may improve oxygenation and outcomes when advanced rescue therapies such as ECMO are not available.

Department and Institution Where Work Was Done

Critical Care Department, Shree Hindu Mandal Hospital, Dar es Salaam, Tanzania.

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Consent

Written informed consent for publication was obtained from the patient or patient/guardian(s) and is available on request.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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