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ORIGINAL ARTICLE

Prevalence and predictors of malaria-associated acute kidney injury among adults with severe malaria in Tanzania

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ABSTRACT

Introduction: Severe *Plasmodium falciparum* malaria is a major public health challenge in sub-Saharan Africa, particularly in endemic regions like Tanzania. Among its complications, acute kidney injury (AKI) is one of the most severe, contributing to prolonged hospital stays, poor outcomes, and high mortality especially where dialysis services are limited. Despite its clinical importance, malaria-associated AKI (MAKI) remains under-recognised, and data on its predictors, recovery patterns and long-term kidney outcomes are limited. We report the prevalence, predictors and outcomes of AKI among patients with severe falciparum malaria admitted to Muhimbili National Hospital in Dar es Salaam, Tanzania.

Method: A hospital-based prospective cohort study was conducted in the nephrology wards of Muhimbili National Hospital. Patients with severe *Plasmodium falciparum* malaria admitted between January and October 2020 were consecutively enrolled. AKI was assessed at admission, after 48 hours, and on day 7. Kidney function was re-evaluated at three months to determine long-term kidney recovery. Associated factors were analysed using chi-squared tests followed by multivariate logistic regression, with a P value of <0.05 considered statistically significant

Results: A total of 318 falciparum malaria patients with a mean age of 40.2 ± 5.1 years were recruited into our study. The prevalence of AKI among severe falciparum malaria patients was 36%. On multivariate logistic regression, we found that advanced age, high parasitaemia count, anaemia and proteinuria were significantly associated with AKI. In-hospital mortality rate for patients with MAKI was 3.5%, and upon 3-monthly follow up, 6.1% of patients with MAKI persisted to chronic kidney disease (CKD).

Conclusion: Advanced age, high parasitaemia, anaemia, and proteinuria were independent predictors of developing acute kidney injury (AKI) among our patients with severe *Plasmodium falciparum* malaria. In addition, malaria-associated AKI was linked to in-hospital mortality and a risk of persistent kidney injury evolving into chronic kidney disease (CKD) at three months, underscoring the importance of early detection and intervention to improve patient outcomes.

Keywords: acute kidney injury, malaria-associated kidney injury, severe falciparum malaria, Kidney Disease Improving Global Outcomes.

INTRODUCTION

Severe *Plasmodium falciparum* malaria continues to pose a major health burden in sub-Saharan Africa (SSA), particularly in endemic regions such as Tanzania [1]. Despite global efforts to reduce malaria-related morbidity and mortality, the disease remains a leading cause of hospital admissions and deaths [2]. Acute kidney injury (AKI) is one of the most serious complications of severe falciparum malaria, significantly contributing to prolonged hospitalisation, poor clinical outcomes, and increased healthcare costs due to the need for kidney replacement therapy [3]. The impact is even more pronounced in settings with limited access to nephrology care, where

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delayed recognition and inadequate management of AKI often lead to increased mortality [4,5].

Despite the high burden of malaria in SSA, AKI remains an under-recognised yet life-threatening complication of severe malaria, affecting up to 45% of adult cases [6,7]. Mortality can reach 75% when dialysis is required but unavailable, a common scenario in many public health facilities across SSA, including Tanzania [6]. Emerging evidence indicates that even minor declines in kidney function are linked to increased risks of morbidity, mortality and progression to CKD [8]. In Tanzania, although the estimated prevalence of malaria-associated AKI (MAKI) is approximately 26%, critical gaps remain in understanding recovery trajectories and long-term kidney outcomes especially from public facilities where more than 80% of the population seek care [9]. Moreover, the clinical course and consequences of malaria-associated AKI vary considerably across settings, shaped by differences in patient characteristics, healthcare infrastructure, and standards of care [1].

To address this critical research gap, we investigated the predictors of acute kidney injury and characterised both short- and long-term kidney recovery patterns following malaria-associated AKI. By generating context-specific evidence from the leading tertiary public hospital in Tanzania, we sought to enhance understanding of disease progression and outcomes. The findings will support improved clinical risk stratification and guide timely interventions to reduce the burden of malaria-associated kidney complications in resource-limited settings.

METHODOLOGY

This was a hospital-based prospective cohort study conducted over a nine-month period (January to October 2020) at Muhimbili National Hospital (MNH), Dar es Salaam, the largest public tertiary hospital in Tanzania. We enrolled all adult patients admitted with severe *Plasmodium falciparum* malaria, defined according to WHO criteria, who met the inclusion criteria and provided informed consent [10,11].

The sample size was calculated using the Kish Leslie formula based on a previously reported prevalence of malaria-associated acute kidney injury of 26%, with a power of 80% and a margin of error of 5%. Patients were consecutively enrolled upon admission until the desired sample size was reached.

A total of 318 patients with severe *Plasmodium falciparum* malaria were included in the study. Their mean age was 40.2 ± 5.1 years. Most participants (75%) were male and had no known comorbidities (77%).

All patients presenting with clinical features of malaria were initially screened using the ParaHit malaria rapid diagnostic test (RDT), a lateral flow immunoassay that detects *Plasmodium falciparum*-specific histidine-rich protein II (HRP2) in blood. Those who tested positive underwent confirmatory testing with thick and thin blood smears. Thin smears were prepared by spreading blood at a 30–45° angle, air-dried, and fixed with methanol. Thick smears were stained with Field's stain A and B, and malaria parasites were quantified by counting against 200 white blood cells under a microscope. Parasitaemia severity was classified as mild (1–500 parasites/200 WBCs), moderate (501–1500/200 WBCs), and high (>1500/200 WBCs), corresponding approximately to <20,000, 20,000–60,000, and >60,000 parasites/μL, respectively.

Kidney function was evaluated by measuring serum creatinine by the Jaffe method, and acute kidney injury was diagnosed using the Kidney Disease: Improving Global Outcomes (KDIGO) classification criteria. Urinalysis was performed using the dipstick method to detect proteinuria. AKI was assessed throughout the course of hospital stay until discharge. For patients with persistent AKI at discharge, kidney function was reassessed at three months to determine whether kidney injury had resolved or progressed to chronic kidney disease (CKD), which was defined as an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2, persisting for ≥3 months, consistent with KDIGO guidelines [11].

An interviewer-administered questionnaire was used to collect patients' demographic data, clinical history, laboratory results, and treatment details. All patients received standard malaria treatment with artemisinin-based combination therapy as per the Tanzanian Standard Treatment Guidelines. Those diagnosed with AKI were managed by nephrologists in accordance with hospital protocols. Dialysis was initiated based on KDIGO indications including severe acidosis, refractory hyperkalemia, volume overload, or uremic complications.

Data were analysed using SPSS version 25. The prevalence of AKI during the hospital stay was determined based on the KDIGO criteria. Associations between potential predictors and AKI were initially assessed using chi-squared tests. Variables with P values less than 0.2 in univariate analysis were entered into multivariate logistic regression models to identify independent predictors. All statistical tests were two-tailed, with a P value of <0.05 considered statistically significant.

RESULTS

At admission, the majority of patients (59%) presented with mild parasitaemia, anaemia defined as haemoglobin

<11 g/dL (55%), thrombocytopenia with platelet counts <150 × 10³/mm³ (67%) and 73% had negative urine protein. The prevalence of AKI during hospitalisation was 36%, with most cases (49%) classified as AKI stage 3 (Table 1).

Table 1. Sociodemographic and clinical characteristics of study population (N = 318).

Characteristics	N (%)
Age (years)	
18–35	164 (52)
36–65	120 (38)
>65	34 (11)
Mean (SD)	40.1 (5)
Sex	
Male	238 (75)
Female	80 (25)
Comorbidities	
None	244 (77)
Hypertension	16 (5)
Diabetes	10 (3)
HIV	25 (8)
Others	23 (7)
Parasitaemia at admission (/200 WBCs)	
0	29 (9)
Mild (1–500)	187 (59)
Moderate (501–1500)	85 (27)
Severe (>1500)	17 (5)
Haemoglobin at admission (g/dL)	
<11	174 (55)
≥11	144 (45)
Mean (SD)	10.6 ± 2.7
Platelets at admission (×10³/mm³)	
≤ 50	43 (14)
51–100	97 (31)
101–150	73 (23)
>150	105 (33)
Median (IQR)	113.4 (69.1–162.5)
Urine dipsticks for protein	
None	233 (73)
+1	48 (15)
≥ +2	37 (12)
AKI	
Yes	114 (36)
No	204 (64)
AKI staging (KDIGO) (N = 114)	8 (42)
Stage 1	23 (20)
Stage 2	35 (31)
Stage 3	56 (49)

Abbreviations: SD, standard deviation; HIV, human immunodeficiency virus; WBC, white blood cells; IQR, interquartile range; AKI, acute kidney injury; KDIGO, Kidney Disease Improving Global Outcomes.

In the multivariate logistic regression analysis, several factors were found to be significantly associated with the presence of AKI: age 36–65 years (OR: 3.59, P = 0.003) and over 65 years (OR: 3.87, P = 0.04); moderate parasitaemia (501–1500/200 WBCs) (OR: 10.45, P = 0.003); severe parasitaemia (>1500/200 WBCs) (OR: 16.64, P = 0.018); anaemia (haemoglobin <11 g/dL) (OR: 5.66, P < 0.001); and presence of proteinuria, with progressively increasing odds for +1 (OR: 39.61, P < 0.001) and ≥+2 (OR: 44.20, P < 0.001) categories (Table 2).

The mean duration of hospital stay was 7.3 (±3.1) days for AKI patients and 2.5 (±1.1) days for non-AKI patients. Dialysis was required for 43% of patients diagnosed with MAKI. The in-hospital mortality rate among patients with MAKI was 3.5%, with a total of four deaths reported. At 90-day follow-up, seven patients (6.1%) had persistent kidney dysfunction consistent with chronic kidney disease (CKD) (Table 4).

DISCUSSION

Our study provides valuable insight into the clinical profile and outcomes of patients with malaria-associated acute kidney injury admitted to a tertiary referral hospital in Tanzania. Most patients were young adults without pre-existing comorbidities. A substantial number developed AKI during hospitalisation. Key clinical predictors of AKI included advancing age, high parasitaemia levels, anaemia, and the presence of proteinuria. Notably, dialysis was required in approximately half of those who developed AKI, and a small proportion experienced persistent kidney dysfunction at follow-up, meeting the criteria for chronic kidney disease.

In our study, AKI was observed in approximately one-third of patients on admission, indicating a substantial burden. This prevalence is slightly higher than that reported in the only previously published study from Tanzania, which documented an AKI prevalence of 26% among malaria patients admitted to a private tertiary facility in Dar es Salaam [9]. The higher prevalence observed in our study could be attributed to differences in study settings; our research was conducted in a public tertiary referral hospital that serves a larger and more diverse patient population and included those with severe falciparum malaria. In contrast, the previous study was conducted in a private hospital, where access may have been limited to patients with better health-seeking behaviour and resources. In addition, it included both severe and non-severe cases of *Plasmodium falciparum* malaria, which may have contributed to a lower observed incidence of AKI. Our findings are consistent with a growing body of literature from SSA highlighting that AKI is still a common and serious complication among

Table 2. Multivariate logistic regression analysis of factors associated with AKI among patients with severe falciparum malaria.

Parameter	Odds Ratio	95% confidence interval	P value
Sex			
Female	Ref.	Ref.	Ref.
Male	2.35	0.9–5.7	0.07
Age (years)			
18–35	Ref.	Ref.	Ref.
36–65	3.59	1.5–8.4	0.003
>65	3.87	1.1–13.9	0.04
Comorbidities			
None	Ref.	Ref.	Ref.
Hypertension	0.37	0.1–1.9	0.23
Diabetes	6.71	0.6–75.9	0.12
HIV	0.38	0.1–1.8	0.23
Others	1.56	0.4–6.4	0.54
Parasitaemia (/200 WBCs)			
0	Ref.	Ref.	Ref.
Mild (1–500)	1.77	0.4–8.0	0.46
Moderate (501–1500)	10.45	2.2–50.4	0.003
Severe (> 1500)	16.64	1.6–171.4	0.018
Haemoglobin (g/dL)			
<11	5.66	2.4–13.2	<0.001
>11	Ref.	Ref.	Ref.
Urine dipstick protein			
None	Ref.	Ref.	Ref.
+1	39.61	11.5–136.9	<0.001
≥ +2	44.20	8.3–235.4	<0.001

Abbreviation: Ref, reference; HIV, human immunodeficiency virus; WBC, white blood cells.

patients hospitalised with severe malaria. Studies from countries such as Ethiopia, Nigeria and Uganda have reported similar or even higher prevalence rates of MAKI, further underscoring the need for timely recognition and appropriate management strategies in endemic and resource-limited settings [6,12,13].

We found that age between 36 and 65 years, high parasitaemia, anaemia, and the presence of proteinuria were significantly associated with the occurrence of malaria-associated acute kidney injury. The association between high parasitaemia and AKI has been reported in several studies on severe malaria and is supported by multiple pathogenic mechanisms through which *Plasmodium falciparum* can directly cause kidney injury [7,9,12,14]. These include parasite sequestration in renal microvasculature, endothelial dysfunction, oxidative stress, and immune-mediated damage [1,15]. In addition, the presence of proteinuria remained the only significant factor associated with ongoing AKI at seven days, likely reflecting underlying glomerular and tubular injury, as well as continued endothelial activation and renal inflammation central to the pathogenesis of AKI in severe malaria [14].

In our study, nearly half the patients with MAKI required dialysis, underscoring the severe impact of *Plasmodium falciparum*-related renal complications and aligning with previous data in SSA for which AKI requiring dialysis ranged from 40% to 70% of patients [12,13,16]. This high demand for dialysis significantly increases the cost of care, particularly in resource-limited settings where malaria is endemic and dialysis services are both scarce and expensive with most patients paying out of pocket [17,18]. Although most patients recovered, a small but clinically significant proportion experienced persistent kidney dysfunction beyond three months, progressing to chronic kidney disease. Moreover, AKI, even when followed by apparent full recovery, is increasingly recognised as an independent risk factor for both CKD and cardiovascular disease [8]. These findings suggest that patients recovering from MAKI remain at risk, with uncertain long-term outcomes. The possibility of subclinical or unresolved kidney damage progressing silently

further highlights the importance of structured follow-up and surveillance to identify those at risk early and the implementation of appropriate interventions.

Although our study demonstrated that nearly half of those patients with MAKI required dialysis, this result may not be generalisable to all malaria cases due to selection bias. Nonetheless, independent predictors of AKI, such as advanced age, high parasitaemia, anaemia and proteinuria, highlight key risk factors that can inform early identification and targeted interventions. Strengthening malaria case detection and initiating prompt management remain critical to preventing AKI and its associated complications. Early recognition is particularly important in resource-limited settings, where progression to chronic kidney disease further strains already burdened healthcare systems.

Our study, having been conducted at the largest public tertiary and referral hospital in Tanzania and providing access to a diverse patient population, allowed for comprehensive evaluation and management, including access to nephrology services and dialysis, which strengthens the reliability of our findings. However, a notable limitation is that these results may not be generalisable to lower-level health facilities, which constitute over 90% of healthcare centres in Tanzania. Such facilities often lack specialised nephrology care and dialysis services, which could result in different clinical outcomes and management patterns for patients with malaria-associated AKI. Consequently, the overall burden and outcomes of AKI across the wider population may be underestimated in this report.

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Ethics statement

Ethical approval was sought from the MUHAS Research Ethics Committee (MUHAS-REC-06-2020-245). Informed written consent was obtained from all participants before data collection. Permission to conduct the study was obtained from the administration of Muhimbili National Hospital.

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Conflict of interest

The authors have no conflicts of interest to declare.

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