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Acute kidney injury among children with severe malaria at St. Francis Hospital Nsambya in Kampala City, Uganda: A retrospective study

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Abstract

Background

Acute kidney injury (AKI) is a common complication of severe malaria, arising from multiple pathophysiological processes. AKI is increasingly recognized as a critical contributor to morbidity and mortality in pediatric populations in Sub-Saharan Africa. This study assessed the prevalence of AKI and its associated factors among children diagnosed with severe malaria at St. Francis Hospital Nsambya.

Methods

This was a retrospective cross-sectional study in which the medical records of 198 children aged 2 months to 12 years admitted between 1st January 2019 and 31st December 2023 were reviewed. AKI was defined using the Kidney Disease Improving Global Outcomes (KDIGO) criteria based on fold change in admission creatinine from estimated baseline. A minimum creatinine value of 0.4mg/dL was required to be considered AKI. Logistic regression analysis was performed to assess factors associated with AKI. A $p < 0.05$ was considered statistically significant.

Results

The median (IQR) age of participants was 5 (2–7) years, and the majority were males 130 (65.7%). Overall, 1 in 2 children had AKI (49.5%) with 31.6% (198) participants having stage 3, 24.5% stage 2 AKI, and 15.3% required dialysis. Mortality was confined to children with AKI, with a mortality rate of 4.1% in AKI and highest in stage 3 AKI (9.7%). On multivariable analysis, younger age (aOR 0.6, 95% CI 0.51–0.71), higher BUN (aOR 1.1 per mg/dL, 95% CI 1.03–1.12), and lower hemoglobin levels (aOR 1.3, 95% CI 1.1–1.48) were independently associated with AKI.

Conclusion

This study found a high prevalence of AKI in children with severe malaria with younger children and children with lower hemoglobin most at risk. Routine early screening and close monitoring of renal function is recommended for all severe malaria cases in hyperendemic areas.

Introduction

Globally, the number of malaria cases was estimated at 263 million in 2023, with an incidence of 60.4 cases per 1000 population at risk [1]. The African region continues to carry the heaviest burden of the disease, accounting for an estimated 94% of global malaria cases and 95% of the 597,000 global malaria

deaths, with Uganda among the top five countries for malaria burden, accounting for 5% of global malaria cases and 3% of global deaths [1].

Malaria is a leading cause of child mortality in Uganda, responsible for an estimated 4,817 deaths in 2022 [2]

Complications of severe malaria involve the nervous, respiratory, renal, and hematopoietic systems [3]. Among the complications of severe malaria, acute kidney injury (AKI) is increasingly recognized as a critical contributor to morbidity and mortality in pediatric populations in Sub-Saharan Africa, with a stepwise increase in mortality across AKI stages [4, 5]. AKI in malaria often arises from multiple pathophysiological processes, including intravascular hemolysis, hypovolemia, renal hypoperfusion, and immune-mediated injury [6]. Using the Kidney Disease Improving Global Outcomes (KDIGO) criteria to define AKI, an estimated 24–59% of African children with severe malaria have AKI, with most AKI community-acquired [5]. AKI is also a risk factor for post-discharge mortality and is associated with increased long-term risk of neurocognitive impairment and behavioral problems in survivors [5].

In Uganda, it has been shown that over 47% of children with severe malaria develop AKI, with higher rates observed in children presenting with delayed care, dehydration, concurrent infections, or low socio-economic status [7]. Early identification of AKI is crucial, as timely intervention can prevent progression to chronic kidney disease or death. However, limited data exist on the burden and associated risk factors of AKI in pediatric malaria cases in Uganda, particularly in urban tertiary hospitals. There is evidence that even small changes in kidney function are associated with increased morbidity, mortality, and the risk of developing chronic kidney disease (CKD) in children with severe malaria [8]. This study aimed to provide insights into the epidemiology of acute kidney injury among pediatric patients with severe malaria and determine the associated risk factors.

Materials and methods

Study design and setting

This was a retrospective cross-sectional study conducted between June and December 2024, using hospital records obtained between 1st January 2019 and 31st December 2023. The study was conducted at St. Francis Hospital Nsambya. The hospital is a private, not-for-profit (PNFP) tertiary referral hospital located 4.7 km from the capital city, Kampala, with a total bed capacity of 400. The hospital receives over 30 children with malaria per day, who receive a wide range of services including initial stabilization, outpatient and inpatient management, specialist physician consultations, ICU admissions, dialysis, and others. AKI management at St. Francis Hospital Nsambya involves antimalarial treatment according to Uganda Clinical Guidelines, fluid resuscitation where necessary, management of electrolyte and acid-base imbalances, supportive care, and renal replacement therapy, including hemodialysis or peritoneal dialysis.

Study population

This comprised of children aged 2 months to 12 years with severe malaria admitted at the pediatric ward of St. Francis Hospital Nsambya over one year. presenting with one or more features of severe disease or danger signs**,** including impaired consciousness or coma, prostration (inability to sit, stand, or drink), repeated convulsions, severe anemia (hemoglobin <5 g/dL or hematocrit <15%), hypoglycemia (<2.2 mmol/L), respiratory distress or metabolic acidosis, acute renal failure (urine output <0.5 ml/kg/hour or raised serum creatinine), jaundice with evidence of other organ dysfunction, pulmonary oedema, significant bleeding or shock, hemoglobinuria, or hyper parasitemia, requiring urgent parenteral antimalarial treatment and inpatient management [9]. These features were extracted from patient records. children with any form of malnutrition, preexisting kidney diseases, and other conditions that cause chronic kidney injury, such as hypertension, sickle cell disease, and chronic glomerulonephritis were excluded.

Sampling method and Sample size estimation

The study employed a census sampling approach, in which all available patient files meeting the inclusion criteria were reviewed.

Study variables

Study outcome

The primary outcome was AKI, which was defined using the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria [10] based on the fold change in admission creatinine from estimated baseline. Stage 1 AKI was a 1.5 to <2.0-fold increase in creatinine, stage 2 AKI was a 2.0 to <3.0-fold increase, stage 3 AKI was ≥3.0-fold increase in creatinine. Baseline creatinine was estimated assuming a normal GFR of 120mL/min per $1.73m^2$ and using age-based equations to back-calculate baseline creatinine[11]. A minimum creatinine value of 0.4mg/dL was required to be considered AKI. Secondary outcomes included receipt of hemodialysis and in-hospital mortality.

Independent variables included sex**,** age in years, and selected clinical and laboratory parameters at admission, namely blood urea nitrogen (BUN, mg/dL)**,** hemoglobin level (g/dL)**,** and serum potassium (mmol/L)**,** whose values were extracted from patient records.

Data collection process and procedure

The data was collected by the principal investigator (PI) and three trained research assistants. All physical files of children managed for severe malaria between 1st January 2019 to 31st December 2023 were retrieved from the hospital records office and assessed for eligibility.

Data extraction was guided by a Google Forms questionnaire to collect de-identified data from patient files, and were entered online by research assistants using password protected accounts.

Management of missing data

Prior to data extraction, all selected files were reviewed for data completeness and accuracy. Patient files with major missing variables essential for diagnosing acute kidney injury (e.g., serum creatinine or urine output and clinical features of severe malaria) were excluded. Files with more than 10% missing data of other variables were also excluded, with 35 files excluded from the study due to incomplete data.

Statistical analysis

Data analysis was performed using STATA version 16.0. Descriptive statistics such as means, medians, and standard deviations were used to summarize continuous variables, while frequencies and percentages were used for categorical variables. The prevalence of AKI was defined as the proportion of participants who met the KDIGO criteria for AKI among all participants recruited. A modified Poisson regression analysis was used to assess the associated factors. All variables with $p<0.2$ on bivariate analysis and a known biological plausibility were considered for multivariate analysis. The final multivariate model was built using the stepwise selection and $p<0.005$ was considered statistically significant.

Results

The study involved 198 children admitted with severe malaria, with a median (IQR) age of 5 (2.1 – 7) years, and male predominance (65.7%, n=130). Anemia was highly prevalent, with 59.1% (n=117) having hemoglobin of 5-11 g/dL, and 9.6% (n=19) had severe anemia of <5 g/dL. Hypokalemia was present in 41.4% (n=82) of children, hyperkalemia was noted in 17 (8.5%), and 4 children (2.0%) died during admission (***Table 1***).

Table 1: Sociodemographic, clinical, and laboratory characteristics of pediatric patients with severe malaria at St. Francis Hospital Nsambya

Variable	N=198
Age (years), median (IQR)	5 (2.1 – 7)
Age category, n (%)	
<2	30 (15.1)
2-5	63 (31.8)
6-10	72 (36.4)
>10	33 (16.7)
Sex, n (%)	
Male	130 (65.7)
Female	68 (34.3)
Laboratory parameters	
Creatinine (mg/dl)	0.5 (0.41 – 0.52)
Creatinine category, n (%)	
<0.3	20 (10.1)

0.3 – 0.7	141 (71.2)
>0.7	37 (18.7)
BUN (mg/dl)	9.33 (9.33 0 16.01)
BUN category	
< 5	8 (4.0)
5-18	144 (72.7)
>18	46 (72.7)
Hemoglobin (mg/dL)	10.2 (7.6 – 11.7)
Hemoglobin category, n (%)	
<5	19 (9.6)
5-11	117 (59.1)
≥12	62 31.3
Serum potassium (mmol/L)	3.56 (3.24 – 4.42)
Potassium category, n (%)	
< 3.5	82 (41.4)
3.5 – 5.5	99 (50.0)
>5.5	17 (8.5)
Outcomes	
Received hemodialysis, n (%)	16 (8.1)
Died, n (%)	4 (2.0)

Data presented as median (interquartile range) or n (%)

Prevalence of AKI in severe malaria.

Based on KDIGO criteria, the prevalence of AKI was 49.5% (n=98/198), for which 31.6% (n=31/98) had stage 3 AKI, 24.5 (n=24/398) had stage 2 AKI, and 15.3% (n=15/98) had received renal replacement therapy (hemodialysis). In-hospital mortality was noted in 4.1% (n=4) of children with AKI in severe malaria (**Table 2**).

Table 2: Prevalence of AKI, AKI stage, renal replacement therapy and mortality among children with severe malaria at St. Francis Hospital Nsambya

Variable	Frequency (n=198)	Percentage
Diagnosis of AKI		
Yes	98	49.5
No	100	50.5
Stage of AKI (n=98)		
One	43	43.9
Two	24	24.5
Three	31	31.6
Renal replacement therapy (n=98)	15	15.3
In hospital mortality (n=98)	4	4.1

Factors associated with AKI in children with severe malaria

Using logistic regression analysis, younger age, higher blood urea nitrogen (BUN) levels, and lower hemoglobin concentrations were independently associated with AKI among children with severe malaria. Each increasing year of age was associated with a 40% reduction in the odds of AKI (aOR 0.6, 95% CI 0.51–0.71; $p < 0.001$), while rising BUN levels significantly increased the odds of AKI (aOR 1.1 per mg/dL increase, 95% CI 1.03–1.12; $p < 0.001$).

Lower hemoglobin levels were also independently associated with AKI (aOR 1.3, 95% CI 1.1–1.48; $p = 0.001$). Although female sex and elevated serum potassium were associated with AKI in unadjusted analyses, these associations did not remain statistically significant after adjustment (**Table 3**).

Table 3: Factors associated with AKI in children with severe malaria

Variable	cOR [95% CI]	P-Value	aOR [95% CI]	P-Value
Sex				
Male	1		1	
Female	1.5 [.75 - 2.43]	0.318	1.8 [0.84 - 4.07]	0.127
*Age (years)	0.7 [0.64 - 0.8]	<0.001	0.6 [0.51 - 0.71]	**<0.001**
*BUN (mg/dl)	1.1 [1.02 - 1.09]	0.02	1.1 [1.03 - 1.12]	**<0.001**
*Hemoglobin (mg/dl)	1.1 [0.98 - 1.18]	0.013	1.3 [1.1 - 1.48]	**0.001**
*Serum potassium (mmol/L)	2.12 [1.49 - 3.04]	<0.001	1.4 [0.9 - 2.33]	0.129

**Continuous variables*

Association between acute AKI and mortality in children with severe malaria.

Mortality was significantly higher among children with AKI (4.1%) compared to those without AKI (0.0%). Furthermore, mortality increased with AKI severity, with the highest mortality observed among children with stage 3 AKI (9.7%) (**Table 4**).

Table 4: Association between acute AKI and mortality in children with severe malaria.

Variable	Died	Survived	P-Value
Diagnosis			
No AKI	0 (0.0%)	100 (100%)	0.041
AKI	4 (4.1%)	94 (95.9%)	
AKI stage			
No AKI	0 (0.0)	100 (100.0)	0.008
Stage 1	1 (2.3)	42 (97.7)	
Stage 2	0 (0.0)	24 (100.0)	
Stage 3	3 (9.7)	28 (90.3)	

Discussion

This was a retrospective chart review study to determine the prevalence and factors associated with acute kidney injury among children with severe malaria at a tertiary hospital in Uganda with access to

specialized nephrology services. The prevalence of AKI was 49.5%, consistent with other studies conducted in Uganda [8, 12, 13]. Among children with AKI, 15% required hemodialysis, and mortality was 4% among patients with AKI, increasing to 9.7% among children with stage 3 AKI. Compared to global estimates and past studies in African children with severe malaria-associated AKI requiring dialysis, mortality was low, suggesting severe malaria-associated AKI is amenable to intervention with good clinical recovery when recognized and complications managed.

Plasmodium falciparum is known to cause significant intravascular hemolysis, microvascular sequestration of parasitized erythrocytes, and intense inflammatory responses, all of which impair renal perfusion and precipitate acute tubular necrosis [15]. The similarity of prevalence across Jinja, Mulago, Kiryadongo, and the current study suggests a high burden of malaria-associated AKI in endemic, resource-limited settings, reflecting both the severity of disease at presentation and limited access to early diagnostic and supportive renal care. These findings are, however, lower than reported in other studies in the region, where an AKI prevalence of 38% was noted in Nigeria [8, 11] and 23.6% in the Democratic Republic of Congo [16]. The discrepancies may be attributed to differences in AKI definitions, timing of assessment, disease severity, age of the population, and the epidemiology of malaria and underlying population immunity across settings.

The present study found a significant association between AKI in severe malaria and younger age. Consistent with our results, younger age has been identified in other research as a risk factor for AKI in severe malaria [17], possibly reflecting greater vulnerability of renal function to hypoperfusion and metabolic stress in younger children.

Elevated BUN has also been associated with AKI and adverse outcomes in severe malaria, reflecting greater degrees of renal dysfunction or prerenal azotemia due to dehydration, hypovolemia, and impaired renal perfusion [18]. In the AQUAMAT study, a BUN above 20mg/dL was identified as an independent predictor of mortality, while recent efforts to refine

thresholds to identify patients at increased risk of mortality recommend a BUN above 28mg/dL.

In the present study, there was an increase in AKI among children with relatively high hemoglobin levels. As the study was conducted at a private hospital where children may come from higher-income backgrounds, be older, and have more limited exposure to malaria, the frequency of severe anemia was relatively low at < 10%. However, acute hemolysis and release of nephrotoxic hemoglobin pigments in malaria may contribute to renal tubular damage even when measured hemoglobin is relatively higher. Hemolysis and impaired microcirculation have been implicated in the pathogenesis of malaria-associated AKI in prior studies [8]. Given the retrospective nature of the study, we were unable to assess the relationship among AKI, hemoglobin, parasite density, and hemoglobinuria.

Study Strength and limitations

As this was a retrospective cross-sectional study, there were limitations in the availability of information collected, as it relied on investigations ordered during hospitalization. As a result, data that were not systematically collected and recorded during clinical care were excluded, and approximately 7% of records with more than 10% missing data were excluded. However, as data were collected over an entire year, we were able to capture seasonality. As the study was conducted at a private not-for-profit facility with specialized nephrology services, routine assessment of renal function resulted in > 90% of children hospitalized with severe malaria included in the analysis. Further, as an urban site with dialysis access, this study provides important insights into clinical outcomes when care is available, despite limitations in sample size.

Conclusion

This study confirms a high prevalence of AKI in children with severe malaria. Routine early screening and close monitoring of renal function should be integrated into the management of all children with severe malaria, with particular attention to younger children. Appropriate AKI management with timely initiation of dialysis was associated with low mortality.

Declarations

Ethical approval and consent to participate

Approval for the research was obtained from St. Francis Hospital Nsambya Research Ethics Committee number-NH/DDCS/RESCH/24/24. We did not require consent for participant participation but a waiver of consent to access hospital data, which was obtained from St.

Francis Hospital Nsambya Research Ethics Committee.

Consent for publication

Not applicable

Availability of data and materials

All data generated/analyzed during this study are included in this manuscript. The datasets generated and/or analyzed during the study are also available from the author on request.

Competing interests

The authors declare that they have no competing interests

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Authors' information (optional)

Not applicable

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