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Acute Kidney Injury and Its Short-Term Outcomes among Children with Malaria Admitted to the National Institute of Child Health

Abdul Qadeer Shaikh[1*], Bilquis Naeem[2], Hina Fatima[2], Lubna Aman[2] and Wajid Hussain[1]

[1]Department of Pediatric Medicine, National Institute of Child Health, Karachi, Pakistan
[2]Department of Pediatric Nephrology, National Institute of Child Health, Karachi, Pakistan

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***Corresponding Author:**
Abdul Qadeer Shaikh
Department of Pediatric Medicine, National Institute of Child Health, Karachi, Pakistan
shaikhqadeer751@gmail.com

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ABSTRACT

In Pakistan, the overall reported contribution of malaria to acute kidney injury (AKI) is not well studied. **Objectives:** To determine the frequency and short-term outcomes of AKI in children presenting with malaria. **Methods:** This analytical, cross-sectional study was conducted at the National Institute of Child Health, Karachi, Pakistan, during 13th January 2025 to 13th July 2025. Children aged 1-16 years with confirmed malaria were analyzed. Detailed demographic, clinical, and laboratory data were collected. AKI was staged using KDIGO criteria. Outcomes included need for dialysis, hospital stay, and mortality. Data were analyzed using IBM-SPSS Statistics, version 26.0. Statistical significance was set at $p<0.05$. **Results:** Among 237 children, 135(57.0%) were male, while the mean age was 7.9 ± 3.6 years. AKI was identified in 28 (11.8%; 95% CI: 7.9-16.5%) children. Fever was universally present in all children. Oliguria was significantly more frequent in children with AKI (64.3% vs. 7.2%, $p<0.001$). Oliguria (64.3% vs. 7.2%, $p<0.001$), dehydration (57.1% vs. 22.0%, $p<0.001$), and hypotension (25.0% vs. 4.3%, $p<0.001$) were significantly more common among children with AKI. Dialysis or renal replacement therapy was required in 21.4% children with AKI ($p<0.001$). Mortality occurred 10.7% children with AKI vs. 0% without AKI ($p<0.001$). **Conclusions:** AKI affects a notable proportion of children hospitalized with malaria. AKI in malaria is linked to more severe clinical presentation and significantly worse short-term outcomes.

INTRODUCTION

Malaria is considered to be a major public health issue, especially in endemic regions, affecting millions of children annually. Globally, around 500 million individuals suffer from malaria [1]. Local data reports pooled malaria prevalence around 23.3% [2]. Mortality due to malaria can be multifactorial. Severe forms of malaria can lead to multiple organ dysfunction, with acute kidney injury (AKI) being one of the severe and under-recognized complications in pediatric populations [3]. AKI in pediatric patients is not commonly reported, presumably as a result of a low suspicion index. In Pakistan, the reported contribution of AKI to malaria ranges between 2-39%, but in the pediatric population, there is a significant lack of data [4]. Malaria-associated AKI can be influenced by the severity of the disease, host immunity, and co-existing comorbidities [4]. The pathophysiology involves hemodynamic instability, intravascular hemolysis, and immune-mediated renal damage and dehydration [5]. The early diagnosis of AKI in malaria and identifying key risk factors can help develop targeted interventions [6]. The impact of AKI on the duration of hospitalization, need for dialysis, complete or partial recovery, and electrolyte imbalance, in particular with hyperkalemia, is not well understood in the pediatric population [7]. The rising

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incidence of malaria in children and the potential for fatal outcomes due to AKI necessitate research in this subject [8]. Studies from high-burden regions describe AKI in 24–59% of children with severe malaria, with clear associations with longer hospital stays, dialysis requirement, neurodisability at discharge, and elevated mortality that rises stepwise with AKI severity [9]. Despite the growing recognition of malaria-associated AKI in adults, significant gaps remain in understanding its burden, clinical profile, and outcomes in children, particularly in South Asian settings where malaria epidemiology differs from African regions. Pediatric AKI may be underdiagnosed due to limited routine monitoring of renal function, variability in clinical presentation, and lack of standardized surveillance in resource-constrained environments. Existing reports from Pakistan largely describe adult populations, leaving substantial uncertainty regarding the true frequency, severity, and short-term consequences of AKI among children with malaria.

Generating local pediatric data is essential to guide early recognition, inform management protocols, improve prognosis, and support resource allocation in high-volume tertiary centers. This study was therefore undertaken to address this evidence gap by evaluating the frequency and short-term outcomes of AKI in children presenting with malaria. This study aimed to determine the frequency and short-term outcomes of AKI in children presenting with malaria.

METHODS

This analytical, cross-sectional study was conducted across all medical units and the Department of Nephrology at the National Institute of Child Health (NICH), Karachi, Pakistan, from 13th January 2025 to 13th July 2025, following approval from the Institutional Ethical Review Board (IERB-53/2024). Written informed consent was obtained from parents or legal guardians after providing a thorough explanation of the study objectives and procedures. A sample size of 237 was calculated, taking the anticipated frequency of AKI in malaria as 33.2% [10], with a 95% confidence level and 6% margin of error. Using non-probability consecutive sampling, children aged 1 to 16 years, admitted with a confirmed diagnosis of malaria, were included. Malaria diagnosis was established using Giemsa-stained thick and thin blood films or the malaria parasite immunochromatographic test. Pre-existing chronic kidney disease (CKD), congenital renal anomalies, or sepsis unrelated to malaria, or current use of nephrotoxic medications were excluded. For each enrolled child, demographic data (age, gender, residential status) and detailed clinical information including presenting symptoms, duration of fever, dehydration status, vital signs, oliguria, type of therapy provided, and the stage of AKI. AKI was defined and staged according to the Kidney-Disease: Improving Global Outcomes (KDIGO) guidelines [11]. Stage 1 AKI was defined as an increase in serum creatinine to 1.5–1.9 times baseline or an absolute rise of ≥0.3 mg/dL within 48 hours, or a reduction in urine output to <0.5 mL/kg/h for 6–12 hours. Stage 2 AKI was defined as an increase in serum creatinine to 2.0–2.9 times baseline or urine output <0.5 mL/kg/h for more than 12 hours. Stage 3 AKI was defined as an increase in serum creatinine to ≥3.0 times baseline, or to ≥4.0 mg/dL, initiation of renal replacement therapy, or, in children younger than 18 years, a decrease in estimated glomerular filtration rate (eGFR) to <35 mL/min/1.73 m^2; urine output <0.3 mL/kg/h for more than 24 hours or anuria for ≥12 hours. All patients received standard management for malaria and AKI according to institutional protocols. Short-term renal outcomes like need for dialysis or renal replacement therapy (RRT), along with the length of stay, and in-hospital mortality, were recorded. All data were collected using a standardized data collection proforma. Statistical analysis was performed using IBM-SPSS Statistics version 26.0. Quantitative data were presented as means with standard deviation (SD) or median with interquartile ranges (IQR), as assessed for normality using the Shapiro-Wilk test. Quantitative data were compared using an independent sample t-test, or Mann-Whitney U test, while chi-square test or Fisher's exact were employed for the comparison of categorical data. Survival analysis was performed using Kaplan-Meier survival analysis and the log-rank test. Variables with $p<0.10$ in univariate analysis were entered into a multivariable binary logistic regression model to identify independent predictors of AKI. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) were reported. Model fitness was assessed using the Hosmer–Lemeshow test, and multicollinearity was evaluated through variance inflation factors. A p-value <0.05 was considered statistically significant for all inferential statistics.

RESULTS

In a total of 237 children, 135 (57.0%) were males, with a mean age of 7.9 ± 3.6 years. Among these, 165 (69.6%) resided in urban areas. AKI was identified in 28 (11.8%; 95% CI: 7.9-16.5%) children with malaria. Of these 28 children, 13 (46.4%) were classified as Stage-1, 8 (28.6%) as Stage-2, and 7 (25.0%) as Stage-3. Fever was universally present in all children. Oliguria was significantly more frequent in children with AKI (64.3% vs. 7.2%, $p<0.001$). Children with AKI were significantly more likely to be clinically dehydrated (57.1% vs. 22.0%, $p<0.001$) and had a higher incidence of hypotension at admission (25.0% vs. 4.3%, $p<0.001$). Significantly lower mean hemoglobin ($p<0.001$) and lower platelet count ($p=0.001$) were noted among children with AKI (Table 1).

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Table 1: Comparison of Study Variables (n=237)

Characteristics	AKI (n=28)	Non-AKI (n=209)	p-value
Male	16 (57.1%)	119 (56.9%)	0.984
Female	12 (42.9%)	90 (43.1%)	
Age (Years)	8.2 ± 3.3	7.9 ± 3.7	0.684
Residence (Urban)	21 (75.0%)	144 (68.9%)	0.510
Residence (Rural)	7 (25.0%)	65 (31.1%)	
Fever	28 (100%)	209 (100%)	1
Dehydration	16 (57.1%)	46 (22.0%)	<0.001
Hypotension	7 (25.0%)	9 (4.3%)	<0.001
Hemoglobin (g/dL)	8.9 ± 1.6	10.2 ± 1.8	<0.001
Platelets (109/L)	110 (75-135)	146 (120-185)	<0.001
Leukocyte Count (109/L)	13.2 ± 5.1	12.0 ± 4.8	0.219
Serum Creatinine (mg/dL)	2.2 (1.8-3.0)	0.7 (0.5-0.9)	<0.001
Blood Urea Nitrogen (mg/dL)	32 (22-48)	14 (10-21)	<0.001
Alanine Aminotransferase (U/L)	49 (31-87)	41 (26-63)	0.140
Aspartate Aminotransferase (U/L)	68 (44-102)	52 (36-81)	0.115

In terms of outcomes, children with AKI had a significantly longer median hospital stay compared to those without AKI (8 (6–10) days vs. 5 (4–7) days, p<0.001). The requirement for dialysis or RRT was limited to the AKI group (21.4% vs. 0%, p<0.001). In-hospital mortality was confined to the AKI children (10.7% vs. 0%, p<0.001) (Table 2).

Table 2: Comparison of Short-Term Outcomes (n=237)

Outcomes	AKI (n=28)	Non-AKI (n=209)	p-value
Required Dialysis / Renal Replacement Therapy	6 (21.4%)	–	<0.001
In-Hospital Mortality	3 (10.7%)	–	<0.001
Hospital Stay (Days)	8 (6-10)	5 (4-7)	<0.001

Kaplan–Meier survival curves showed significantly lower survival probabilities among children with AKI compared with those without AKI (log-rank p=0.002). The survival probability at Day 10 was 0.90 in the AKI group and 1.00 in the non-AKI group. Median survival time could not be estimated for either group because survival remained above 50% throughout the hospitalization period. All deaths occurred in the AKI group, whereas all non-AKI children were censored at discharge (Figure 1).

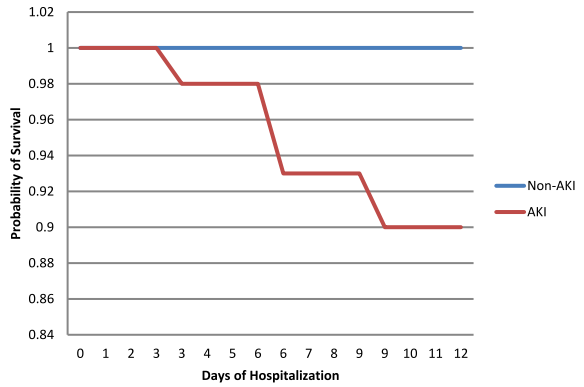

Figure 1: Kaplan-Meier Survival Curve

Dehydration (aOR 4.21, p=0.002) and hypotension at admission (aOR 5.94, p=0.004) remained strong independent predictors of AKI. Lower hemoglobin levels independently increased AKI likelihood (aOR 1.31 per 1 g/dL decrease, p=0.028). Higher blood urea nitrogen was associated with AKI (aOR 1.04 per mg/dL, p=0.013). Platelet count showed a borderline association (p=0.062). The details about multivariate binary logistic regression are shown (Table 3).

Table 3: Multivariate Binary Logistic Regression Analysis for the Predictors of Acute Kidney Injury in Children with Malaria

Predictor*	Adjusted Odds Ratio (95% Confidence Interval	p-value
Dehydration	4.21 (1.72-10.33)	0.002
Hypotension at Admission	5.94 (1.78-19.79)	0.004
Hemoglobin (per 1 g/dl decrease)	1.31 (1.03-1.68)	0.028
Platelet Count Per (10^9/L decrease)	1.01 (1.00-1.02)	0.062
Blood Urea Nitrogen (mg/dl increase)	1.04 (1.01-1.07)	0.013

*Serum creatinine was removed due to multicollinearity with blood urea nitrogen

DISCUSSION

This study showed that AKI was detected in 11.8% of hospitalized children with malaria. Kwambele and colleagues [12], in a study from Uganda, documented AKI prevalence of 47.7% in children with malaria, while Namazzi *et al.* reported an AKI frequency of 45.3% in a large multicenter cohort [7]. Oshomah-Bello *et al.* also documented AKI in 59% hospitalized children for severe malaria in Nigeria [13]. These higher frequencies are likely multifactorial and may reflect differences in malaria epidemiology, healthcare access, study inclusion criteria, and the spectrum of disease severity across populations. Several contextual factors might explain the lower AKI prevalence found in the current study. Pakistan is characterized by a mix of Plasmodium species, with Plasmodium vivax predominating, in contrast to sub-Saharan Africa, where Plasmodium falciparum is more frequently encountered and associated with more severe systemic and renal complications. Local malaria case management protocols, relatively earlier healthcare access, and broader inclusion of both moderate and severe cases in this study may have also contributed to lower AKI detection rates. Bugti *et al.* observed renal failure in 54.2% of malaria admissions, underscoring the wide geographic variation in AKI prevalence [14]. Some differences in AKI frequency may also arise from the criteria and timing used for AKI assessment, as studies incorporating serial creatinine measurements or biomarker-based diagnostics such as Cystatin C or NGAL have tended to identify more cases, especially in early or evolving stages, compared to single-point creatinine estimation. Hawkes *et al.* found higher rates of AKI in non-malarial febrile illness compared

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to malaria, but found severe AKI to be comparably prevalent in both groups [15]. This further suggests that population context, comorbidities, and care practices influence reported AKI rates. Children with malaria-associated AKI experienced longer hospitalizations, higher need for RRT, and markedly higher in-hospital mortality. The clear stepwise decline in survival among AKI patients, as demonstrated by the Kaplan-Meier analysis, mirrors findings from studies such as Conroy *et al.* who noticed increased mortality with greater AKI severity [16]. A recently published meta-analysis of over 133,000 pediatric AKI cases worldwide similarly noted an overall in-hospital mortality rate of 18.3%, rising from 8.2% in Stage 1 to nearly 28% in Stage 3 AKI [17]. The present study's observed mortality for children with AKI (10.7%) aligns most closely with mortality rates for moderate (Stage-2) AKI reported in the global literature, although the absolute mortality may be somewhat lower, potentially reflecting differences in patient mix and access to early supportive interventions [17]. The need for dialysis or RRT was observed in 21.4% of AKI patients, consistent with data from Teuwafeu et al. who reported that nearly three-quarters of children with AKI required dialysis, though only a minority received it due to resource constraints [18]. In contrast, the current study site, as a large tertiary center, was able to provide RRT to all indicated patients, which may explain the absence of mortality in non-AKI children and the relatively lower mortality rate among AKI cases compared to resource-limited settings where dialysis is less accessible. The consistently high mortality observed among children requiring dialysis across studies emphasizes the urgent need for improved access to RRT and early detection of AKI to prevent progression to advanced stages [19, 20]. Namazzi *et al.* found that 15.6% of pediatric severe malaria cases with AKI had persistent kidney dysfunction at one-month follow-up [7]. Chisavu *et al.* highlighted that persistent AKI was associated with increased risk of CKD and higher mortality [21]. Barriers to timely AKI diagnosis and management remain substantial, with access to laboratory testing, dialysis, and pediatric nephrology expertise often concentrated in urban referral centers [22, 23]. These disparities are further exacerbated by socioeconomic determinants, as children with less educated caregivers were at increased risk of AKI, emphasizing the need for broader community education and health system strengthening [12]. Future strategies to address these barriers may include capacity building for district and rural hospitals, decentralized training on AKI detection, and establishment of referral networks to facilitate rapid access to specialist care. Expanded use of point-of-care creatinine testing and novel biomarkers may further improve early detection and risk stratification, especially where laboratory infrastructure is limited [24, 25].

A shortcoming of this study is that generalizability may be limited due to single center to other settings with different malaria epidemiology and healthcare access. In addition, AKI assessment relied largely on single-point serum creatinine measurements, potentially underestimating early or evolving AKI compared with studies using serial measurements or novel biomarkers. Larger multicenter studies are required to confirm predictors, evaluate stage-dependent risk gradients, and assess long-term renal outcomes in pediatric malaria.

CONCLUSIONS

This study demonstrated that AKI complicates a significant proportion of pediatric malaria admissions among hospitalized children with malaria. AKI in children with malaria is associated with more severe clinical and laboratory profiles at presentation and predicts adverse short-term outcomes. Routine risk assessment, enhanced monitoring, and timely interventions for AKI should be prioritized in pediatric malaria care, especially in endemic regions, to mitigate morbidity and mortality related to this preventable complication.

Authors' Contribution

Conceptualization: BN, LA
Methodology: AQS, BN, HF
Formal analysis: LA
Writing and Drafting: WH
Review and Editing: AQS, BN, HF, LA, WH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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