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Original Article

Predictors and Clinical Outcomes of Acute Renal Failure in Patients with *Plasmodium falciparum* Malaria: A Prospective Cohort Study

Amrita Sadhwani[*], Abdul Manan Junejo[1], Muhammad Ali[1], Sandia Kumari[1], Reema Rehman[1] and Muneeba Asif[2]

[1]Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan
[2]Department of Medicine, Muhammad Medical College and Hospital, Ibn-e-Sina University, Mirpurkhas, Pakistan

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***Corresponding Author:**
Amrita Sadhwani
Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan
amrita.sadhwani1@gmai.com

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ABSTRACT

ARF is considered a serious complication of *Plasmodium falciparum* malaria and a major indicator of morbidity and mortality. Currently, there are no prospective studies from Pakistan investigating the prevalence and risk factors of ARF. **Objectives:** To ascertain the prevalence of ARF in adults suffering from *Plasmodium falciparum* malaria and to determine its predictors and clinical outcomes. **Methods:** A prospective cohort study was undertaken in the Department of Nephrology, Jinnah Postgraduate Medical Centre (JPMC), Karachi. 230 patients, aged between 18 and 60 years, suffering from microscopically confirmed *P. falciparum* malaria, constituted the study population. ARF was defined using KDIGO 2012 criteria. The renal function was assessed upon admission and on the second and seventh day of admission. The measured outcomes included the requirement for RRT, in-hospital mortality, length of hospital stay, renal recovery, and CKD. The statistical analyses were done with the help of SPSS version 26. **Results:** Prevalence of ARF was 18.3%. The prevalence of ARF requiring hemodialysis and exhibiting KDIGO stage 3 kidney dysfunction accounted for 52.4%. Higher in-hospital mortality was observed in patients with ARF as compared to patients without ARF. While amongst survivors, most showed renal recovery, some developed CKD. **Conclusions:** 18.3% of the studied adults admitted with *P. falciparum* malaria developed ARF. Mortality rate was significantly higher in patients with ARF, by almost ten times, and at a higher risk of developing CKD. Some preventable causes contributing to ARF are cardiovascular disorders, metabolic disorders, and delayed presentation in hospitals.

INTRODUCTION

Malaria is a communicable disease caused by various species of Plasmodium, transmitted to humans via mosquito bite [1]. Out of all the Plasmodium species infecting humans, namely *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi*, *P. falciparum* is responsible for causing the deadliest kind of malaria and accounts for nearly 90% of total deaths from malaria [2, 3]. As per recent data by the World Health Organization (WHO), 597,000 deaths and 263 million cases occurred globally due to malaria in 2023 [4]. About 95% of the deaths from malaria occurred in the WHO African Region, where interventions have failed to stop this menace. Pakistan stands as one of the endemic countries with approximately two million cases annually, of which, in 2022, there was a sharp increase to 2.7 million cases due to flooding, and it started decreasing since 2024 [5, 6]. Renal involvement in the form of ARF is a life-threatening complication of malaria. In this context, ARF in the setting of malaria refers to acute kidney injury (AKI) characterized by an absolute increase in serum creatinine of more than 0.3 mg/dL within

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48 hours; an absolute increase of more than 1.5 times baseline creatinine value within seven days; or urine output less than 0.5 mL/kg/hour for six or more hours [7]. The incidence of AKI in malaria patients increases the risk of mortality, prolongs the period of hospital stay, and may progress further to CKD [8, 9]. Malaria caused by *Plasmodium falciparum* remains a major public health concern in many tropical and subtropical countries, particularly in South Asia and sub-Saharan Africa. Among the severe complications of *falciparum* malaria, acute renal failure is associated with substantial morbidity and mortality, especially in hospitalized patients [9]. The development of renal impairment is believed to result from multiple mechanisms, including microvascular obstruction, hemolysis, dehydration, immune-mediated injury, and metabolic disturbances. Delayed diagnosis and inadequate treatment further increase the risk of poor clinical outcomes in affected individuals [10]. Despite advances in antimalarial therapy and supportive care, acute renal failure continues to pose a serious challenge in resource-limited healthcare settings where access to early diagnostic and renal replacement facilities may be restricted. Therefore, identification of clinical and laboratory predictors associated with renal complications is essential for timely intervention, improved patient management, and reduction of malaria-related mortality [11].

No prospective cohort data currently exist for the prevalence, risk factors, and outcomes of ARF in *P. falciparum* patients. This study aimed to determine the prevalence of ARF amongst adults suffering from *P. falciparum*; independent predictors of ARF amongst these patients were sought, and the clinical outcomes measured, including RRT, renal recovery, CKD, and mortality rate.

METHODS

A prospective cohort study was carried out at the Department of Nephrology, Jinnah Postgraduate Medical Center (JPMC), Karachi, after approval from the Research Ethics Unit of JPMC, F.2-81/2025-GENL/378/JPMC, dated 17 July 2025. Data collection took place over six months starting from 18 July 2025 to 17 January 2026. The sample size was calculated based on a previously reported prevalence of 18.3% by Muhamed Hussein *et al.* using a 95% confidence level, 5% margin of error, and OpenEpi (version 3.01). With an estimated sample size of 230 patients, the ratio of events per variable comes to 8.4, adequate for conducting multiple regressions. Consenting patients who met the inclusion criteria of the study were recruited using simple random sampling. Simple random sampling was used to reduce the potential for investigator selection during participant recruitment. Eligible patients were identified from the study population and selected according to the predefined sampling procedure. Adults aged 18 to 60 years admitted to the Department of Nephrology, JPMC, suffering from microscopically confirmed *P. falciparum* malaria were included. Patients with documented pre-existing CKD or previous AKI were excluded. Other potential causes of acute kidney injury, including bacterial sepsis, recent exposure to nephrotoxic medications, and urinary tract obstruction, were assessed using clinical history, physical examination, laboratory investigations, and relevant imaging findings where indicated. After obtaining written consent, information was obtained using a pre-designed pro forma along with measurements of anthropometric values. BMI was measured as the body mass in kg divided by the square of height in meters (kg/m^2). Categories for BMI values were: underweight (<18.5); normal (18.5–24.9); overweight (25–29.9); obese (≥30). Upon admission, blood film and complete blood counts were taken. Serum creatinine (mg/dL), serum urea (mmol/L), and estimated GFR (mL/min/1.73 m^2) were used for assessment of renal function upon admission, day two, and day seven of admission. AKI was classified as per KDIGO Stages 1, 2, and 3 on admission, day two, and day seven of admission. Stage 1: Increase in serum creatinine ≥0.3 mg/dL within 48 hours, or ≥1.5 to ≤1.9 times baseline serum creatinine within seven days. Stage 2: Increase in serum creatinine ≥2.0 to ≤2.9 times baseline serum creatinine within seven days. Stage 3: Increase in serum creatinine ≥3.0 times baseline serum creatinine, or serum creatinine ≥4.0 mg/dL with absolute minimum increase of ≥0.5 mg/dL within four hours, or initiation of RRT. Renal recovery was operationally defined as an eGFR ≥60 mL/min/1.73 m^2 at three months after the AKI episode. Because premorbid serum creatinine values were not available for all participants, this definition was used as a pragmatic follow-up measure rather than confirmation of return to individual premorbid renal function.

Statistical analysis was conducted using SPSS Version 26 (IBM Corp., Armonk, NY). Normality of distribution was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were presented as mean ± standard deviation, while categorical variables as frequency and percentages. Comparison of normally distributed continuous variables was made using an independent-samples t-test, while categorical variables were compared using a Chi-Square test. Where required, Fisher's exact test was also used. Multivariable logistic regression was used to identify independent predictors of ARF. Adjusted odds ratios (aORs) with 95% confidence intervals were reported. Model discrimination and calibration were assessed using AUC and the Hosmer-Lemeshow test, respectively. Bootstrap internal validation was performed, with the corrected AUC and 95% confidence interval reported.

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RESULTS

Among adults admitted with *P. falciparum* malaria complicated by acute renal failure (ARF), patients were found to be generally older and heavier than other non-ARF malaria patients. More specifically, age in ARF malaria patients was significantly higher (mean ± SD: 47.2 ± 9.4 years) than in the rest (37.9 ± 10.6 years), with p<0.001. ARF malaria patients were also heavier, as measured by BMI (mean ± SD: 26.1 ± 4.2 vs 24.2 ± 3.7 kg/m^2), p=0.004. Moreover, there was a higher proportion of males in ARF malaria patients (78.6% vs. 61.2%), p=0.036. Obesity, diabetes, hypertension, and active smoking were more prevalent in ARF patients, compared to non-ARF patients (p=0.023, p=0.002, p=0.001, p=0.015, respectively). Finally, patients aged over 40 were significantly more prone to developing ARF (p<0.001). For continuous variables, comparisons were done using an independent samples t-test, while a chi-square test was employed for categorical variables (Table 1).

Table 1: Baseline Demographic and Comorbidity Profile Stratified by Acute Renal Failure Status

Variables	Overall (n=230), Mean ± SD / n (%)	ARF Absent (n=188), Mean ± SD / n (%)	ARF Present (n=42), Mean ± SD / n (%)	p-value	Crude OR (95% CI)
Continuous Variables					
Age (years)	39.8 ± 11.2	37.9 ± 10.6	47.2 ± 9.4	<0.001	–
BMI (kg/m^2)	24.6 ± 3.9	24.2 ± 3.7	26.1 ± 4.2	0.004	–
Sex					
Male	148 (64.3%)	115 (61.2%)	33 (78.6%)	0.036	2.35 (1.05–5.24)
Female	82 (35.7%)	73 (38.8%)	9 (21.4%)	0.036	Ref
BMI Category					
Underweight (<18.5)	18 (7.8%)	16 (8.5%)	2 (4.8%)	0.420	–
Normal Weight (18.5–24.9)	118 (51.3%)	102 (54.3%)	16 (38.1%)	0.067	Ref
Overweight (25.0–29.9)	72 (31.3%)	56 (29.8%)	16 (38.1%)	0.289	1.82 (0.86–3.84)
Obese (≥30.0)	22 (9.6%)	14 (7.4%)	8 (19.0%)	0.023	3.67 (1.37–9.84)
Comorbidities					
Diabetes Mellitus	38 (16.5%)	24 (12.8%)	14 (33.3%)	0.002	3.41 (1.58–7.37)
Hypertension	46 (20.0%)	30 (16.0%)	16 (38.1%)	0.001	3.22 (1.55–6.68)
Hiv	9 (3.9%)	6 (3.2%)	3 (7.1%)	0.230	2.31 (0.55–9.61)
Current Smoking	72 (31.3%)	52 (27.7%)	20 (47.6%)	0.015	2.38 (1.18–4.82)
Age Category					
18–40 Years	127 (55.2%)	112 (59.6%)	15 (35.7%)	<0.001	Ref
>40 Years	103 (44.8%)	76 (40.4%)	27 (64.3%)	<0.001	2.66 (1.30–5.43)

Relationship between symptoms and ARF was tested using chi-square test, while independent samples t-test was used for symptom duration and ARF relationship testing. ARF patients exhibited a significantly higher frequency of fatigue (p=0.004; OR = 3.26, CI 1.41 – 7.52), and vomiting (p=0.004; OR = 2.83, CI 1.38 -5.79), compared to other malaria patients. Furthermore, ARF was significantly related to more than five days of symptoms (p=0.004; OR = 2.72, CI 1.37 -5.39). In addition, patients with ARF experienced a significantly higher number of days before seeking medical care (p<0.001; mean ± SD: 6.7 ± 3.1 days for ARF vs 4.4 ± 2.3 days in other malaria patients). However, none of the remaining symptoms, including chills, sweating, headache, and nausea, had a significant relationship with ARF (Table 2).

Table 2: Presenting Clinical Symptom Profile Stratified by Acute Renal Failure Status

Symptoms / Features	Overall, n (%)	ARF Absent, n (%)	ARF Present, n (%)	p-value	OR (95% CI)
Fever	230 (100%)	188 (100%)	42 (100%)	–	–
Chills	178 (77.4%)	142 (75.5%)	36 (85.7%)	0.148	1.93 (0.78–4.76)
Sweating	165 (71.7%)	134 (71.3%)	31 (73.8%)	0.731	1.13 (0.54–2.37)
Headache	152 (66.1%)	124 (66.0%)	28 (66.7%)	0.932	1.03 (0.51–2.08)
Fatigue	140 (60.9%)	106 (56.4%)	34 (81.0%)	0.004	3.26 (1.41–7.52)
Nausea	118 (51.3%)	92 (48.9%)	26 (61.9%)	0.131	1.70 (0.85–3.39)
Vomiting	112 (48.7%)	83 (44.1%)	29 (69.0%)	0.004	2.83 (1.38–5.79)
Symptom Duration >5 Days	96 (41.7%)	70 (37.2%)	26 (61.9%)	0.004	2.72 (1.37–5.39)
Symptom Duration, Days (Mean ± SD)	4.8 ± 2.6	4.4 ± 2.3	6.7 ± 3.1	<0.001	–

Clinical laboratory data indicate that serum creatinine level in ARF patients upon admission was significantly higher (mean ± SD: 4.6 ± 1.8 mg/dL for ARF vs. 1.1 ± 0.3 mg/dL for other malaria patients), compared to patients in the other group. The same pattern holds for serum creatinine level on Day 2 (4.9 ± 1.6 vs. 1.0 ± 0.3 mg/dL) and on Day 7 (3.2 ± 1.5 vs. 1.0 ± 0.2 mg/dL), as well

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as for blood urea ($p<0.001$ for all tests). ARF patients also exhibited significantly lower estimated glomerular filtration rate (eGFR) on admission (mean ± SD: 32 ± 11 vs. 89 ± 14 mL/min/1.73 m^2). Almost half (52.4%) of patients in the ARF group had been identified as stage 3 ARF patients requiring haemodialysis treatment (Table 3).

Table 3: Renal Biochemistry Over Time and KDIGO AKI Staging (n=230)

Parameters	ARF Absent (n=188), Mean ± SD \ n (%)	ARF Present (n=42), Mean ± SD / n (%)	p-value	Clinical Note
Serum Creatinine (mg/dL)				
Admission Creatinine	1.1 ± 0.3	4.6 ± 1.8	<0.001	4.2× higher in ARF group at presentation
Day 2 Creatinine	1.0 ± 0.3	4.9 ± 1.6	<0.001	Peak creatinine; further rise from admission
Day 7 Creatinine	1.0 ± 0.2	3.2 ± 1.5	<0.001	34.7% decline from Day 2; partial recovery
Estimated GFR (mL/min/1.73 m^2) CKD-EPI 2021 Equation				
Admission eGFR	89 ± 14	32 ± 11	<0.001	ARF group mean within KDIGO Stage 3b range
Blood Urea (mmol/L)				
Admission Urea	7.2 ± 2.1	22.8 ± 7.4	<0.001	Markedly elevated; hypercatabolic state
Day 7 Urea	6.9 ± 1.9	15.3 ± 6.8	<0.001	Declining; persistently elevated in ARF group
KDIGO AKI Stage Distribution in ARF Group (n=42)				
Stage 1 (Cr ×1.5–1.9 or +0.3 mg/dL)	—	8 (19.0%)	—	Mild AKI; managed conservatively
Stage 2 (Cr ×2.0–2.9)	—	12 (28.6%)	—	Moderate AKI; intensive monitoring required
Stage 3 (Cr ×≥3.0 or RRT Initiated)	—	22 (52.4%)	—	Severe AKI; all 22 required haemodialysis

The outcome measures confirm the necessity of renal replacement therapy in ARF patients ($p<0.001$), along with significantly higher in-hospital mortality ($p=0.001$) in ARF patients. Length of stay was also significantly higher in ARF patients (mean ± SD: 11.6 ± 4.2 vs. 5.8 ± 2.7 days). At three months, chronic kidney disease incidence was significantly higher ($p<0.001$) among survivors in the ARF group (mean ± SD of three-month eGFR: 58.4 ± 18.2 mL/min/1.73 m^2 vs. 91.2 ± 12.6 mL/min/1.73 m^2). Renal recovery was observed in most patients (88.2%). Only a small number of patients were lost to follow-up after three months (4 patients in the ARF group vs. 11 in the other group). Complete case analysis excluding these patients did not influence the main outcomes (Table 4).

Table 4: Clinical Outcomes Stratified by Acute Renal Failure Status

Clinical Outcomes	ARF Present (n=42), n (%) / Mean ± SD	ARF Absent (n=188), n (%) / Mean ± SD	p-value	95% CI / Effect Size
Renal Replacement Therapy				
RRT (Haemodialysis) Required	22 (52.4%)	0 (0%)	<0.001	RR = Not estimable; attributable solely to ARF
KDIGO Stage 3 Receiving RRT	22/22 (100%)	—	—	All Stage 3 patients initiated RRT
Median Sessions/Patient (IQR)	6 (4–9)	—	—	Range: 2–18 sessions
In-Hospital Mortality				
In-Hospital Mortality	8 (19.0%)	4 (2.1%)	<0.001	OR 10.7 (3.05–37.6); RD (risk Difference) 16.9%
Mortality in RRT-Requiring Patients	5/22 (22.7%)	—	—	Stage 3 AKI subgroup
Hospitalization and Recovery				
Length of Stay, Days	11.6 ± 4.2	5.8 ± 2.7	<0.001	Mean difference 5.8 days (95% CI 4.6–7.0)
Recovery from ARF within 3 Months	30/34* (88.2%)	—	—	*Excludes 8 in-hospital deaths
Mean Time To Recovery, Days	18.4 ± 6.1	—	—	Range: 7–42 days
Three-Month Renal Outcomes				
Progression to CKD (eGFR <60 for >3 Months)	6/34* (17.6%)	0	<0.001	All 6 had KDIGO Stage 3 AKI
eGFR at 3 Months, (Survivors)	58.4 ± 18.2	91.2 ± 12.6	<0.001	Mean difference 32.8 mL/min/1.73 m^2
Lost to Follow-Up at 3 Months	4 (9.5%)	11 (5.9%)	0.350	Sensitivity analysis performed

Relative risk was not estimable because no RRT events occurred in the non-ARF group

Finally, the study summarizes independent predictors of ARF according to multivariable logistic regression analysis. Significant predictors were diabetes (OR 2.98, p=0.009) and hypertension (OR 2.75, p=0.012). In addition, independent predictors of ARF were vomiting at admission (OR 2.21, p = 0.031), age above 40 (OR 2.12, p=0.046), and active smoking (OR 1.98, p=0.047)(Table 5).

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Table 5: Multivariable Logistic Regression: Independent Predictors of Acute Renal Failure

Predictor Variables	Adjusted OR	95% CI	p-value	Clinical Interpretation
Diabetes Mellitus	2.98	1.31–6.76	0.009	Strongest modifiable predictor; ~3× increased odds of ARF
Hypertension	2.75	1.25–6.04	0.012	Pre-existing hypertension nearly triples ARF risk
Vomiting on Presentation	2.21	1.08–4.52	0.031	Clinical proxy for systemic severity and volume depletion
Age >40 Years	2.12	1.01–4.47	0.046	Age-related nephron loss and higher comorbidity burden
Current Smoking	1.98	1.01–3.88	0.047	Endothelial dysfunction and impaired tubular reserve

Model performance: AUC-ROC = 0.81 (95% CI: 0.73–0.89) | Hosmer-Lemeshow: χ^2 = 7.42, p = 0.62 (good calibration) | Nagelkerke R^2 = 0.38 | Bootstrap-corrected AUC = 0.79 (1,000 iterations) | EPV (Events per Variable) = 8.4

DISCUSSION

The present study was carried out in a tertiary care nephrology center in Karachi, Pakistan. ARF was recorded in 18.3% of adult *P. falciparum* malaria patients. The result concurs with findings of a study carried out among children in Tanzania, reporting a comparable rate of ARF, and of several studies in South and Southeast Asian regions documenting a 18.3% rate of ARF within the 15–30% range. ARF associated with malaria thus seems to be a common complication of *falciparum* malaria, and not limited to any particular geographic location [12, 13]. As noted in the Introduction, malaria constitutes an important burden in low and middle-income countries, contributing to morbidity and mortality in acquired AKI. As per the literature, it belongs to the major infections causing AKI and accounting for up to 45% of cases in some studies [14, 15]. Regarding data from sub-Saharan African regions, patients require dialysis less often, but in-hospital mortality is higher, presumably due to late diagnosis and lack of dialysis access facilities [16]. In this study, dialysis necessity among ARF patients was high (52.4%). This result is comparable to findings of a study on RRT requirements in severe malaria-associated AKI in Pakistan and South Asia. Several Indian studies on RRT requirements in severe malaria also support the importance of kidney function in *P. falciparum* malaria outcomes [17, 18]. Metabolic disorders increase susceptibility to acute ischemic kidney injury. Diabetic nephropathy is marked by glomerular hyperfiltration, podocyte destruction, and tubulointerstitial fibrosis, impairing ischemia resistance [19]. Arteriolar sclerosis and poor renal perfusion control mechanisms characterize hypertensive patients and increase the risk of injury. Endothelial dysfunction and compromised microvascular integrity due to smoking also make one susceptible to injury [20]. The findings of this study emphasize the importance of early recognition and continuous monitoring of renal function in patients suffering from *Plasmodium falciparum* malaria. Patients presenting with severe clinical manifestations, delayed hospital admission, or abnormal biochemical parameters were more likely to develop acute renal failure and experience unfavorable outcomes. Prompt diagnosis, effective antimalarial treatment, and supportive renal care may significantly improve recovery and decrease complications. These results highlight the need for strengthened clinical protocols and awareness among healthcare professionals managing severe malaria cases.

This study has several limitations. The single-center design and relatively small sample size may limit the generalizability of the findings. The use of simple random sampling may also introduce selection bias depending on the completeness of the sampling frame. In addition, the absence of premorbid creatinine values for all participants limited definitive assessment of baseline renal function and recovery. In addition, the prevalence estimate used for sample size calculation was derived from published data from a different population, which may limit the applicability of the assumed prevalence to our setting. The exclusion of patients with other potential causes of AKI was based on clinical and laboratory assessment and may have involved some degree of clinical judgment. The relatively small number of ARF events resulted in a low events-per-variable ratio in the multivariable model, which may have increased the risk of model overfitting. Finally, the three-month follow-up limited assessment of long-term renal outcomes. Larger multicenter prospective studies with standardized baseline renal assessment, adequate statistical power, and longer follow-up are recommended.

CONCLUSIONS

In conclusion, ARF occurred in 18.3% of adults with *Plasmodium falciparum* malaria in this prospective cohort. Diabetes, hypertension, age above 40 years, active smoking, and vomiting at admission were associated with higher odds of ARF in the multivariable analysis. Patients with ARF also had higher rates of renal replacement therapy, in-hospital mortality, prolonged hospitalization, and adverse renal outcomes at three months. These findings highlight the importance of early assessment and close monitoring of renal function in patients with severe falciparum malaria. However, the findings should be interpreted in view of the single-center design, limited number of ARF events, and limitations in assessment of premorbid renal function.

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Authors' Contribution

Conceptualization: AS
Methodology: AS, MA[1], RR
Formal analysis: SK
Writing and Drafting: AS, AMJ, MA[1], SK, RR, MA[2]
Review and Editing: AS, AMJ, MA[1], SK, RR, MA[2]

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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