

PREVALENCE AND OUTCOME OF ACUTE KIDNEY INJURY IN COMMON TROPICAL FEVERS: A HOSPITAL-BASED PROSPECTIVE OBSERVATIONAL STUDY FROM A TERTIARY CARE CENTRE IN RAJASTHAN, INDIA

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ABSTRACT

Background: Acute kidney injury (AKI) is a frequent and potentially fatal complication of tropical acute febrile illnesses (TAFI). Its burden in this region of Rajasthan, where dengue, scrub typhus and malaria co-circulate, has not been well described. Aim: To determine the prevalence, severity, need for dialysis and short-term outcome of AKI in adults hospitalised with common tropical fevers. **Materials and Methods:** This hospital-based prospective observational study enrolled 200 consecutive adults admitted to the Department of Medicine, SMS Medical College and Attached Hospitals, Jaipur, between April 2023 and May 2024 with malaria, scrub typhus, dengue, typhoid fever, leptospirosis or chikungunya. Patients with chronic kidney disease and pregnant women were excluded. AKI was defined and staged by KDIGO criteria, and renal parameters were measured on admission and on days 3, 7 and 14. **Results:** Mean age was 41.0 ± 12.6 years. Dengue (44.5%) was the commonest diagnosis, followed by scrub typhus (23.5%) and malaria (19.5%). AKI occurred in 71 patients (35.5%; 95% CI 28.9–42.6): KDIGO stage 1 in 19.7%, stage 2 in 52.1% and stage 3 in 28.2%. AKI was most frequent in malaria (69.2%) and scrub typhus (44.7%) and least frequent in dengue (16.9%) ($p < 0.001$); compared with dengue, the odds of AKI were 11.1-fold higher in malaria (95% CI 4.6–26.7). Haemodialysis was required in 16 of 71 AKI patients (22.5%), 12 of whom had malaria. Two patients (1.0%) died, both with AKI (in-hospital mortality 2.8% among AKI vs 0% without AKI; $p = 0.12$). Serum creatinine and blood urea fell and urine output rose significantly from admission to day 14 ($p < 0.001$). **Conclusion:** About one in three adults admitted with a common tropical fever developed AKI, most often of moderate severity. Malaria and scrub typhus carried the highest risk and malaria accounted for most dialysis requirement. With early recognition and timely renal replacement therapy, renal function recovered in most patients and mortality was low.

KEYWORDS

Acute Kidney Injury; Tropical Fever; Malaria; Scrub Typhus; Dengue; Kdigo; Dialysis; India

INTRODUCTION

Acute kidney injury (AKI) is an abrupt decline in kidney function that encompasses both structural injury and functional impairment. The Kidney Disease: Improving Global Outcomes (KDIGO) criteria define AKI as a rise in serum creatinine of ≥ 0.3 mg/dL within 48 hours, a rise to ≥ 1.5 times baseline within 7 days, or urine output < 0.5 mL/kg/h for 6 hours.^{1,2} AKI is usually multifactorial, and in tropical regions infection is one of its leading community-acquired causes.

Tropical acute febrile illnesses (TAFI) — dengue, malaria, scrub typhus, enteric fever and leptospirosis — remain endemic across India, and their burden is rising with urbanisation, climate change and population mobility.^{3,4} AKI complicates a substantial proportion of these infections: an Indian tertiary-centre study found AKI in 41.1% of patients with TAFI, with AKI independently associated with death,³ and scrub typhus — once thought rarely to involve the kidney — causes AKI in about half of affected patients.⁵ The mechanisms differ between infections and include haemodynamic instability and hypovolaemia, microvascular obstruction by parasitised erythrocytes in malaria, direct tubulointerstitial invasion, rhabdomyolysis, haemolysis and immune-mediated glomerular injury.^{2,3} The resulting AKI is often reversible if recognised early, but severe cases require renal replacement therapy, which is not uniformly available.

The spectrum of TAFI and the frequency of associated AKI vary considerably between regions and seasons.^{6–8} Data from Rajasthan, where dengue, scrub typhus and malaria co-circulate, are limited. We therefore studied the prevalence, severity and short-term outcome of AKI in adults hospitalised with common tropical fevers at a tertiary care hospital in Jaipur, Rajasthan.

Materials and Methods

Study design, setting and period

This hospital-based prospective observational study was conducted in the inpatient wards of the Department of Medicine, SMS Medical College and Attached Group of Hospitals, Jaipur, from April 2023 to May 2024. The study was approved by the Institutional Ethics Committee (approval number and date to be inserted), and written informed consent was obtained from all participants or their legally authorised representatives.

Participants

Consecutive adults (≥ 18 years) hospitalised with fever and a confirmed diagnosis of malaria, scrub typhus, dengue, typhoid fever, leptospirosis or chikungunya were eligible. Patients with known chronic kidney disease and pregnant women were excluded. Diagnoses were established as follows: malaria by peripheral smear and/or rapid antigen test; dengue by NS1 antigen and/or IgM ELISA; scrub typhus by IgM ELISA; typhoid fever, leptospirosis and chikungunya by blood culture/Widal, leptospira IgM, chikungunya IgM.

Sample size

Assuming an AKI prevalence of 9.3% among patients with dengue,⁸ a 95% confidence level and an absolute precision of 5%, the minimum sample size was 134; to improve precision, 200 patients were enrolled.

Clinical and laboratory evaluation

All participants underwent a detailed history, physical examination and laboratory evaluation including haemoglobin, total and differential leucocyte counts, haematocrit, platelet count, blood urea, serum creatinine, serum electrolytes, liver enzymes, urinalysis, chest radiograph and ultrasonography of the kidneys, ureters and bladder. Blood urea, serum creatinine and 24-hour urine output were recorded on admission and on days 3, 7 and 14 (or at discharge).

Definitions and outcomes

AKI was diagnosed and staged according to KDIGO criteria,¹ using the lowest available/admission creatinine as baseline, and the highest stage reached during hospitalisation was recorded. The primary outcome was the prevalence of AKI. Secondary outcomes were KDIGO stage, requirement for haemodialysis, in-hospital mortality and the trajectory of renal parameters during follow-up. Indications for dialysis followed standard clinical criteria (refractory hyperkalaemia, metabolic acidosis, volume overload, uraemic complications or progressive oliguria).

Statistical analysis

Data were analysed with SPSS version 27 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean $\pm$ standard deviation and categorical variables as number (%). Prevalence was

reported with exact (Clopper–Pearson) 95% confidence intervals (CI). Categorical variables were compared with the chi-square or Fisher's exact test, and odds ratios (OR) with 95% CI were calculated for AKI by diagnosis, using dengue as the reference. Changes in renal and haematological parameters across time points were analysed with repeated-measures ANOVA. A two-sided p-value < 0.05 was considered significant.

RESULTS

Baseline characteristics and spectrum of tropical fevers

A total of 200 patients were enrolled; their mean age was 41.02 ± 12.56 years, and the largest age group was 31–40 years (31.0%) (Table 1). Dengue was the commonest diagnosis (89, 44.5%), followed by scrub typhus (47, 23.5%), malaria (39, 19.5%), typhoid fever (20, 10.0%), leptospirosis (3, 1.5%) and chikungunya (2, 1.0%) (Table 2).

Table 1. Age distribution of the study participants (n = 200)

Age group (years)	n (%)
18–30	46 (23.0)
31–40	62 (31.0)
41–50	41 (20.5)
51–60	35 (17.5)
> 60	16 (8.0)
Mean $\pm$ SD	41.02 ± 12.56

Table 2. Distribution of patients by diagnosis (n = 200)

Diagnosis	n (%)
Dengue	89 (44.5)
Scrub typhus	47 (23.5)
Malaria	39 (19.5)
Typhoid fever	20 (10.0)
Leptospirosis	3 (1.5)
Chikungunya	2 (1.0)
Total	200 (100)

Prevalence and severity of AKI

AKI developed in 71 patients (35.5%; 95% CI 28.9–42.6). Most had KDIGO stage 2 AKI (37, 52.1%); 20 (28.2%) had stage 3 and 14 (19.7%) stage 1 (Table 3).

Table 3. Prevalence and KDIGO stage of AKI

Variable	n (%)
AKI present (n = 200)	71 (35.5)
AKI absent	129 (64.5)
KDIGO stage among AKI (n = 71)	
Stage 1	14 (19.7)
Stage 2	37 (52.1)
Stage 3	20 (28.2)

AKI according to diagnosis

The prevalence of AKI differed significantly between diagnoses ($p < 0.001$). It was highest in malaria (27/39, 69.2%) and scrub typhus (21/47, 44.7%), intermediate in typhoid fever (25.0%) and lowest in dengue (16.9%). Compared with dengue, the odds of AKI were 11.1 times higher in malaria and 4.0 times higher in scrub typhus (Table 4, Figure 1). Two of three patients with leptospirosis and one of two with chikungunya developed AKI, but these numbers are too small for meaningful comparison.

Table 4. Prevalence of AKI according to diagnosis

Diagnosis	Total	AKI present, n (%)	AKI absent, n (%)	95% CI for AKI (%)	OR (95% CI) vs dengue
Dengue	89	15 (16.9)	74 (83.1)	9.8–26.3	1 (reference)
Scrub typhus	47	21 (44.7)	26 (55.3)	30.2–59.9	4.0 (1.8–8.9)
Malaria	39	27 (69.2)	12 (30.8)	52.4–83.0	11.1
Typhoid fever	20	5 (25.0)	15 (75.0)	8.7–49.1	1.6 (0.5–5.2)
Leptospirosis	3	2 (66.7)	1 (33.3)	9.4–99.2	—
Chikungunya	2	1 (50.0)	1 (50.0)	1.3–98.7	—
Total	200	71 (35.5)	129 (64.5)	28.9–42.6	

$p < 0.001$ (chi-square test for dengue, scrub typhus, malaria and typhoid fever). OR, odds ratio; CI, confidence interval (exact for proportions; Woolf method for OR). —, not estimated because of very small numbers.

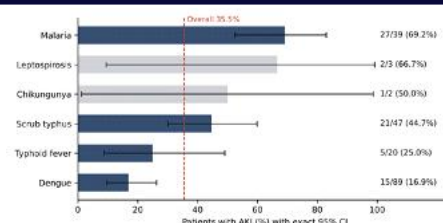


Figure 1. Prevalence of AKI by type of tropical fever with exact 95% confidence intervals. Grey bars indicate groups with fewer than five patients. The dashed line shows the overall prevalence (35.5%).

Management of AKI

Of the 71 patients with AKI, 55 (77.5%) were managed conservatively and 16 (22.5%; 95% CI 13.5–34.0) required haemodialysis. Malaria accounted for 12 of the 16 patients who needed dialysis (44.4% of malaria-associated AKI), and scrub typhus for the remaining 4 (19.0%). No patient with dengue, typhoid fever, leptospirosis or chikungunya required dialysis (Table 5). Dialysis was significantly more frequent in malaria-associated AKI than in AKI from other causes (OR 8.0; $p < 0.001$).

Table 5. Management of AKI according to diagnosis (n = 71)

Diagnosis	AKI, n	Conservative, n (%)	Haemodialysis, n (%)
Dengue	15	15 (100)	0
Scrub typhus	21	17 (81.0)	4 (19.0)
Malaria	27	15 (55.6)	12 (44.4)
Typhoid fever	5	5 (100)	0
Leptospirosis	2	2 (100)	0
Chikungunya	1	1 (100)	0
Total	71	55 (77.5)	16 (22.5)

Outcome

Two patients (1.0%) died — one with scrub typhus and one with malaria — and both had AKI. In-hospital mortality was therefore 2.8% (2/71) among patients with AKI and 0% (0/129) among those without AKI; the difference was not statistically significant given the small number of deaths (Fisher's exact $p = 0.12$) (Table 6).

Table 6. In-hospital mortality according to AKI status and diagnosis AKI present vs absent: Fisher's exact $p = 0.12$.

Group	Total	Died, n (%)	Survived, n (%)
AKI present	71	2 (2.8)	69 (97.2)
AKI absent	129	0	129 (100)
By diagnosis			
Dengue	89	0	89 (100)
Scrub typhus	47	1 (2.1)	46 (97.9)
Malaria	39	1 (2.6)	38 (97.4)
Typhoid fever / leptospirosis / chikungunya	25	0	25 (100)
Total	200	2 (1.0)	198 (99.0)

Changes in renal and haematological parameters during follow-up

Mean serum creatinine fell from 1.71 ± 1.11 mg/dL on admission to 0.93 ± 0.41 mg/dL on day 14, and blood urea from 48.3 ± 43.2 to 21.3 ± 11.2 mg/dL, while mean urine output rose from 1125 ± 415 to 1813 ± 297 mL/24 h (all $p < 0.001$). Haemoglobin and total leucocyte count did not change significantly (Table 7, Figure 2).

Table 7. Haematological and renal parameters during follow-up (mean $\pm$ SD)

Parameter	Admission	Day 3	Day 7	Day 14	p-value
Haemoglobin (g/dL)	13.9 ± 1.3	13.2 ± 1.5	12.8 ± 1.3	12.5 ± 1.5	0.12
Total leucocyte count (/mm ³)	6924 ± 3119	6875 ± 3014	6683 ± 3713	6398 ± 3952	0.63
Blood urea (mg/dL)	48.3 ± 43.2	41.7 ± 29.4	31.8 ± 15.8	21.3 ± 11.2	< 0.001
Serum creatinine (mg/dL)	1.71 ± 1.11	1.53 ± 1.02	1.19 ± 0.75	0.93 ± 0.41	< 0.001
Urine output (mL/24 h)	1125 ± 415	1394 ± 319	1558 ± 308	1813 ± 297	< 0.001

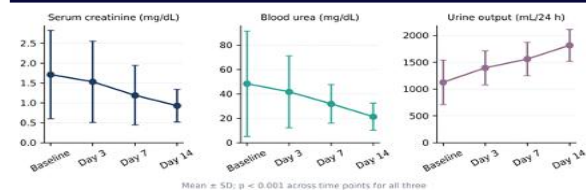


Figure 2. Trends in serum creatinine, blood urea and urine output from admission to day 14 (mean ± SD).

DISCUSSION

In this prospective study of 200 adults hospitalised with common tropical fevers, AKI occurred in 35.5%. It was usually moderate (KDIGO stage 2), was most frequent in malaria and scrub typhus, and required haemodialysis in about one in five affected patients. Renal function improved in most patients during follow-up, and in-hospital mortality was low (1.0% overall; 2.8% among patients with AKI).

The spectrum of illness — dengue followed by scrub typhus and malaria — mirrors the epidemiology of north-western India, where dengue predominates during the post-monsoon season and scrub typhus has re-emerged. Aggarwal et al.⁸ from north India similarly found dengue (43%) to be the commonest TAFI, followed by malaria and scrub typhus, and Cherian et al.⁷ reported dengue in 82% of their patients. In contrast, scrub typhus predominated in the south Indian series of Basu et al.,³ and vivax malaria and leptospirosis in the coastal Karnataka series of Nair et al.,⁹ underlining the strong regional variation in TAFI aetiology.⁶ The mean age of our patients (41 years) was higher than in a Thai cohort (median 33 years)¹⁰ but lower than in a Korean scrub typhus cohort (mean 58 years).¹¹

Our AKI prevalence of 35.5% lies within the range of 28–54% reported from Indian centres^{3,7,9} and is almost identical to the 35.7% found by Cherian et al.⁷ It is much higher than the 6.8% reported from Thailand by Omar et al.,¹⁰ whose cohort was dominated by dengue. Differences in case-mix, in AKI definitions (RIFLE, AKIN or KDIGO) and in the frequency of creatinine measurement largely explain this variability.

Malaria carried the greatest risk of AKI (69.2%) and accounted for three-quarters of dialysis requirement. Aggarwal et al. and Cherian et al. likewise found the highest AKI rate in malaria (56.5% and 61.5%),^{7,8} and Basu et al. reported the highest rates of AKI and renal replacement therapy in falciparum malaria.³ Sequestration of parasitised erythrocytes in the renal microcirculation, haemolysis and systemic inflammation underlie malaria-associated AKI.¹² Scrub typhus was the second commonest cause of AKI (44.7%), consistent with the 35.9% reported by Hwang et al. in Korea¹¹ and 53% by Kumar et al. in north India.⁵ AKI in dengue (16.9%) was less frequent and milder, none of these patients requiring dialysis; dengue-associated AKI is related mainly to plasma leakage, shock and rhabdomyolysis.¹³ Leptospirosis is a classical cause of severe AKI,¹⁴ and two of our three patients with leptospirosis developed AKI, although the numbers are too small to draw conclusions.

Haemodialysis was needed in 22.5% of patients with AKI, comparable to 20.3% reported by Omar et al.¹⁰ and higher than the 13.6% of Cherian et al.;⁷ published rates for TAFI-associated AKI range widely from about 8% to 45%.^{3,6,9,15} Mortality in our study (2.8% among AKI patients) was considerably lower than in the series of Cherian et al. (22.6%)⁷ and Mehta et al. (12.2%),⁶ possibly reflecting early referral, the predominance of moderate AKI and ready access to dialysis at our centre. Both deaths occurred in patients with AKI, consistent with the strong association between AKI and mortality described by Basu et al.,³ but with only two deaths our study lacked power to confirm this association statistically.

The progressive fall in serum creatinine and blood urea and the rise in urine output over 14 days indicate that TAFI-associated AKI is largely reversible when managed promptly, as also observed by Aggarwal et al.⁸ The modest decline in haemoglobin during admission was not statistically significant.

Strengths and limitations

Strengths of this study include its prospective design, consecutive enrolment, use of the current KDIGO definition and serial measurement of renal parameters. Its limitations include the single-centre setting; very small numbers of leptospirosis and chikungunya

cases; the absence of a known pre-morbid baseline creatinine in most patients, which may lead to misclassification of AKI stage; lack of species-wise malaria data and of multivariable analysis to identify independent predictors of AKI; and follow-up limited to 14 days, so that long-term renal outcomes are unknown.

CONCLUSION

Acute kidney injury affected about one in three adults hospitalised with common tropical fevers in this tertiary care setting and was most often of KDIGO stage 2. Malaria and scrub typhus carried the highest risk of AKI, and malaria accounted for most patients requiring haemodialysis. With early recognition, careful monitoring of renal function and timely dialysis, renal recovery was the rule and mortality was low. Routine creatinine monitoring in all patients admitted with tropical fever, particularly malaria and scrub typhus, is recommended. Larger multicentre studies are needed to identify predictors of severe AKI and its long-term renal consequences.

Declarations

Ethics approval: Approved by the Institutional Ethics Committee, SMS Medical College, Jaipur. Written informed consent was obtained from all participants.

Conflicts of interest: None declared.

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