Original Research Article

Acute Kidney Injury in Acute Febrile Illness, a prospective observational study

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Abstract

Background:

Acute kidney injury (AKI) is a frequent and serious complication of acute febrile illness (AFI) in tropical regions, contributing significantly to morbidity and mortality. Infection-related AKI remains underrecognized due to overlapping clinical presentations and limited diagnostic resources. This study aimed to determine the incidence, etiology, clinical profile, and outcomes of AKI in patients admitted with AFI.

Methods:

A prospective observational study was conducted over 18 months in a tertiary care hospital. Adults with AFI (<14 days duration) were enrolled, and AKI was diagnosed using KDIGO 2012 criteria. Patients with pre-existing chronic kidney disease, pregnancy, or obstructive uropathy were excluded. Demographic, clinical, and laboratory data were analyzed to assess the incidence, severity, and outcomes of AKI.

Results:

Among 300 patients with AFI, 96 (32%) developed AKI. The mean age was 46.8 ± 14.2 years, and males constituted 60.4%. Leptospirosis (58%) and scrub typhus (42%) were the predominant causes of severe AKI, while dengue (28%) and malaria (22%) were the most common infections overall.

According to KDIGO staging, 40% had stage 1, 35% stage 2, and 25% stage 3 AKI. Dialysis was required in 18 patients (18.7%), mostly in leptospirosis. The mean hospital stay was significantly longer in AKI patients (10.8 ± 4.5 days) compared to non-AKI cases (6.1 ± 2.8 days). Complete renal recovery was observed in 70.8%, partial recovery in 12.5%, and mortality in 10.4% of AKI cases. Independent predictors of mortality included stage 3 AKI, shock, leptospirosis, and need for dialysis ($p<0.05$).

Conclusion:

AKI complicates nearly one-third of acute febrile illnesses in tropical regions, predominantly due to leptospirosis and scrub typhus. Although most cases recover with supportive care, severe AKI and dialysis requirement significantly increase mortality. Early detection, aggressive management, and prevention of infection-related AKI are crucial to improving outcomes.

Keywords: Acute kidney injury; Acute febrile illness; Leptospirosis; Scrub typhus; KDIGO; Dialysis; Mortality

Introduction

Acute Kidney Injury (AKI) is a sudden decline in renal function characterized by the accumulation of nitrogenous waste products, disturbances in fluid and electrolyte balance, and impaired excretory and endocrine functions of the kidney. It is a common complication in patients presenting with acute febrile illness (AFI), particularly in tropical regions where infections such as malaria, dengue, leptospirosis, and scrub typhus are prevalent (1,2). AKI in these settings may result from direct pathogen-induced renal injury, systemic inflammatory responses, hypovolemia, or multi-organ dysfunction. The spectrum of clinical manifestations varies widely, ranging from asymptomatic elevations in serum creatinine to overt renal failure requiring renal replacement therapy (3,4).

The global burden of AKI in AFI is significant. Epidemiological studies suggest that AKI complicates 10–40% of severe febrile illnesses, with higher incidence in hospitalized patients and those with comorbidities such as diabetes, hypertension, or pre-existing chronic kidney

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disease (5,6). AKI is associated with increased morbidity, prolonged hospitalization, requirement for intensive care support, and elevated mortality. For example, patients with dengue-associated AKI have reported mortality rates up to 30%, while leptospirosis-related AKI is a leading cause of death in endemic regions (7,8). Despite its clinical significance, the early recognition of AKI remains challenging due to overlapping symptoms with the underlying infection, non-specific clinical signs, and limited availability of early biomarkers in many healthcare settings (9,10).

Rationale

Although AFI is common in tropical countries, there is limited prospective data assessing the incidence, risk factors, and outcomes of AKI in this population. Most existing studies are retrospective, single-center, or focus on specific infections, such as malaria or dengue, which limits the generalizability of findings (11,12). There is a pressing need for systematic, prospective studies to provide robust data on AKI in AFI. Understanding the burden and predictors of AKI is essential for several reasons: first, early recognition of at-risk patients can guide timely interventions, including fluid management, avoidance of nephrotoxic drugs, and early initiation of renal replacement therapy if required; second, it can inform clinical protocols and hospital resource allocation, particularly in settings with limited intensive care and dialysis facilities; and third, it contributes to the global understanding of infection-related AKI, which is underreported compared to other causes (13,14).

The heterogeneity in causative pathogens, patient demographics, and healthcare infrastructure emphasizes the need for region-specific data. Prospective observational studies allow for systematic evaluation of temporal relationships between febrile illness, onset of AKI, clinical and laboratory predictors, and outcomes. Such studies are critical to identify modifiable risk factors and develop strategies to reduce AKI-related morbidity and mortality.

Objective of the Study

This prospective observational study was designed to evaluate the incidence, clinical characteristics, risk factors, and outcomes of AKI in patients hospitalized with AFI. Standardized criteria, such as KDIGO (kidney disease: Improving Global Outcomes) or RIFLE (Risk, Injury, Failure, Loss, End-stage) classifications, were used to diagnose and stage AKI. Comprehensive demographic, clinical, and laboratory data were collected to assess the association of AKI with patient characteristics, severity of illness, type of infection, and hospital outcomes. By providing detailed evidence on AKI in AFI, the study aims to guide early recognition, optimize management strategies, and ultimately improve patient outcomes in resource-limited settings where the burden of AFI is highest (15,16).

Material and method: -

Study Design and Setting

This was a prospective observational study conducted in the Department of General Medicine and Nephrology at a tertiary care teaching hospital in Konaseema institute of medical science Amalapuram AP India over a period of 18 months, from July 2021 to December 2022. The study was approved by the Institutional Ethics Committee (IEC No.011 /2021). Written informed consent was obtained from all participants before enrolment.

Study Population

All adult patients (≥18 years) admitted with acute febrile illness (AFI)—defined as fever ≥38°C lasting less than 14 days—were screened for eligibility. Patients with pre-existing chronic kidney disease (CKD), known renal structural abnormalities, or those on nephrotoxic drugs prior to admission were excluded.

Inclusion Criteria

Patients presenting with acute febrile illness of infectious etiology.
Age ≥18 years.
Willingness to participate and provide informed consent.

Exclusion Criteria

Known cases of CKD (eGFR <60 mL/min/1.73 m² for ≥3 months).
Pregnant or postpartum women.
Patients with obstructive uropathy or renal transplant recipients.
Patients on nephrotoxic agents prior to admission (e.g., aminoglycosides, NSAIDs).

Data Collection and Clinical Evaluation

Demographic data including age, sex, and comorbidities were recorded. Detailed clinical history regarding duration of fever, associated symptoms, possible exposure history, and drug intake were obtained. Physical examination findings such as blood pressure, signs of dehydration, icterus, rash, and organomegaly were noted.

All patients underwent baseline investigations including complete blood count, renal function tests (serum creatinine, urea, electrolytes), liver function tests, urinalysis, and imaging studies when indicated. Etiological investigations for fever were carried out based on clinical suspicion and included malarial antigen test, dengue NS1 and IgM, leptospira IgM ELISA, scrub typhus IgM, and blood/urine cultures.

Diagnosis and Classification of AKI

AKI was diagnosed and staged according to the KDIGO 2012 criteria (15):
Stage 1: Increase in serum creatinine by ≥0.3 mg/dL within 48 hours or 1.5–1.9 times baseline.
Stage 2: Increase in serum creatinine 2.0–2.9 times baseline.
Stage 3: Increase ≥3 times baseline or serum creatinine ≥4.0 mg/dL, or initiation of renal replacement therapy.
Baseline creatinine was taken as the lowest known value within the past three months or estimated using the MDRD equation assuming a baseline GFR of 75 mL/min/1.73 m^2 in patients with unknown previous values (16).

Urine output was monitored and recorded throughout hospitalization. The RIFLE (Risk, Injury, Failure, Loss, End-stage renal disease) classification (4) was used for additional comparison to ensure diagnostic consistency.

Outcome Measures

Primary outcomes included:

Incidence of AKI among patients with AFI.
Severity and staging of AKI according to KDIGO criteria.
Secondary outcomes included:
Etiological distribution of AFI among AKI and non-AKI groups.
Length of hospital stay, need for dialysis, and in-hospital mortality.
Recovery pattern of renal function at discharge (complete, partial, or non-recovery).

Statistical Analysis

Data were entered and analyzed using SPSS software version 26.0 (IBM Corp, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range) as appropriate, and categorical variables as frequency and percentage.
The Chi-square test or Fisher's exact test was used for categorical variables.
The Student's t-test or Mann–Whitney U test was applied for continuous variables.
Multivariate logistic regression was performed to identify independent predictors of AKI.
A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study adhered to the principles of the Declaration of Helsinki (2013 revision). Confidentiality of patient data was strictly maintained, and no financial incentives were provided for participation.

Results

A total of 300 patients with acute febrile illness (AFI) were enrolled in the study during the 18-month study period. The mean age of participants was 42.6 ± 15.4 years, with a male-to-female ratio of 1.6:1. The most common comorbidities were hypertension (22%), diabetes mellitus (18%), and chronic liver disease (6%).

Out of 300 patients, 96 (32%) developed Acute Kidney Injury (AKI) as per KDIGO 2012 criteria. Among those with AKI, 58 (60.4%) were males and 38 (39.6%) were females.

Table 1. Baseline characteristics of study participants (n = 300)

Parameter	**Total (n=300)**	**AKI (n=96)**	**Non-AKI (n=204)**	**p-value**
Mean age (years)	42.6 ± 15.4	46.8 ± 14.2	40.7 ± 15.6	0.021*
Male sex, n (%)	186 (62)	58 (60.4)	128 (62.7)	0.71
Diabetes mellitus, n (%)	54 (18)	28 (29.1)	26 (12.7)	0.001*

Hypertension, n (%)	66 (22)	32 (33.3)	34 (16.6)	0.002*
Mean systolic BP (mmHg)	112 ± 16	106 ± 18	116 ± 14	0.04*
Mean duration of fever (days)	6.3 ± 2.7	6.9 ± 3.1	6.0 ± 2.6	0.08
Oliguria (<400 mL/day), n (%)	34 (11.3)	29 (30.2)	5 (2.4)	<0.001*

*Statistically significant ($p < 0.05$)

Etiological Spectrum of AFI

The most common causes of AFI were dengue fever (28%), malaria (22%), leptospirosis (16%), scrub typhus (14%), and bacterial sepsis (12%). Mixed infections were seen in 5% of cases, and 3% remained undiagnosed despite evaluation.

AKI incidence was highest among patients with leptospirosis (58%), followed by scrub typhus (42%), malaria (36%), and dengue (22%).

Table 2. Etiological distribution and AKI incidence among AFI cases

Etiology	**Total cases (n=300)**	**AKI cases (n=96)**	**Incidence of AKI (%)**
Dengue fever	84	18	21.4
Malaria	66	24	36.4
Leptospirosis	48	28	58.3
Scrub typhus	42	18	42.8
Bacterial sepsis	36	6	16.6
Mixed infection	15	2	13.3
Undiagnosed AFI	9	0	0

Severity and Clinical Course of AKI

Among the 96 patients with AKI, stage 1 AKI was seen in 38 (39.6%), stage 2 in 34 (35.4%), and stage 3 in 24 (25%) patients table 3).

Out of these, 18 (18.7%) required dialysis during hospitalization.

Mean duration of hospital stay was 10.8 ± 4.5 days among AKI patients compared to 6.1 ± 2.8 days in non-AKI patients ($p < 0.001$).

Table 3 Distribution of AKI severity according to KDIGO staging

KDIGO Stage	Number of Patients	Percentage (%)
Stage 1	38	39.6
Stage 2	34	35.4
Stage 3	24	25.0

Outcome Analysis

Outcomes were assessed at discharge. Among the 96 patients with AKI:

Complete renal recovery occurred in 68 (70.8%),

Partial recovery in 16 (16.6%), and

No recovery (persistent renal dysfunction) in 12 (12.5%).

The overall in-hospital mortality among AKI patients was 10.4% (10/96), compared to 2.9% (6/204) in non-AKI patients ($p = 0.02$).

Predictors of poor outcome identified on multivariate logistic regression were:

Stage 3 AKI (OR = 5.6; 95% CI 2.3–13.4; $p = 0.001$)

Presence of shock (OR = 4.1; 95% CI 1.7–9.8; $p = 0.003$)

Leptospirosis etiology (OR = 3.8; 95% CI 1.5–9.6; $p = 0.005$)

Need for dialysis (OR = 6.7; 95% CI 2.9–15.5; $p < 0.001$)

Table 4. Outcomes among AKI patients (n = 96)

Outcome	Number (%)
Complete renal recovery	68 (70.8)
Partial recovery	16 (16.6)
Persistent renal dysfunction	12 (12.5)
Required dialysis	18 (18.7)
In-hospital mortality	10 (10.4)

The overall incidence of AKI among hospitalized AFI patients was 32%, consistent with other studies from tropical regions (1,3,6).

Leptospirosis and scrub typhus were the leading causes associated with severe AKI.
Higher AKI stages correlated strongly with increased mortality and dialysis requirement.
Most patients recovered completely with supportive management, though a minority had residual renal dysfunction at discharge.

Discussion

The present prospective study evaluated the incidence, etiology, clinical profile, and outcomes of acute kidney injury (AKI) among patients admitted with acute febrile illness (AFI). In our study, the incidence of AKI was 32%, which is consistent with prior reports from tropical countries where infection-related AKI contributes substantially to the overall burden of renal disease (25,26).

Incidence and Demographic Correlation

he reported incidence of AKI in AFI varies widely, ranging from 10% to 40%, depending on local epidemiology, diagnostic criteria, and population characteristics (27). Our incidence of 32% aligns closely with studies by Gopalakrishnan et al. (28) and Wani et al. (29), who reported AKI rates of 34% and 31%, respectively, in similar cohorts. The slightly higher incidence in our series may be attributable to referral bias, as our institution is a tertiary care center receiving severe cases from peripheral hospitals.

Male predominance (60.4%) among AKI patients observed in our study parallels findings from earlier studies (30,31). This trend may reflect both occupational exposure to vector-borne infections and health-seeking differences between genders in low-resource settings. The mean age of patients with AKI (46.8 ± 14.2 years) also indicates that AKI affects the economically active population, leading to significant social and financial implications.

Etiological Spectrum and Pathophysiology

The etiological distribution in this study highlights dengue fever (28%), malaria (22%), leptospirosis (16%), and scrub typhus (14%) as the major causes of AFI. Among these, leptospirosis (58%) and scrub typhus (42%) showed the highest incidence of AKI. These findings corroborate the results of Pappachan et al. (32) and Kaur et al. (33), who emphasized the nephrotoxic potential of Leptospira interrogans and Orientia tsutsugamushi.

The mechanisms underlying AKI in these infections are multifactorial, involving hypovolemia, systemic inflammation, sepsis-induced hypotension, cytokine storm, rhabdomyolysis, and direct renal tubular injury (34,35). In leptospirosis, non-oliguric AKI often predominates due to direct tubular involvement and interstitial nephritis, while in scrub typhus and malaria, prerenal and ischemic mechanisms are more common (36).

Severity and Clinical Course

In our study, 60% of AKI cases were stage 2 or 3, and 18.7% required dialysis. The proportion of dialysis-requiring AKI (D-AKI) was similar to the 15–20% reported by Prakash et al. (37) and Gopalakrishnan et al. (28). The need for renal replacement therapy (RRT) was primarily in patients with leptospirosis and scrub typhus, suggesting that these etiologies are associated with more severe renal dysfunction and systemic involvement.

The mean hospital stay among AKI patients (10.8 ± 4.5 days) was significantly longer than non-AKI cases (6.1 ± 2.8 days), reflecting increased morbidity and healthcare costs. This finding is consistent with prior studies demonstrating prolonged hospitalization and higher resource utilization among AKI patients (38,39).

Outcomes and Predictors of Mortality

Among the 96 AKI patients, 70.8% achieved complete renal recovery, while 12.5% had persistent renal dysfunction, and 10.4% died during hospitalization. These outcomes are comparable to those reported by Kumar et al. (40), who observed complete recovery in 68% and mortality in 9.8% of AFI-associated AKI cases.

Multivariate analysis in our study revealed that Stage 3 AKI, shock, leptospirosis, and dialysis requirement were independent predictors of poor outcome. The strong association between advanced AKI stage and mortality has been confirmed by Bagshaw et al. (41), who demonstrated an exponential rise in mortality from 8% in stage 1 to over 35% in stage 3. Similarly, infection-related hemodynamic instability and multiorgan dysfunction markedly increase mortality risk (42).

Patients requiring dialysis had a 6.7-fold higher mortality risk, consistent with Pannu et al. (43), who identified the need for RRT as an independent predictor of in-hospital death. Interestingly, although dengue was the most common etiology in our series, its renal involvement was usually mild and reversible, echoing observations from Chung et al. (44).

Table 5: - Comparative Analysis with Previous Studies

A comparison of our findings with major regional studies is summarized below:

Study	Year	Sample size	AKI incidence (%)	Mortality (%)
Gopalakrishnan et al. (28)	2019	420	34	11
Prakash et al. (37)	2020	280	30	9
Kaur et al. (33)	2021	350	28	12
Wani et al. (29)	2022	310	31	10
Present study	**2025**	**300**	**32**	**10.4**

Our findings are consistent with these reports, reaffirming that tropical infection-associated AKI remains a major cause of preventable renal injury in developing nations.

Public Health and Clinical Implications

The study underscores the need for early identification and aggressive management of AKI in AFI cases. Simple measures such as timely fluid resuscitation, avoidance of nephrotoxic drugs, and early referral to nephrology services can reduce the incidence of severe AKI and mortality (45).

Routine monitoring of renal parameters in all febrile patients, particularly those with leptospirosis, scrub typhus, or malaria, is strongly recommended.

Community-level prevention strategies, including vector control, sanitation improvement, and public education, are vital to reduce the burden of infection-related AKI.

Limitations

Our study has several limitations. First, it was a single-center study with a limited sample size, potentially affecting the generalizability of results. Second, long-term renal outcomes were not assessed beyond hospital discharge. Third, renal biopsy was not performed to delineate histopathological patterns due to practical and ethical constraints. Future multicentric studies with larger cohorts and follow-up data are warranted to validate these findings.

Conclusion

AKI is a common and serious complication of acute febrile illness in tropical regions, with a prevalence of 32% in our study. Leptospirosis and scrub typhus are the leading causes associated with severe and dialysis-requiring AKI. Most cases recover completely with timely management; however, advanced AKI stage, hemodynamic shock, and need for dialysis significantly increase mortality. Early recognition, supportive therapy, and preventive public health measures remain key to improving outcomes in this potentially reversible condition.

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