

## PREVALENCE OF ACUTE KIDNEY INJURY IN TROPICAL ACUTE FEBRILE ILLNESS AND ITS OUTCOME IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY.

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### ABSTRACT

#### Background

Tropical acute febrile illness (TAFI) accounts for the majority of hospitalizations in our country. It is one of the most frequent causes of acute kidney injury (AKI) leading to very high morbidity and mortality in the Indian sub-continent. This study was conducted to evaluate the prevalence and outcome of AKI associated with TAFI.

#### Methods

This observational study was carried out on 100 patients of TAFI belonging to the age group of 15-89 years of both genders, admitted in the medicine ward fulfilling the inclusion and exclusion criteria in a tertiary care government teaching hospital in Eastern Odisha, India from June 2021 to October 2022. After obtaining informed consent, they were thoroughly evaluated for clinical signs and symptoms along with routine laboratory investigations. Kidney Disease Improving Global Outcomes (KDIGO) criteria were followed for AKI diagnosis and classification. Outcomes in terms of duration of hospital stay, treatment with dialysis, the requirement for intensive care unit (ICU) support, survival, and mortality were analyzed and recorded.

#### Results

Out of 100 patients of TAFI, 58% of patients developed AKI among whom 20 (34.4%) patients required hemodialysis. The majority (77.6%) of AKI patients improved, around 15.5% of patients progressed to chronic kidney disease (CKD) and mortality was seen in about 6.8% of patients.

#### Conclusion

The spectrum of TAFI in this present study shows malaria (38%) followed by dengue (27%), scrub typhus (16%), and leptospirosis (12%). The most common etiology of AKI in TAFI is leptospirosis (75%).

#### Recommendations

Recommendations include early diagnosis and management of tropical acute febrile illness (TAFI) and acute kidney injury (AKI), preventive measures targeting common causes, and a multi-disciplinary approach to patient care to reduce morbidity and mortality in tropical regions.

**Keywords:** Tropical Acute Febrile Illness, Acute Kidney Injury, Chronic Kidney Disease, Kidney Disease Improving Global Outcomes, Renal Replacement Therapy.

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### INTRODUCTION

Tropical Acute Febrile Illness (TAFI) is defined as all acute febrile syndromes with oral temperature over 37.7 degrees C within the last 24 hours and less than two weeks, in tropical and sub-tropical developing countries with non-specific symptoms that include all the symptoms that will not help us to localize to a particular system and include the typical symptoms of an acute febrile illness, such as fever,

headache, altered sensorium, loose stools, vomiting, leg and body edema, decreased urine production, dyspnea, coughing, and others and non-specific signs that include all the signs that will not help us to localize to a particular system like fever, tachycardia, myalgia, conjunctival congestion, rashes, joint pains and others [1,2,3]. In tropical countries, epidemics of acute febrile illness are manifested in the form of bacterial, viral, and parasitic

infections like malaria, dengue fever, enteric fever, scrub typhus, leptospirosis, rickettsia, and influenza. These infections are mostly transmitted by vectors like mosquitoes, house flies, and rodents. All of these infections can increase morbidity as well as mortality by causing renal failure, respiratory failure, and multi-organ dysfunction. TAFI with AKI is a major cause of mortality [3]. The pathophysiology of TAFI remains unclear. It is likely multifactorial and may differ based on infectious etiologies and their clinical presentation [4]. AKI management demands a better syndromic approach, early treatment, and prevention of complications with the latest guidelines [5,6]. This study was conducted to evaluate the prevalence and outcome of AKI associated with TAFI.

## METHODS

### study design

A prospective cross-sectional observational study was designed.

### Study setting

The study was conducted in the Department of General Medicine of a Government Medical College and Hospital in eastern Odisha, India, from June 2021 to Oct 2022.

### Study population

A total number of 100 patients of TAFI of either sex above the age of 15 years admitted to the Department of General Medicine fulfilling the inclusion-exclusion criteria were taken in this study and were thoroughly evaluated after obtaining informed written consent.

### Inclusion criteria

For inclusion criteria, patients were required to have experienced fever for less than 14 days with a temperature exceeding 99.9 degrees Fahrenheit (or 37.7 degrees Celsius). Additionally, participants needed to be aged over 15 years.

### Exclusion criteria

Exclusion criteria encompassed immunocompromised individuals, those with malignancy, tuberculosis, systemic hypertension, diabetes mellitus, autoimmune diseases, sepsis with localized foci of infection, and pre-existing renal diseases.

### Data collection and procedure

All the patients enrolled in the study underwent a detailed clinical and physical examination. The clinical symptoms like fever, headache, seizure, altered sensorium, myalgia, respiratory symptoms of dyspnea, cough, chest pain, abdominal pain, vomiting, diarrhea, gastrointestinal (GI) bleed, jaundice, dysuria, oliguria, and pedal edema were

evaluated. Thorough physical examinations were carried out for the findings of conjunctival suffusion, icterus, facial puffiness, lymphadenopathy, skin rash, eschar, and pedal edema, and findings on systemic examination of meningoencephalitis, pneumonia, abdominal tenderness, hepatomegaly, and splenomegaly.

### Clinical assessment

A routine blood and urine investigations including blood culture for enteric fever, peripheral smear, and ICT for malaria, a standard set of febrile serological investigations including leptospiral IgM ELISA, scrub typhus ELISA, dengue IgM-IgG ELISA were done. Phosphokinase, lactate dehydrogenase, arterial blood gas analysis (ABG), ultrasound abdomen and pelvis, and chest x-ray were done. KDIGO guidelines were used for AKI diagnosis and classification. All patients were monitored till the end of their hospital stay and management was based on standard guidelines. Patients who developed acute kidney injury were studied in detail and followed up till discharge and for 3 months after discharge. Outcomes in terms of duration of hospital stay, treatment with dialysis, the requirement for intensive care unit (ICU) support, survival, and mortality were analyzed and recorded.

### Statistical analysis

All the observational data was tabulated and analyzed by the SPSS version 21. Mann-Whitney U test and chi-square test were used to report and compare the continuous and categorical variables. Medians (as percentiles) and frequencies (as percentages) of different variables were also obtained. Pearson's Correlation coefficient and P value were calculated to find the statistical significance. Variables were considered to be significant at a P value <0.05.

### Ethical considerations

Ethical clearance was obtained from the Government Medical College and Hospital Ethics Committee before the commencement of the study. The study was done by the guidelines of the Declaration of Helsinki 2008.

## RESULTS

The study involved 100 eligible participants out of 110 initially recruited. Ten were excluded due to various reasons like immunocompromised status, malignancy, tuberculosis, systemic hypertension, diabetes mellitus, autoimmune diseases, sepsis with localized infection, or pre-existing renal conditions, aiming for a homogeneous sample. The eligible participants were thoroughly assessed for acute febrile illness and AKI, following KDIGO criteria, with outcomes analyzed including hospital stay, dialysis, ICU support, survival, and mortality.

In the present study, most of the acute febrile illness affects the young and adult age groups of 21-35 years (46.6%) (Table 1).

**Table 1: Age-wise distribution of AKI among acute febrile illness**

Age group in years	AKI present (N=58) n (%)	AKI Absent (N=42) n (%)
< 20	8 (13.8)	3 (7.1)
21 – 35	27 (46.6)	15 (35.7)
36 – 50	8 (13.8)	7 (16.7)
51 – 65	11 (19.0)	16 (38.1)
66 – 80	3 (5.2)	1 (2.4)
> 80	1 (1.7)	0 (0)
Total	58 (100)	42 (100)

The spectrum of TAFI in the present study shows malaria (38%) followed by dengue (27%), scrub typhus (16%), and leptospirosis (12%). The most common etiology of AKI in TAFI is leptospirosis (75%) (Table 2).

**Table 2: Tropical disease frequency and etiology of AKI**

Diseases (n=100)	Frequency (N)	Percentage (%)	AKI present (N=58) n (%)	AKI Absent (N=42) n (%)
Malaria	38	38	22 (57.9)	16 (42.1)
Dengue	27	27	13 (48.1)	14 (51.9)
Scrub typhus	16	16	11 (68.8)	5 (31.3)
Leptospirosis	12	12	9 (75.0)	3 (25.0)
Enteric fever	7	7	3 (42.9)	4 (57.1)

Fever lasted longer in duration among the AKI patients in comparison to the non-AKI patients showing a highly significant p-value. In the majority of cases (72.2%), fever lasted for more than 10 days (Table 3).

**Table 3: Duration and outcome of fever among AKI and non-AKI**

Duration of fever	AKI present	AKI absent	Outcome		
	(N=58) n (%)	(N=42) n (%)	Improved (N=87) n (%)	CKD (N=9) n (%)	Death (N=4) n (%)
3 – 5 days	10(47.6)	11(52.4)	19 (90.5)	2 (9.5)	0(0)
6 – 8 days	23(69.7)	10(30.3)	27 (81.8)	3 (9.1)	3 (9.1)
9 - 10 days	12(42.9)	16(57.1)	24 (85.7)	3 (10.7)	1 (3.6)
> 10 days	13(72.2)	5(27.8)	17 (94.4)	1(5.6)	0(0)

(P value=0.01 i.e., highly significant)

**Table 4: Serum urea and serum creatinine in AKI among acute febrile illness**

Renal function Test	AKI present (N=58)	AKI Absent (N=42)	P value
	Mean ± SD		
S. Urea (mg/dL)	96.82 ± 54.87	27.14 ± 10.22	0.001
S. creatinine (mg/dL)	3.91 ± 2.67	0.94 ± 0.28	0.001

(P value very highly significant)

Among 58 AKI patients, about 18 patients (31%) had serum creatinine values less than 1.2mg/dL at the time of admission. The remaining 40 patients (68.9%) developed acute kidney injury during their stay in hospital.

**Table 5: Urine output and dialysis in AKI**

Renal performance		AKI present (N=58) n (%)	AKI Absent (N=42) n (%)	P value
Urine output	Oliguric	45 (77.6)	0 (0)	0.0001
	Non oliguric	13 (22.4)	42 (100)	
Dialysis	Done	20 (34.5)	0 (0)	0.0001
	Not done	38 (65.5)	42 (100)	

*(P value very very highly significant)*

Around 34.5% (n=20) of AKI patients required dialysis. The remaining 38 patients (65.5%) did not require dialysis due to early recovery from the renal insult (Table 5). AKI

progressed to CKD patients requiring Renal Replacement Therapy (RRT) and underwent hemodialysis.

**Table 6: Outcome of AKI in acute tropical febrile illness**

Outcome	AKI present (N=58) n (%)	AKI Absent (N=42) n (%)	P value
Improved	45 (77.6)	42 (100)	0.001
CKD	9 (15.5)	0 (0)	
Death	4 (6.9)	0 (0)	

*(P value very highly significant)*

The majority (77.6%) of AKI patients improved and were discharged and were followed up for 3 months. Around 15.5% of patients progressed to chronic kidney disease (CKD) and mortality was seen in about 6.8% of patients. The cause of death in these patients was multiple organ dysfunction syndrome (MODS) and acute respiratory distress syndrome (ARDS).

## DISCUSSION

The study found that malaria (38%), dengue (27%), scrub typhus (16%), leptospirosis (12%), and enteric fever (7%) constituted the spectrum of Tropical Acute Febrile Illness (TAFI) in decreasing order of prevalence among participants. This study is similar to a study conducted by Nair JJ et al [7] in coastal Karnataka where the most common etiology was malaria (48.1%) followed by leptospirosis (25.2%) and dengue fever (14.2%). In contrast to both of our studies, the spectrum of TAFI was different in studies of Chrispal A et al [8], where the leading cause was scrub typhus (47.5%), and Kasper MR et al [6], where influenza was most frequent.

The present study shows most of the patients who suffered from TAFI were in the age group of 21-35 years (42%) and the majority of patients affected were males (62%). This suggests that young adults, particularly males,

are more susceptible to TAFI, highlighting potential demographic trends in the incidence of this illness. A contrast is seen in Abhilash KP et al [9] study, where 42.2% were male.

Out of 58 AKI cases in the present study, 34(58.6%) cases were found in males. But there was no reason for the gender difference of AKI. Acute kidney injury was more common in the age group of 21-35 years (46.6%). These findings suggest that while AKI was more common among males and individuals aged 21-35 years in the study population, further investigation may be needed to understand the underlying factors contributing to these demographic patterns in AKI occurrence.

In the present study among 38 malaria patients, 22 patients developed acute kidney injury, which comes to around 57.9% only. Leptospirosis (n=9) and Scrub typhus (n=11) patients presented with the highest proportion of AKI around 75% & 68.8% respectively. Dengue (n=27) and Typhoid (n=7) patients presented with AKI around 48% and 42% respectively. These numbers highlight the varying degrees of kidney involvement among different tropical febrile illnesses, with leptospirosis and scrub typhus showing higher AKI rates compared to malaria, dengue, and typhoid fever. The spectrum of AKI differs from the studies of Nair JJ et al [7] and Basu G et al [2].

Duration of fever is one of the striking features of comparison between the AKI Group and the non-AKI Group. In the Non-AKI Group around 57% of patients had a fever for 6-8 days and only a few percent (5%) of patients had a fever for more than 10 days. But in AKI patients (22%), the duration of fever lasts longer which is around 10 days. This suggests that a longer duration of fever, particularly exceeding 10 days, may be associated with a higher risk of developing acute kidney injury, highlighting the potential clinical significance of fever duration in these patients.

The present study shows that 41.6% of patients had elevated creatinine levels (baseline) at the time of admission and the remaining 58.1% of patients have normal creatinine (<1.2 mg/dl). The mean serum creatinine at admission was significantly higher among the patients with AKI than the non-AKI patients. This suggests that elevated baseline creatinine levels and higher mean serum creatinine at admission may be predictive factors for AKI development in these patients.

Out of 58 AKI cases, 45 (77.6%) cases were oliguric and 13 cases were non-oliguric, malaria (n=18), being the leading etiology. Out of 45 oliguric patients having AKI, 25 patients improved with IV fluids, and the remaining 20 patients needed renal replacement therapy (RRT). Hemodialysis was the mode of RRT used in our study. This indicates that oliguric AKI is a common presentation, especially in cases of malaria, and that IV fluid therapy is effective for a significant portion of patients, while others may require more advanced renal support such as hemodialysis.

In the present study, 58 patients had AKI due to TAFI among which 20 patients required RRT which is around 34%. This indicates that a significant proportion of AKI cases in the context of TAFI necessitated advanced renal support through RRT, highlighting the severity of kidney involvement in these patients. It was also seen in the Nair JJ et al study where about 10% of AKI patients required RRT [7]. RRT initiation and a greater number of times dialyzed had statistical significance as a predictor of in-hospital mortality similar to studies by Nair JJ et al [7] and Palevsky PM et al [10].

Among 20 patients supported with RRT, 11 patients improved, nine patients developed CKD and four died as a result of multiorgan dysfunction syndrome and acute respiratory distress syndrome. This underscores the varied outcomes and challenges faced in managing severe cases of Acute Kidney Injury (AKI) requiring advanced renal support. In another study conducted in Karnataka, the in-hospital mortality was 18(3%) among TAFI patients, of which 17(94.4%) had AKI, of which 15(88.2%) were of AKI stage 3, and of which 9(60%) patients died before the initiation of RRT and of which all 9(100%) had leptospirosis [7].

## Generalizability

The study sheds light on AKI prevalence in Tropical Acute Febrile Illness (TAFI), revealing 58% incidence with 34.4% requiring hemodialysis. Most AKI patients (77.6%) improved, 15.5% progressed to CKD, and mortality stood at 6.8%. Leptospirosis emerged as the primary AKI cause. Early TAFI and AKI diagnosis, preventive measures, and multi-disciplinary care are recommended to reduce morbidity and mortality in tropical regions. Further research on larger populations is needed for broader applicability.

## STUDY LIMITATIONS

A larger sample size may provide more significant results. The present study cannot represent the entire spectrum of tropical acute febrile illness-related AKI.

## CONCLUSION

The most common etiology of TAFI is malaria and AKI in TAFI is leptospirosis. The mortality rate is increased when TAFI is associated with AKI. To reduce the burden of the disease, emphasis must be given to early detection of AKI and renal function assessment.

## LIST OF ABBREVIATIONS

TAFI- Tropical Acute Febrile Illness  
AKI-Acute Kidney Injury  
CKD-Chronic Kidney Disease  
KDIGO-Kidney Disease Improving Global Outcome  
RRT- Renal Replacement Therapy  
MODS-Multiorgan Dysfunction Syndrome  
ARDS-Acute Respiratory Distress Syndrome

## AUTHORS' CONTRIBUTIONS

The authors declare that all the named authors have contributed equally to this article.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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