



Original Article

Study of Microbiological Spectrum and Renal Outcomes in Patients of Acute Febrile Illness with Thrombocytopenia: An Observational and Retrospective Study

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ABSTRACT

Background: Acute febrile illness (AFI) with thrombocytopenia is a common clinical syndrome in tropical regions, frequently complicated by acute kidney injury (AKI). However, region-specific data on microbiological spectra and renal outcomes remain limited, particularly in Bihar, eastern India.

Methods: This observational retrospective study analyzed 400 patients aged ≥ 18 years admitted with AFI (< 14 days duration) and thrombocytopenia (platelet count $< 150,000/\mu\text{L}$) at a tertiary care hospital in Bihar. Demographic, clinical, laboratory, and microbiological data were extracted from medical records. AKI was diagnosed and staged using KDIGO criteria. Patients were compared between AKI and non-AKI groups to identify risk factors and clinical outcomes.

Results: The mean age was 41.8 years with male predominance (62%). Scrub typhus (33%) was the most common etiology, followed by dengue (23.5%), leptospirosis (11.5%), and malaria (10.5%). AKI occurred in 35.5% of patients, with 43.7% Stage 1, 31% Stage 2, and 25.3% Stage 3. Scrub typhus (46.5%, $p < 0.0001$) and leptospirosis (19.7%, $p = 0.0002$) showed the strongest associations with AKI. Independent risk factors included high-grade fever, hyperbilirubinemia, respiratory failure, hypotension, severe thrombocytopenia, and elevated ALT. AKI patients had significantly worse outcomes: ICU admission (38% vs. 10.1%), dialysis requirement (16.9% vs. 0%), MODS (26.8% vs. 6.2%), prolonged hospitalization (9.8 vs. 5.7 days), and mortality (11.3% vs. 1.6%), all $p < 0.0001$.

Conclusion: AKI affects over one-third of AFI patients with thrombocytopenia, with scrub typhus and leptospirosis as the most renal-pathogenic infections. AKI significantly increases morbidity, healthcare resource utilization, and mortality, emphasizing the need for early diagnosis and region-specific management protocols.

Keywords: Acute febrile illness, thrombocytopenia, acute kidney injury, scrub typhus, leptospirosis, dengue, KDIGO criteria, tropical infections, Bihar, India.

INTRODUCTION

Acute febrile illness (AFI) with thrombocytopenia represents a common yet diagnostically challenging clinical syndrome in tropical and subtropical regions, particularly in resource-limited settings like India [1]. Defined as fever of short duration (<14 days) without an obvious localized source, AFI frequently overlaps with vector-borne and zoonotic infections that induce hematological abnormalities and multi-organ involvement, including acute kidney injury (AKI) [1-2]. In Bihar, an eastern Indian state with endemic tropical diseases, seasonal monsoon patterns exacerbate transmission of pathogens such as *Orientia tsutsugamushi* (scrub typhus), dengue virus, *Leptospira* spp., and *Plasmodium* species, leading to significant morbidity [1-3]. Thrombocytopenia in AFI arises from mechanisms including direct bone marrow suppression, immune-mediated platelet destruction, and consumption in disseminated intravascular coagulation [4]. Its presence often signals severe disease and heightens suspicion for complications like AKI [4, 5]. Studies across India report AKI incidence in tropical AFI ranging from approximately 20-41%, with associated mortality up to 12%. A southern Indian prospective study using RIFLE criteria documented AKI in 41.1% of AFI cases, underscoring its burden in tertiary care [4, 5]. Common etiologies exhibit distinct renal tropism. Scrub typhus, increasingly recognized as a leading cause of AFI in eastern and northern India, causes AKI through vasculitis, rhabdomyolysis, and direct tubular injury; up to 35% of hospitalized scrub typhus patients develop AKI [4, 6-8]. Dengue fever contributes via capillary leak, hypovolemia, and cytokine storm, with thrombocytopenia nearly universal in severe cases; AKI severity often correlates with dengue positivity and shock. Leptospirosis frequently presents with Weil's disease featuring jaundice and AKI due to tubulointerstitial nephritis, while malaria (especially falciparum) induces AKI through hemolysis, cytoadherence, and hypovolemia [4, 6-8]. Standardized AKI diagnosis employs KDIGO criteria, which integrate serum creatinine rise, oliguria, and staging to predict outcomes reliably. Higher KDIGO stages associate with greater risks of dialysis, prolonged hospitalization, multi-organ dysfunction syndrome (MODS), and mortality. Risk factors for AKI in this context include high-grade fever, hyperbilirubinemia, respiratory failure, hypotension, and delayed presentation—factors often compounded by diagnostic delays in undifferentiated fever [4, 9].

Despite the high prevalence, comprehensive data on microbiological spectra and renal outcomes specific to Bihar remain limited. Most studies focus on single pathogens or southern/western Indian cohorts, leaving gaps in region-specific etiology, co-infections, and prognosis. Retrospective analyses from similar settings highlight that early etiology-specific therapy (e.g., doxycycline for scrub typhus/leptospirosis, supportive care for dengue) alongside supportive renal management can improve recovery, yet ICU admission, dialysis needs, and mortality persist in severe cases [4-7, 9].

This observational retrospective study at a tertiary care hospital in Bihar addresses these gaps by evaluating the microbiological spectrum in AFI with thrombocytopenia and characterizing AKI incidence, staging (per KDIGO), risk factors, complications, and outcomes. By comparing AKI versus non-AKI groups and stratifying by etiology, it seeks to inform syndromic, region-tailored approaches. This study seeks to answer the research question: *What is the microbiological spectrum of acute febrile illness (AFI) accompanied by thrombocytopenia, and what are the incidence, severity, risk factors, and clinical outcomes of acute kidney injury (AKI) in these patients presenting to a tertiary care hospital in Bihar, India?* The primary objective is to determine the incidence and etiology of AKI using KDIGO criteria, while secondary objectives include identifying clinical and laboratory risk factors, analyzing severity across infectious etiologies (scrub typhus, dengue, leptospirosis, malaria), and assessing outcomes such as ICU admission, dialysis requirement, multi-organ dysfunction, and mortality, with comparison of prognosis and recovery between AKI and non-AKI groups to highlight the importance of early diagnosis and region-specific management in improving patient outcomes.

MATERIALS AND METHODS

This study was conducted as a single-center, observational, retrospective analysis in a tertiary care hospital in Eastern India. It involved the review of medical records of patients admitted with acute febrile illness (AFI) and thrombocytopenia to evaluate the microbiological spectrum and renal outcomes, particularly acute kidney injury (AKI).

Study Population

The study population comprised patients aged 18 years and above who were admitted with acute febrile illness of less than 14 days duration and thrombocytopenia, defined as a platelet count below 150,000/ μ L. Patients with documented microbiological evidence or strong clinical suspicion of tropical infections such as scrub typhus, dengue, leptospirosis, malaria, or other bacterial and viral fevers were included. Patients with pre-existing chronic kidney disease stage 3 or higher, hematological malignancies, chemotherapy-induced thrombocytopenia, chronic liver disease with portal hypertension, incomplete medical records lacking essential laboratory data, pregnant women, and those with fever due to localized bacterial infections without systemic features were excluded.

Sampling Method & Sample Size

Eligible patients were identified retrospectively from hospital records using ICD codes for fever and thrombocytopenia. The sample size was calculated based on the primary outcome, i.e., the incidence of AKI in AFI with thrombocytopenia. Using the formula for estimation of a single population proportion and referencing the study by Saran et al. (2026) [9], where AKI incidence was 36.1%, the minimum sample size was calculated as 355. Allowing for 10% incomplete records

or exclusions, the final targeted sample size was approximately 400 patients.

Outcome Parameters

The primary outcome was the incidence and staging of AKI according to KDIGO criteria. Secondary outcomes included the microbiological spectrum of AFI, risk factors associated with AKI, severity of AKI across different infectious etiologies, requirement for dialysis, ICU admission, occurrence of multi-organ dysfunction syndrome (MODS), in-hospital mortality, length of hospital stay, and renal recovery rates at discharge.

METHODOLOGY

Eligible patients were identified from hospital records, and detailed demographic, clinical, laboratory, and microbiological data were extracted. Clinical presentation such as fever grade, duration, and associated symptoms were recorded along with laboratory parameters including complete blood count, renal and liver function tests, and coagulation profile. Microbiological results such as dengue NSI/IgM, scrub typhus IgM, leptospira IgM, malaria antigen/smear, and blood cultures were documented. AKI was diagnosed and staged using KDIGO serum creatinine and urine output criteria. Patients were categorized into AKI and non-AKI groups, and etiological diagnosis was based on serological, molecular, or rapid diagnostic test results available in the records.

Data Collection

Data were collected using a structured proforma in Microsoft Excel. Two independent investigators extracted the data to minimize transcription errors, and discrepancies were resolved by consensus or consultation with a senior investigator. Patient identifiers were removed, and unique study IDs were assigned to maintain confidentiality.

Statistical Analysis

Data were analyzed using SPSS version 26.0 and R software. Continuous variables were expressed as mean $\pm$ standard deviation or median with interquartile range depending on distribution. Categorical variables were presented as frequencies and percentages. Comparisons between AKI and non-AKI groups were performed using Student's t-test or Mann-Whitney U test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Multivariate logistic regression analysis was applied to identify independent risk factors for AKI. A p-value less than 0.05 was considered statistically significant.

Ethical Consideration

Ethical approval was obtained from the Institutional Ethics Committee of the participating tertiary care hospital prior to commencement of the study. As this was a retrospective observational study involving review of existing medical records, the requirement for individual informed consent was waived. Strict confidentiality of patient data was maintained, and the study adhered to the principles of the Declaration of Helsinki and the guidelines of the Indian Council of Medical Research (ICMR).

RESULTS

The study population of 400 patients had a mean age of 41.8 years with male predominance (62%). Significant thrombocytopenia was evident with mean platelet count of 58,400/ μ L, while mean serum creatinine of 1.38 mg/dL suggested early renal involvement. Over half presented with high-grade fever, and gastrointestinal symptoms were common. Jaundice (18.5%), bleeding (14%), hypotension (13%), and breathlessness (16.5%) indicated substantial systemic involvement and disease severity [Table 1].

Table 1. Baseline demographic and clinical characteristics of study participants (N = 400)

Variable	Frequency (%) / Mean $\pm$ SD
Age (years)	41.8 $\pm$ 16.3
Male	248 (62.0)
Female	152 (38.0)
Fever duration (days)	6.2 $\pm$ 2.5
High-grade fever ($>102^{\circ}\text{F}$)	228 (57.0)
Vomiting	154 (38.5)
Abdominal pain	102 (25.5)
Bleeding manifestations	56 (14.0)

Jaundice	74 (18.5)
Breathlessness	66 (16.5)
Hypotension	52 (13.0)
Platelet count ($\times 10^3/\mu\text{L}$)	58.4 ± 29.1
Hemoglobin (g/dL)	11.4 ± 2.1
Serum creatinine (mg/dL)	1.38 ± 0.92

Scrub typhus emerged as the predominant etiology (33%), followed by dengue (23.5%), leptospirosis (11.5%), and malaria (10.5%). Enteric fever accounted for 5.5%, while non-specific viral infections comprised 9.5% and mixed infections were documented in 3% of cases. The diverse etiological spectrum underscores the diagnostic challenges and need for comprehensive testing in endemic tropical settings [Table 2].

Table 2. Microbiological spectrum of acute febrile illness (N = 400)

Etiology	n	%	95% CI of %
Scrub typhus	132	33.0	28.4 – 37.6
Dengue	94	23.5	19.4 – 27.6
Leptospirosis	46	11.5	8.4 – 14.6
Malaria	42	10.5	7.5 – 13.5
Enteric fever	22	5.5	3.3 – 7.7
Viral fever (non-specific)	38	9.5	6.6 – 12.4
Mixed infection	12	3.0	1.3 – 4.7
Others	14	3.5	1.7 – 5.3

AKI was observed in 35.5% of patients. Among AKI cases, 43.7% had Stage 1, 31% had Stage 2, and 25.3% had Stage 3 severity. The presence of Stage 3 AKI in one-quarter of affected patients highlights the significant burden of severe renal impairment requiring intensive monitoring and potential renal replacement therapy [Table 3].

Table 3. Incidence and severity of acute kidney injury according to KDIGO criteria (N = 400)

Etiology	n	%	95% CI of %
No AKI	258	64.5	59.9 – 69.1
AKI	142	35.5	30.9 – 40.1
KDIGO Stage 1	62	43.7*	35.5 – 51.9
KDIGO Stage 2	44	31.0*	23.2 – 38.8
KDIGO Stage 3	36	25.3*	18.1 – 32.5

*Percentage calculated among AKI patients (n = 142).

Scrub typhus showed the strongest association with AKI (46.5% vs. 26.4%, $p < 0.0001$), followed by leptospirosis (19.7% vs. 7.0%, $p = 0.0002$). Dengue and malaria showed no significant association with AKI. Non-specific viral fevers were significantly more common in non-AKI patients (14.0% vs. 1.4%, $p < 0.0001$), confirming differential renal pathogenicity across various tropical infections [Table 4].

Table 4. Comparison of microbiological etiology between AKI and non-AKI groups

Etiology	AKI (n=142)	Non-AKI (n=258)	p-value (Fisher's Exact Test)
Scrub typhus	66 (46.5%)	68 (26.4%)	< 0.0001
Dengue	28 (19.7%)	66 (25.6%)	0.2181
Leptospirosis	28 (19.7%)	18 (7.0%)	0.0002
Malaria	12 (8.5%)	30 (11.6%)	0.3950
Enteric fever	4 (2.8%)	18 (7.0%)	0.1078
Viral fever	2 (1.4%)	36 (14.0%)	< 0.0001
Mixed/Others	2 (1.4%)	24 (9.3%)	0.0013

High-grade fever (78.9% vs. 45.0%), hyperbilirubinemia (45.1% vs. 14.7%), respiratory failure (25.4% vs. 7.0%), hypotension (23.9% vs. 7.0%), severe thrombocytopenia (67.6% vs. 36.4%), and elevated ALT (40.8% vs. 24.0%) were all significantly associated with AKI ($p < 0.0001$). These factors reflect the inflammatory burden, hemodynamic instability, and multiorgan dysfunction driving renal injury in this population [Table 5].

Table 5. Risk factors associated with the development of AKI

Variable	AKI (n=142)	Non-AKI (n=258)	p-value
High-grade fever	112 (78.9%)	116 (45.0%)	<0.0001
Hyperbilirubinemia	64 (45.1%)	38 (14.7%)	<0.0001
Respiratory failure	36 (25.4%)	18 (7.0%)	<0.0001
Hypotension	34 (23.9%)	18 (7.0%)	<0.0001
Platelet count <50,000/ μ L	96 (67.6%)	94 (36.4%)	<0.0001
Serum creatinine (mg/dL)	2.62 $\pm$ 1.08	0.86 $\pm$ 0.24	<0.0001
ALT >100 IU/L	58 (40.8%)	62 (24.0%)	<0.0001

AKI patients had significantly worse outcomes with higher ICU admission (38.0% vs. 10.1%), dialysis requirement (16.9% vs. 0%), MODS (26.8% vs. 6.2%), prolonged hospital stay (9.8 vs. 5.7 days), and in-hospital mortality (11.3% vs. 1.6%), all $p < 0.0001$. The more than seven-fold increase in mortality underscores AKI as a critical prognostic marker in acute febrile illness with thrombocytopenia [Table 6].

Table 6. Clinical outcomes among AKI and non-AKI patients

Outcome	AKI (n=142)	Non-AKI (n=258)	p-value
ICU admission	54 (38.0%)	26 (10.1%)	<0.0001
Dialysis required	24 (16.9%)	0	<0.0001
MODS	38 (26.8%)	16 (6.2%)	<0.0001
Mean hospital stay (days)	9.8 $\pm$ 3.4	5.7 $\pm$ 2.1	<0.0001
In-hospital mortality	16 (11.3%)	4 (1.6%)	<0.0001

DISCUSSION

The present study of 400 patients with acute febrile illness and thrombocytopenia at a tertiary care hospital in Bihar revealed scrub typhus as the predominant etiology, accounting for one-third of cases, followed by dengue, leptospirosis, and malaria. The overall incidence of acute kidney injury was 35.5%, with scrub typhus and leptospirosis demonstrating the strongest associations with renal impairment. Risk factors significantly associated with AKI included high-grade fever, hyperbilirubinemia, respiratory failure, hypotension, severe thrombocytopenia, and elevated liver enzymes. Patients with AKI experienced substantially worse outcomes, including higher rates of ICU admission, dialysis requirement, multi-organ dysfunction, prolonged hospitalization, and significantly increased mortality.

Our finding of scrub typhus as the leading etiology (33%) aligns closely with Saran et al. (2026), who reported scrub typhus in 41.8% of their AFI cohort, confirming its endemic dominance in eastern India [9]. However, our dengue prevalence (23.5%) was comparatively lower than the 29.5% reported by Saran and the 38.3% documented by Kundu et al. (2024) in Eastern India, possibly reflecting regional and seasonal variations in disease transmission patterns [9, 10]. Agrawal et al. (2025) in Central India reported dengue as the leading cause (25%), with scrub typhus at only 7.5%, suggesting a westward decline in scrub typhus prevalence and corresponding increase in dengue dominance across different geographical zones [11]. Similarly, Yadav et al. (2026) found dengue as the most prevalent etiology at 32.5%, with non-specific viral fever comprising 18.3% and malaria 17.5%, indicating that dengue emerges as the predominant pathogen in certain regions while scrub typhus dominates in others, highlighting the importance of region-specific diagnostic algorithms [12].

The AKI incidence of 35.5% in our study is remarkably consistent with Saran et al. (2026) who reported 36.1%, reinforcing that renal impairment affects approximately one-third of hospitalized AFI patients with thrombocytopenia [9]. This figure is substantially higher than the 24.2% reported by Yadav et al. (2026) and the 23.5% observed by Singhi et al. (2017) in critically ill ICU patients, suggesting that thrombocytopenia may serve as a marker of more severe disease with higher renal complications [12, 13].

Our identification of scrub typhus as having the strongest association with AKI (46.5% of AKI cases) corroborates Saran et al. (2026), who found scrub typhus AKI rates of 47.1%, and Bajpai et al. (2008), who documented that scrub typhus, alongside leptospirosis, was a leading cause of fatal AFI during monsoon seasons [9, 15]. Leptospirosis showed a similarly robust association with AKI (19.7% of AKI cases) in our study, consistent with Kundu et al. (2024), who identified severe renal involvement—including AKI in 29.5% and Weil's disease in 4.4%—as the major driver of the highest individual mortality rate observed in leptospirosis [10]. Risk factor analysis in our study identified high-grade fever, hyperbilirubinemia, respiratory failure, hypotension, severe thrombocytopenia, and elevated ALT as significant predictors of AKI, findings that closely parallel Saran et al. (2026), who reported high-grade fever ($p = 0.00001$), hyperbilirubinemia

($p=0.00276$), and respiratory failure ($p=0.0253$) as key correlates [9]. Yadav et al. (2026) similarly identified age over 60, admission hypotension, high serum creatinine, and thrombocytopenia as independent predictors of poor outcomes [12], while Ray et al. (2019) demonstrated that acidemia, altered sensorium, and coagulopathy predicted mortality in critically ill AFI patients [15]. Our outcome data showing significantly worse prognosis in AKI patients—with ICU admission rates of 38%, dialysis requirement of 16.9%, MODS in 26.8%, and in-hospital mortality of 11.3%—are consistent with the existing literature. Lee et al. (2024) found that mortality surged to 29.6% in AKI patients and reached 50% in those with advanced renal failure, closely mirroring our observation of higher mortality with increasing AKI severity [16]. This gradient likely reflects differences in illness severity at presentation, with higher mortality in studies specifically targeting critically ill populations compared to our broader hospitalized cohort. The dialysis requirement of 16.9% in our AKI patients aligns with Singhi et al. (2017), who reported that 9% of critically ill AFI patients required renal replacement therapy [13], and Lee et al. (2024), who noted that 9.3% of SFTS patients required continuous renal replacement therapy for an average of 10 days [16]. These consistent observations across multiple Indian studies underscore the substantial healthcare resource burden imposed by AKI in tropical AFI, including prolonged hospitalization (9.8 vs. 5.7 days in our study) and intensive care requirements. Interestingly, Hu et al. (2025) highlighted a different dimension of complications in severe febrile illness, reporting that 45% of SFTS patients developed secondary bacterial or fungal co-infections, with multidrug-resistant organisms comprising 20.1% of bacterial isolates [17]. While our study did not specifically investigate superinfections, this finding suggests that the clinical course of severe AFI may be further complicated by nosocomial infections, particularly in patients requiring prolonged ICU stays and invasive procedures. The lack of a control group of AFI patients without thrombocytopenia limits our ability to determine whether thrombocytopenia independently contributes to AKI risk or merely reflects disease severity. The study also could not assess long-term renal outcomes beyond discharge, such as persistent kidney dysfunction or progression to chronic kidney disease.

CONCLUSION

In conclusion, our study reinforces the substantial burden of AKI in tropical AFI with thrombocytopenia, confirms scrub typhus and leptospirosis as the most renal-pathogenic infections, and validates previously identified risk factors and prognostic indicators. Early recognition of AKI risk factors, prompt etiological diagnosis, and aggressive supportive renal management are essential to improve outcomes in this high-risk population. Future prospective studies incorporating biomarkers of early kidney injury and evaluating targeted therapeutic interventions are warranted to further reduce morbidity and mortality associated with AKI in tropical acute febrile illness.

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