Chinese Journal of Health Management
Volume 20 Issue 4, Year of Publication 2026, Page 1027-1033 | DoI-10.564220/1674-0815.2026.129

ISSN: 1674-0815

Chinese Journal of Health Management

Chinese Medical Association

Clinical and Laboratory Profile of Scrub Typhus in Children: A Prospective Observational Study from a Tertiary Care Hospital in Eastern India

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Article Information
Received: 17-03-2026
Revised: 04-04-2026
Accepted: 22-04-2026
Published: 25-05-2026

Keywords
scrub typhus; children; Orientia tsutsugamushi; acute febrile illness; eastern India; eschar

ABSTRACT:
Background: Scrub typhus is a re-emerging, vector-borne rickettsiosis and an important treatable cause of acute undifferentiated febrile illness (AUFI) in children, yet pediatric data from eastern India remain limited. We described the clinico-laboratory profile, complications and outcome of children with serologically confirmed scrub typhus. **Methods:** This prospective observational study was conducted over 24 months in the pediatric department of a Fakirmohan Medical College, Odisha, in eastern India. Children aged 1 month–14 years with AUFI of ≥5 days and a positive anti-Orientia tsutsugamushi IgM ELISA were enrolled. **Results:** Of 1,260 AUFI admissions, 96 (7.6%) were confirmed. The mean age was 6.4 ± 3.4 years with a male preponderance (56.3%); 74.0% were rural and 76.0% presented during the monsoon/post-monsoon months. Fever (100%), hepatomegaly (54.2%) and vomiting (42.7%) were common; an eschar was found in 21.9%. Thrombocytopenia (49.0%) and transaminitis (AST 63.5%) were the principal laboratory abnormalities. Complications occurred in 60.4%, most often hepatitis (39.6%) and meningoencephalitis (16.7%). The case-fatality rate was 2.1%. **Conclusion:** Scrub typhus is a frequent and serious cause of pediatric AUFI in eastern India. Because the eschar is often absent, a high index of suspicion with early empirical doxycycline/azithromycin is essential to reduce morbidity and mortality.

INTRODUCTION:
Scrub typhus is an acute, potentially life-threatening zoonosis caused by *Orientia tsutsugamushi*, an obligate intracellular bacterium transmitted to humans through the bite of the larval stage (chigger) of trombiculid mites.[1] The disease is classically confined to the "tsutsugamushi triangle," an area of more than eight million square kilometres bounded by far-eastern Russia and Japan in the north, northern Australia in the south, and Pakistan, Afghanistan and India in the west.[2] Globally, an estimated one billion people are at risk and roughly one million cases occur every year, making it one of the most common and clinically important rickettsioses worldwide.[1,3]

Once considered controlled after the antibiotic era, scrub typhus has re-emerged across India over the past two decades and is now the most frequently reported rickettsial infection from the subcontinent.[3,4] A systematic review of Indian literature confirmed widespread distribution with substantial, though under-recognised, morbidity and mortality, attributing the rise partly to improved diagnostics, reduced empirical tetracycline use and ecological change.[4] Transmission peaks during the rainy, post-monsoon and cooler months, when agricultural activity and contact with scrub vegetation increase mite exposure.[5]

In children, the clinical picture is protean and overlaps with dengue, enteric fever, leptospirosis, malaria and other causes of AUFI. Fever, vomiting, abdominal pain, hepatosplenomegaly, generalised oedema, lymphadenopathy and rash are common, while the pathognomonic eschar — a painless necrotic crust at the site of the chigger bite — is reported in only a minority of pediatric cases.[6,7] When recognition is delayed, the infection can progress to hepatitis, meningoencephalitis, acute kidney injury, myocarditis, acute respiratory distress syndrome (ARDS) and multi-organ dysfunction, with case-fatality rates that may exceed those reported in adults.[7,8]

Despite this burden, most Indian studies are derived from adult populations, and dedicated pediatric series — particularly from eastern India — remain scarce.[9,10] Because the region is highly endemic and the disease is eminently treatable with inexpensive antibiotics, locally generated data are valuable for raising clinical suspicion and informing empirical therapy. The present study was therefore undertaken to determine the seroprevalence, and to describe the clinical features, laboratory abnormalities, complications and immediate outcome, of scrub typhus among children admitted with AUFI to a tertiary care hospital in eastern India.

MATERIALS AND METHODS:

Study design and setting. This hospital-based, prospective observational study was carried out in the Department of Pediatrics of Fakirmohan Medical College, Odisha, India over a 24-month period (January 2023 to December 2024). The institution serves a predominantly rural and semi-urban catchment population and functions as a referral centre for the surrounding districts.

Study population. Consecutive children aged 1 month to 14 years admitted with acute undifferentiated febrile illness — defined as documented fever of ≥5 days without a localising focus or an obvious alternative diagnosis on initial evaluation — were screened for eligibility, in keeping with case definitions used in earlier pediatric series.[9,11]

Inclusion and exclusion criteria. Children with AUFI who tested positive for anti-*O. tsutsugamushi* IgM antibodies were included as confirmed scrub typhus. Children with a confirmed alternative diagnosis (for example culture-positive enteric fever, NS1/IgM-positive dengue, smear-positive malaria), those already on a complete course of an anti-rickettsial antibiotic before admission, and those whose guardians declined consent were excluded.

Case definition and diagnosis. Diagnosis was based on a positive qualitative/quantitative IgM enzyme-linked immunosorbent assay (ELISA) against *O. tsutsugamushi*, which is the most widely used serological method in Indian settings; an optical-density cut-off was applied per the manufacturer's instructions and validated regional thresholds.[4,12] A careful whole-body examination, including the axillae, groin, perineum and retro-auricular areas, was performed in every child to detect an eschar.

Data collection. A structured proforma was used to record demographic details, residence, season of presentation, duration of fever, presenting symptoms and signs, and the presence of an eschar. Laboratory investigations included complete blood count, peripheral smear, liver and renal function tests, serum electrolytes, C-reactive protein, urinalysis, chest radiography and, where indicated, cerebrospinal fluid analysis and echocardiography.

Definitions of complications. Thrombocytopenia was defined as a platelet count <150 × 10⁹/L and anaemia as haemoglobin below age-specific norms. Hepatitis was defined as transaminase elevation greater than three times the upper limit of normal; acute kidney injury and ARDS were defined by standard pediatric criteria; meningoencephalitis required altered sensorium and/or seizures with supportive cerebrospinal fluid or neuro-imaging findings; and myocarditis was defined by clinical, electrocardiographic or echocardiographic evidence of myocardial dysfunction. Shock and multi-organ dysfunction were defined according to consensus pediatric sepsis criteria.[13]

Treatment. All confirmed children received an anti-rickettsial antibiotic — oral or intravenous doxycycline and/or azithromycin — together with supportive and organ-specific care; defervescence time was recorded.[11,14]

Statistical analysis. Data were entered in Microsoft Excel and analysed with SPSS version 25.0. Categorical variables were expressed as frequencies and percentages and continuous variables as mean ± standard deviation or median with range. The chi-square or Fisher's exact test was used to compare proportions between children with and without complications; a two-sided p-value <0.05 was considered statistically significant.

RESULTS

During the study period, 1,260 children were admitted with AUFI, of whom 96 had serologically confirmed scrub typhus, giving a seroprevalence of 7.6%. The mean age was 6.4 ± 3.4 years; the largest group was 1–5 years (39.6%), followed by 6–10 years (35.4%). There was a male preponderance (54 boys, 56.3%; male-to-female ratio 1.29:1), and most children came from rural areas (74.0%). The demographic profile is summarised in Table 1.

Table 1. Demographic profile of children with scrub typhus (N = 96). Mean age 6.4 ± 3.4 years.

Variable	Category	n (%)
Age group	<1 year	6 (6.3)
	1–5 years	38 (39.6)
	6–10 years	34 (35.4)
	11–14 years	18 (18.8)
Sex	Male	54 (56.3)
	Female	42 (43.8)
Residence	Rural	71 (74.0)
	Urban	25 (26.0)
Season	Monsoon/post-monsoon (Aug–Nov)	73 (76.0)
	Other months	23 (24.0)

A clear seasonal clustering was observed, with three-quarters of cases presenting during the monsoon and post-monsoon months and a distinct peak in September–October (Figure 1).

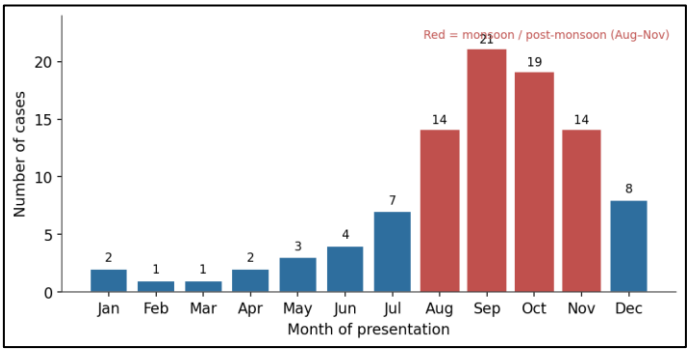

Figure 1. Month-wise distribution of pediatric scrub typhus cases, showing the monsoon/post-monsoon peak (Aug–Nov, red bars).

Fever was universal (100%), with a mean duration of 8.2 days at presentation. The most frequent associated features were hepatomegaly (54.2%), vomiting (42.7%), abdominal pain (34.4%) and splenomegaly (34.4%). An eschar was identified in only 21 children (21.9%), most commonly in the axilla, groin and perineal region. Clinical features are detailed in Table 2 and Figure 2.

Table 2. Frequency of presenting clinical features (N = 96).

Clinical feature	n	%
Fever	96	100.0
Hepatomegaly	52	54.2
Vomiting	41	42.7
Abdominal pain	33	34.4
Splenomegaly	33	34.4
Cough	30	31.3
Edema / facial puffiness	27	28.1
Conjunctival congestion	23	24.0
Headache	22	22.9

Eschar	21	21.9
Lymphadenopathy	19	19.8
Maculopapular rash	18	18.8
Altered sensorium / seizure	14	14.6

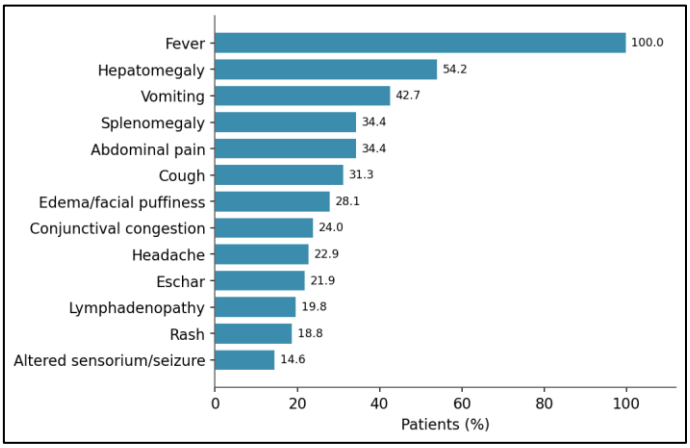

Figure 2. Frequency of major clinical features in children with scrub typhus.

Among laboratory parameters, anaemia (72.9%) and elevated C-reactive protein (83.3%) were the commonest abnormalities, followed by transaminitis (AST elevated in 63.5% and ALT in 57.3%) and thrombocytopenia (49.0%). Hypoalbuminaemia and hyponatraemia were each present in roughly a third of children (Table 3).

Table 3. Principal laboratory abnormalities (N = 96).

Laboratory abnormality	**n**	**%**
Elevated CRP	80	83.3
Anemia (Hb below age norm)	70	72.9
Elevated AST	61	63.5
Elevated ALT	55	57.3
Thrombocytopenia (<150 × 10⁹/L)	47	49.0
Hypoalbuminemia	35	36.5
Hyponatremia	30	31.3
Leukocytosis	22	22.9
Leukopenia	7	7.3

At least one complication developed in 58 children (60.4%). Hepatitis (39.6%) and meningoencephalitis (16.7%) were the most frequent, followed by ARDS/pneumonitis (11.5%), acute kidney injury (9.4%), shock or multi-organ dysfunction (8.3%) and myocarditis (7.3%). The spectrum of complications is shown in Table 4 and Figure 3.

Table 4. Complications among children with scrub typhus (N = 96).

Complication	**n**	**%**
Any complication	58	60.4
Hepatitis	38	39.6
Meningoencephalitis	16	16.7
ARDS / pneumonitis	11	11.5
Acute kidney injury	9	9.4
Shock / multi-organ dysfunction	8	8.3
Myocarditis	7	7.3

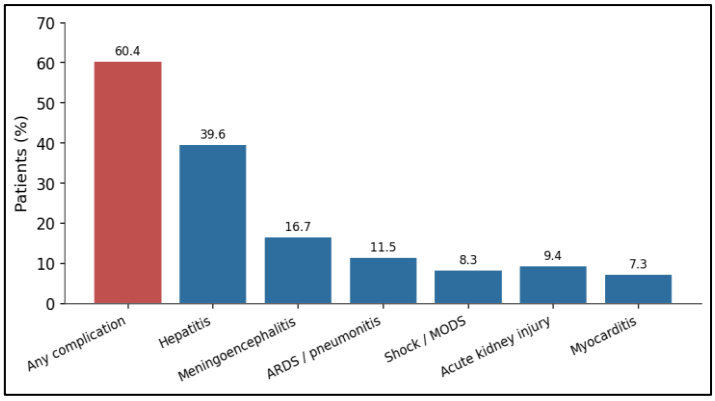

Figure 3. Spectrum of complications. "Any complication" (red) denotes children with one or more of the listed events.

On comparing children with complicated and uncomplicated disease, thrombocytopenia, elevated AST and hypoalbuminaemia at admission were significantly associated with the development of complications, as was a longer duration of fever before presentation (Table 5). The presence of an eschar was not significantly associated with complicated disease.

Table 5. Admission parameters associated with complicated disease, n (%). p-values from chi-square/Fisher's exact test.

Parameter at admission	Complicated (n=58)	Uncomplicated (n=38)	p-value
Thrombocytopenia	37 (63.8)	10 (26.3)	<0.001
Elevated AST (>3× ULN)	31 (53.4)	9 (23.7)	0.004
Hypoalbuminemia	27 (46.6)	8 (21.1)	0.013
Fever >7 days	41 (70.7)	16 (42.1)	0.006
Eschar present	14 (24.1)	7 (18.4)	0.503

All children received an anti-rickettsial antibiotic: doxycycline alone in 70 (72.9%), azithromycin alone in 18 (18.8%) and both agents in 8 (8.3%). Defervescence occurred at a mean of 2.1 days after starting therapy. Nineteen children (19.8%) required intensive care and 7 (7.3%) needed mechanical ventilation. The mean hospital stay was 7.4 days. Ninety-four children (97.9%) recovered, while 2 (2.1%) died, both in the context of multi-organ dysfunction with myocarditis (Table 6).

Table 6. Treatment and immediate outcome (N = 96). Mean defervescence 2.1 days; mean hospital stay 7.4 days.

Treatment / outcome variable	n	%
Doxycycline only	70	72.9
Azithromycin only	18	18.8
Doxycycline + azithromycin	8	8.3
PICU admission	19	19.8
Mechanical ventilation	7	7.3
Recovered	94	97.9
Died (case-fatality rate)	2	2.1

DISCUSSION:

In this prospective study from eastern India, scrub typhus accounted for 7.6% of pediatric AUFI admissions, underscoring its importance as a treatable cause of undifferentiated fever in the region. This seroprevalence is comparable to the 4.5% reported from a tertiary centre in Kolkata[9] and is consistent with the wider Indian literature, which identifies scrub typhus as a major, though frequently overlooked, contributor to acute febrile illness.[3,4] The disease showed striking seasonality, with three-quarters of cases clustering in the monsoon and post-monsoon months — a pattern repeatedly described across India and attributed to increased mite activity and agricultural exposure during these periods.[5,15]

The demographic pattern, with a predominance of young, rural children and a modest male excess, mirrors earlier pediatric series from eastern, southern and north-eastern India.[7,10,16] The high proportion of rural cases is biologically plausible given the rural ecology of the chigger vector and is in keeping with reports linking infection to outdoor activity and proximity to scrub vegetation.[5]

Fever was universal, and gastrointestinal symptoms together with hepatosplenomegaly dominated the clinical picture, as observed in studies from Kolkata, Bhubaneswar and Chennai.[6,7,17] The eschar — although pathognomonic — was detected in only 21.9% of our patients. This low yield is consistent with Indian pediatric data, in which eschar frequency ranges widely from about 11% to 43% and is often lower than in adults, partly because the lesion is small, painless and easily missed in skin folds.[6,11,18] The practical implication, emphasised by several authors, is that the absence of an eschar should never exclude the diagnosis in an endemic setting, and that a deliberate search of the axillae, groin and perineum is essential.[9,19]

Thrombocytopenia and transaminitis were the most consistent laboratory findings, again echoing previous pediatric reports.[7,17,20] Hepatic involvement is characteristic of scrub typhus and reflects the organism's tropism for vascular endothelium and the resulting widespread vasculitis. The frequency of raised inflammatory markers and hypoalbuminaemia further supports a systemic capillary-leak process.

Complications occurred in 60.4% of our cohort, a figure within the broad range reported from Indian tertiary centres, where complication rates vary from roughly 15% to over 70% depending on referral patterns and timing of presentation.[9,11,17] Hepatitis and meningoencephalitis predominated, while myocarditis, acute kidney injury and ARDS were less common but clinically important. The high burden of myocarditis and renal injury reported by Kumar et al. from southern India was interpreted as a marker of late presentation,[17] and our finding that longer fever duration, thrombocytopenia, transaminitis and hypoalbuminaemia were associated with complicated disease is concordant with published predictors of severity in pediatric scrub typhus.[16,21]

Reassuringly, response to anti-rickettsial therapy was prompt, with defervescence within about two days, mirroring the rapid clinical response to doxycycline described elsewhere.[11,14,17] Doxycycline and azithromycin are both effective and well tolerated in children, and short-course doxycycline is no longer considered to pose a meaningful risk of dental staining at the doses used.[14] Our case-fatality rate of 2.1% lies between the very low mortality reported from some centres with early diagnosis and the higher rates seen where treatment is delayed,[16,17] reinforcing the central message that timely empirical therapy is the principal determinant of outcome.

The strengths of this study include its prospective design, serological confirmation of every case, and its contribution to the limited pediatric evidence base from eastern India. Several limitations should be acknowledged. It was a single-centre, hospital-based study at a referral institution, which may overestimate disease severity and complication rates; diagnosis relied on a single IgM ELISA without paired sera or confirmatory polymerase chain reaction, raising the possibility of cross-reactivity and misclassification; and the analysis was restricted to immediate in-hospital outcomes without longer-term follow-up. Multicentre and community-based studies, ideally incorporating molecular diagnostics, would better define the true regional burden.

CONCLUSION:

Scrub typhus is a common and potentially serious cause of acute undifferentiated febrile illness among children in eastern India, with a marked monsoon/post-monsoon predilection and a predominantly rural distribution. Because the diagnostic eschar is frequently absent and the presentation overlaps with other tropical fevers, a high index of clinical suspicion is essential. Thrombocytopenia, transaminitis, hypoalbuminaemia and prolonged fever at admission identify children at higher risk of complications. Early serological testing and prompt empirical treatment with doxycycline or azithromycin produce rapid recovery and low mortality. Strengthening clinician awareness, ensuring access to IgM ELISA in endemic districts, and instituting vector-control and public-health measures are key to reducing the morbidity and mortality of pediatric scrub typhus in this region.

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