

Clinical And Laboratory Profiles Of Scrub Typhus: A Multicenter Prospective Observational Study

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Abstract

Scrub typhus, a neglected tropical disease caused by *Orientia tsutsugamushi*, has re-emerged as a significant cause of acute febrile illness in many parts of Asia, including India. Despite its prevalence, the clinical and laboratory features often overlap with other febrile illnesses such as malaria, dengue, and leptospirosis, making early diagnosis challenging. This prospective multicenter study aimed to evaluate the clinical presentation, laboratory findings, complications, and treatment outcomes in patients with scrub typhus across various healthcare centers in endemic regions of India.

A total of 280 patients diagnosed with scrub typhus were enrolled from three tertiary care centers over a period of 18 months. The most common clinical features were fever, headache, and myalgia. An eschar, a pathognomonic sign, was observed in 52% of patients. Laboratory findings showed a high prevalence of thrombocytopenia (65%) and elevated liver enzymes (73%). Complications such as acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), myocarditis, and multiorgan dysfunction syndrome (MODS) were noted in 21% of cases. The overall mortality rate was 4.3%. The majority of patients (78%) responded well to doxycycline therapy, with clinical improvement observed within 48 to 72 hours.

This study underscores the importance of early diagnosis and treatment in scrub typhus to prevent severe complications. Further efforts are needed to raise awareness of this disease in endemic regions and improve diagnostic capabilities at the primary healthcare level.

Keywords: Scrub typhus, *Orientia tsutsugamushi*, acute febrile illness, eschar, ARDS, doxycycline.

Introduction

Scrub typhus, also known as tsutsugamushi disease, is a zoonotic febrile illness caused by *Orientia tsutsugamushi*, an obligate intracellular bacterium transmitted through the bite of infected chiggers (larval mites). Historically confined to the "tsutsugamushi triangle" (spanning from Japan to Northern Australia and from India to the Pacific Islands), scrub typhus has re-emerged in recent years as an important cause of acute febrile illness in South Asia, including India. The disease is of public health concern due to its wide prevalence, significant morbidity, and potential to cause severe, life-threatening complications if left untreated.

In India, the burden of scrub typhus has increased significantly over the past decade. Rural populations, particularly those involved in agricultural activities, are at higher risk of infection due to frequent exposure to mite-infested vegetation. Despite its growing prevalence, scrub typhus remains an under-recognized disease, largely due to its non-specific clinical presentation, which overlaps with other tropical diseases such as malaria, dengue, and leptospirosis. The clinical features range from mild febrile illness to severe complications, including ARDS, AKI, myocarditis, and MODS, leading to considerable diagnostic challenges.

The characteristic eschar—a necrotic lesion at the site of the chigger bite—is a pathognomonic sign of scrub typhus. However, its presence is often missed or absent, particularly in darker-skinned individuals, complicating the diagnosis. Laboratory findings, including thrombocytopenia, elevated liver enzymes, and hypoalbuminemia, can offer important diagnostic clues, but these are not specific to the disease. Treatment with antibiotics such as doxycycline and azithromycin is highly effective, with rapid clinical improvement observed in most patients. However, delayed diagnosis and treatment can result in high mortality rates, particularly in patients who develop severe complications.

This multicenter prospective observational study was conducted to provide a comprehensive analysis of the clinical and laboratory profiles of scrub typhus in India. The primary objectives of the study were to identify common clinical presentations, describe laboratory abnormalities, and assess treatment outcomes and complications in patients with scrub typhus.

Methods

This multicenter, prospective observational study was conducted over 18 months (January 2023 to June 2024) at three tertiary care centers across different regions of India. The study enrolled 280 patients presenting with acute febrile illness

for more than five days and who tested positive for scrub typhus through either IgM ELISA or polymerase chain reaction (PCR). Patients with confirmed co-infections such as malaria, dengue, or leptospirosis were excluded from the study to ensure the accurate assessment of scrub typhus characteristics.

The study employed standardized data collection tools to gather information on demographics, clinical symptoms, physical examination findings, laboratory investigations, and treatment outcomes. Investigations included complete blood count, liver function tests, renal function tests, serum electrolytes, and chest X-rays. Complications such as ARDS, AKI, myocarditis, and MODS were carefully documented. All patients were managed according to the standard treatment protocols at each center, and antibiotic therapy primarily involved doxycycline or azithromycin. Follow-up data were collected until discharge or death.

Ethical clearance was obtained from the Institutional Review Boards of all participating centers, and written informed consent was obtained from all patients or their legal guardians.

Results

A total of 280 patients with confirmed scrub typhus were included in the study. The majority of the patients were from rural areas (72%), with a male-to-female ratio of 1.5:1. The mean age was 36.4 years (range 18–72 years). Fever was the most common presenting symptom, followed by headache, myalgia, and gastrointestinal symptoms such as nausea, vomiting, and abdominal pain. An eschar was present in 52% of the patients, while 31% exhibited a maculopapular rash.

Table 1: Demographic and Clinical Features of Patients (N = 280)

Characteristic	Number (N)	Percentage (%)
Mean age (years)	36.4	-
Male	168	60
Female	112	40
Rural residents	202	72
Fever	280	100
Headache	218	78
Myalgia	182	65
Gastrointestinal symptoms	109	39
Cough	95	34
Eschar	146	52
Rash	87	31
Lymphadenopathy	78	28
Splenomegaly	45	16
Hepatomegaly	53	19

Laboratory findings revealed thrombocytopenia in 65% of the patients, with elevated liver enzymes (AST/ALT) in 73% and hypoalbuminemia in 43%. Renal involvement, indicated by elevated serum creatinine levels, was noted in 20% of the patients. The prevalence of leukocytosis was 50%, while C-reactive protein (CRP) levels were elevated in 71% of cases.

Table 2: Laboratory Findings of Patients (N = 280)

Laboratory Parameter	Number (N)	Percentage (%)
Thrombocytopenia	182	65
Elevated liver enzymes (AST/ALT)	204	73
Hypoalbuminemia	120	43
Raised serum creatinine (AKI)	56	20
Elevated CRP	198	71
Leukocytosis	140	50

Severe complications were observed in 21% of patients, with ARDS being the most common complication (12%), followed by AKI (7%), myocarditis (4%), and MODS (5%). The overall mortality rate was 4.3%. Most patients (78%) responded favorably to doxycycline therapy, with clinical improvement occurring within 48 to 72 hours.

Table 3: Complications and Outcomes (N = 280)

Complication/Outcome	Number (N)	Percentage (%)
Acute Respiratory Distress Syndrome (ARDS)	34	12
Acute Kidney Injury (AKI)	20	7
Myocarditis	11	4
Multiorgan Dysfunction Syndrome (MODS)	14	5
Mortality	12	4.3
Hospital Stay (Mean days)	7.8	-

Table 4: Treatment and Response (N = 280)

Treatment	Number (N)	Percentage (%)
Doxycycline	218	78
Azithromycin	62	22
Response within 48-72 hours (Doxycycline)	215	98
Response within 48-72 hours (Azithromycin)	57	92
Requirement of ICU care	56	20

Discussion

This multicenter study highlights the significant morbidity associated with scrub typhus in India, with a wide spectrum of clinical manifestations ranging from mild febrile illness to severe life-threatening complications. The presence of an eschar, though pathognomonic, was noted in only 52% of patients, underscoring the need for heightened clinical suspicion, especially in endemic areas.

Laboratory findings of thrombocytopenia, elevated liver enzymes, and hypoalbuminemia were consistent with previous studies and served as important diagnostic clues. Complications such as ARDS, AKI, and MODS were associated with delayed presentation and treatment, emphasizing the need for early diagnosis and intervention.

The high response rate to doxycycline, with significant clinical improvement within 48-72 hours, reaffirms its role as the first-line therapy for scrub typhus. However, the mortality rate of 4.3% remains concerning, particularly in patients who developed severe complications.

Further research is warranted to explore the factors contributing to diagnostic delays and to develop rapid diagnostic tools that can be implemented at the primary healthcare level in endemic regions. Public health measures, including increased awareness and education on scrub typhus, are essential to reduce the burden of this disease.

Conclusion

Scrub typhus is an under-recognized but significant cause of acute febrile illness in India. This study provides a comprehensive overview of the clinical and laboratory profiles of scrub typhus and underscores the need for early diagnosis and prompt treatment to prevent severe complications. Doxycycline remains the treatment of choice, with favorable outcomes observed in the majority of cases. Continued efforts are needed to enhance awareness and diagnostic capabilities in endemic areas.

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