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A study on demographic, clinical profile, and outcome of scrub typhus

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ABSTRACT

Background: Scrub typhus, caused by *Orientia tsutsugamushi*, is an emerging zoonotic infection transmitted through chigger mite bites. It presents with non-specific symptoms and mimics other febrile illnesses, often leading to diagnostic delays and serious complications. **Aims and Objectives:** This study analyzed the demographic, clinical, and laboratory features of patients with scrub typhus and assessed the outcomes based on disease severity. **Materials and Methods:** This prospective observational study was conducted at Dharmapuri Medical College and Hospital in Tamil Nadu. A total of 160 patients who were clinically diagnosed with scrub typhus were included. Demographic details, clinical presentations, laboratory parameters, and outcomes were also recorded. Patients were stratified into three categories based on disease severity: Non-severe, severe, and very severe/fatal. **Results:** Most patients were aged 20–60 years (80%), with a mean age of 40.83 ± 13.79 and 38.77 ± 2.90 years in males and females, respectively. Most cases were from rural areas (80% males and 82.7% females). Fever was present in 100% of cases, followed by vomiting (31.25%), myalgia (30%), abdominal pain (20%), and headaches (19.37%). Eschar was noted in only 6 patients (3.75%). Laboratory abnormalities included hypoalbuminemia (70%), elevated liver enzyme levels (68.75%), and thrombocytopenia (67.5%). Other clinical findings included severe thrombocytopenia (5%), elevated serum triglycerides (50%), and elevated lactate dehydrogenase (43.75%). Complications included electrolyte disturbances (30%), acute renal failure (18.75%), acute respiratory distress syndrome (13.75%), and multi-organ dysfunction syndrome (13.75%). Delayed presentation and very severe disease conditions led to mortality (3.75%). **Conclusion:** Scrub typhus continues to pose a diagnostic challenge because of its varied presentations. Early identification based on clinical suspicion, key laboratory markers, and categorization of disease severity can greatly reduce complications and improve patient outcomes.

Key words: Scrub typhus; Zoonotic infection; Eschar; Hypoalbuminemia; Thrombocytopenia

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INTRODUCTION

Scrub typhus is an acute, life-threatening, undifferentiated febrile illness caused by the obligate intracellular Gram-negative bacterium *Orientia tsutsugamushi*. It is transmitted to humans by the bite of infected larval mites (chiggers) of the *Leptotrombidium* species, which act both as the vector and reservoir of the pathogen.[1] The disease is endemic within a geographical area known as the "tsutsugamushi triangle," which ranges from northern Japan and eastern Russia in the north to northern Australia in the south, and extends westward to Pakistan and Afghanistan.[2] In India, scrub typhus has re-emerged as a significant public health concern, with several outbreaks reported in recent years.[3]

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In India, scrub typhus is found in the Shivalik ranges, Eastern and Western Ghats, Vindhyachal and Satpura ranges, and Southern India experiences outbreaks during the cooler months.[2]

Clinically, scrub typhus manifests after an incubation period of 6–21 days, typically presenting with acute fever, headache, myalgia, rash, and gastrointestinal symptoms such as vomiting and abdominal pain.[4] A key diagnostic clue is the presence of an eschar at the site of mite attachment, usually found in warm, moist, or concealed areas such as the groin, axilla, or waistline.[5] However, the visibility of eschar can vary greatly and is often absent in dark-skinned individuals, particularly in South Asian populations, making diagnosis more challenging.[6] Generalized lymphadenopathy and hepatosplenomegaly are commonly observed, and in untreated cases, systemic involvement may develop during the second week of illness.[7]

Complications can include acute respiratory distress syndrome (ARDS), interstitial pneumonia, meningoencephalitis, myocarditis, gastrointestinal bleeding, and multi-organ dysfunction syndrome (MODS).[8] The disease can mimic other endemic infections, such as dengue, leptospirosis, and typhoid fever, further complicating clinical diagnosis. In tropical countries, co-infections commonly occur alongside scrub typhus infection due to the similarity in clinical features.[9] Laboratory findings often reveal leukopenia or leukocytosis, thrombocytopenia, and elevated liver enzymes.[7]

The Weil–Felix test is inexpensive and widely used, but it has very little specificity and sensitivity because of the use of non-rickettsial antigens for agglutination. Immunoglobulin M (IgM) Enzyme-Linked Immunosorbent Assay (ELISA) offers a sensitivity of 94.2% and a specificity of 93.6%, along with the advantage of automation, making it suitable for large-scale screening. The gold standard remains the indirect fluorescent antibody (IFA) test, which can detect antibodies to various serotypes such as Karp, Gilliam, and Kato, although its use is limited by cost and infrastructure needs.[9] IFA interpretation also requires consideration of endemic cutoff titers, which can vary widely from 1:10 to 1:400, but 1:400 is the most frequently used cutoff.[10]

Doxycycline is the first-line treatment for scrub typhus, typically administered for 7 days. In specific populations, such as children and pregnant women, azithromycin is preferred because of its safety profile. Rifampicin may be used as an adjunct in cases of resistance or non-responsiveness, but it is not recommended as a standalone treatment to prevent the development of antibiotic resistance.[11,12] The disease burden is underestimated due to non-specific clinical symptoms, a lack of pathognomonic signs in many cases, and limited diagnostic awareness among primary healthcare providers. Thus, this study aimed to analyze the demographic characteristics, clinical features, laboratory findings, and outcomes of patients diagnosed with scrub typhus.

MATERIALS AND METHODS

This prospective observational study was conducted on 160 patients clinically suspected of having scrub typhus at Government Dharmapuri Medical College and Hospital, Dharmapuri, from July 2022 to October 2023.

Inclusion criteria

Patients included were aged >12 years, had a febrile illness of 5–28 days duration with a positive serum IgM ELISA for scrub typhus, and had an eschar.

Exclusion criteria

Patients with other proven systemic infections (dengue, leptospirosis, and bacterial infections), positive IgM ELISA only with acute febrile illness and rash, or serious accompanying systemic diseases such as malignancies and autoimmune disorders were excluded.

Methods

Details of the patients, including name, age, sex, address, and occupation, were collected and entered into the data collection form. From each suspected case, 3 mL of blood was collected using BD Vacutainer tubes, red-capped for outpatients and yellow-capped for inpatients. After centrifugation at 6000 rpm for 15 min, 1 mL of serum was separated, labeled, and stored at −80°C. Weil–Felix testing was performed immediately using the PROGEN antigen suspension (Tulip Diagnostics, Goa, India), while ELISA was conducted weekly.

According to disease severity and clinical and laboratory parameters, patients were divided into three categories. Category 1 (non-severe) included no comorbid patients with mild symptoms such as fever, myalgia, cough, or vomiting, and mild derangement of laboratory parameters without complications. These patients had a mean symptom duration of 3.8 days and were treated with doxycycline monotherapy. Category 2 (severe) comprised those with symptoms such as dyspnea, altered sensorium, shock, thrombocytopenia (<1,00,000/mm^3), acute kidney injury not requiring dialysis, and ARDS not requiring ventilation. They did not have any significant association with comorbidities. The mean duration of symptoms was 8.5 days, and the mean hospital stay was 6.5 days. The patient was treated with doxycycline and azithromycin, along with supportive care. Category 3 (very severe/fatal)

included patients with critical features such as severe dyspnea, altered sensorium with meningeal signs, platelet count <20,000/mm^3, renal failure requiring dialysis, MODS, and ARDS needing mechanical ventilation. They did not have any significant association with comorbidities. The mean symptom duration was 12.5 days, and the mean hospital stay was 13.5 days.

Data were analyzed and presented as frequencies and percentages. Data analysis was performed using IBM Statistical Package for the Social Sciences Statistics (version 25), and $P < 0.05$ was considered statistically significant.

Ethical considerations

The Institutional Ethics Committee approved this study (Government Dharmapuri Medical College Institutional Ethics Committee 18/2022), and all patients provided written informed consent before participation. This study adhered to the ethical guidelines for clinical research.

RESULTS

The majority of scrub typhus cases were reported during the monsoon and post-monsoon months, with peak incidences observed in August (30 and 27), September (20 and 18), and October (15 and 12) in both years (Table 1).

In terms of locality, most were from rural areas compared to urban areas (males: 80 vs. 20%, females: 82.7 vs. 17.3%), and most were directly or indirectly involved in agriculture and cattle farming. Age-wise comparison showed that the majority of infections occurred in the 20–40 and 40–60 age groups. The mean age in males was 40.83±13.79 years and in females was 38.77±2.90 years, with no significance (P=0.33) (Table 2).

Fever was the most consistent presenting symptom, observed in all patients (100%); the mean duration of fever was 6.4 days. Other common symptoms included vomiting (31.25%), myalgia (30%), abdominal pain (20%), and headaches (19.37%). On clinical examination, anemia was the most common finding (36.25%), followed by splenomegaly (31.25%) and hepatomegaly (30%). Eschar, though considered a diagnostic marker, was observed in only 3.75% of cases and was commonly observed in the groin, back, and lower extremities (Table 3).

Laboratory evaluation revealed that the most frequent abnormalities were hypoalbuminemia (70%), elevated liver enzymes (68.75%), and thrombocytopenia (67.5%), followed by elevated serum triglyceride (50%) and lactate dehydrogenase (LDH) levels (43.75%). Among the complications, electrolyte disturbances were the most common (30%), followed by acute renal failure (18.75%), ARDS (13.75%), and MODS (13.75%). Polyserositis was observed in 9.37%, whereas encephalopathy and death were each reported in 3.75% of patients; the death occurred only due to delayed presentation and therapy initiation (Table 4).

Table 1: Monthly distribution of cases

Month	2022 (%)	2023 (%)
January	–	4 (5.2)
February	–	2 (2.6)
March	–	2 (2.6)
April	–	1 (1.3)
May	–	1 (1.3)
June	–	2 (2.6)
July	8 (9.5)	7 (9.2)
August	30 (35.7)	27 (35.5)
September	20 (23.8)	18 (23.7)
October	15 (17.9)	12 (15.8)
November	6 (7.1)	–
December	5 (5.9)	–

Table 2: Distribution of locality and age among groups

Parameters	Category	Male (%)	Female (%)
Locality	Rural	68 (80)	62 (82.7)
	Urban	17 (20)	13 (17.3)
Age in years	<20	4 (4.7)	3 (4)
	20–40	32 (37.7)	28 (37.3)
	40–60	36 (42.3)	32 (42.7)
	>60	13 (15.3)	12 (16)

DISCUSSION

Scrub typhus is a dangerous zoonotic infection that is frequently misdiagnosed, can cause serious complications, and has a wide range of clinical manifestations, especially in tropical and rural areas. The lack of certain symptoms, such as eschar, and its resemblance to other common febrile illnesses, lead to delayed diagnosis and treatment, which increases the morbidity and mortality rates. By classifying patients into severity-based categories and comparing clinical features, laboratory abnormalities, and outcomes, this study aimed to highlight patterns in disease presentation and identify early markers of severity to improve clinical suspicion and guide timely management.

In our study, most of the scrub typhus cases were reported during the monsoon and post-monsoon months, particularly August, September, and October. A similar seasonal distribution was observed by Wangrangsimakul et al., who reported that the majority of scrub typhus cases occurred from June to November, with a significant concentration in August, September, and October in Thailand.[13] Kumar

Table 3: Distribution of symptoms and clinical findings

Parameters	Category	Count (%)
Presenting symptoms	Fever	160 (100)
	Headache	31 (19.37)
	Myalgia	48 (30)
	Vomiting	50 (31.25)
	Abdominal pain	32 (20)
	Cough	15 (9.37)
	Dyspnea	25 (15.62)
	Shock	14 (8.75)
	Altered sensorium	13 (8.125)
Clinical finding	Hepatomegaly	48 (30)
	Splenomegaly	50 (31.25)
	Anemia	58 (36.25)
	Hepatosplenomegaly	30 (18.75)
	Eschar	6 (3.75)

Table 4: Distribution of laboratory findings and complications

Parameters	Category	Count (%)
Laboratory findings	Anemia (Hb<11 g/dL)	58 (36.25)
	Leukopenia (<4,000 cells/mm^3)	19 (11.87)
	Leucocytosis (>10,000 cells/mm^3)	46 (28.75)
	Thrombocytopenia (<1,50,000/mm^3)	108 (67.50)
	Severe thrombocytopenia (<20,000/mm^3)	8 (5)
	Elevated liver enzymes	110 (68.75)
	Serum lactate dehydrogenase (>480 IU/L)	70 (43.75)
	Serum triglyceride (Fasting>200 mg/dL)	80 (50)
	Hypoalbuminemia (3.5 g/dL)	112 (70)
	Hyponatremia (<135 mEq/L)	36 (22.5)
	Hypokalemia (<3.5 mEq/L)	23 (14.37)
	Chest infiltrates (interstitial pneumonia, b/l reticulonodular opacity in chest X-ray)	38 (23.75)
	Pleural effusion	37 (23.125)
	CSF WBC (>5 cells/mm^3)	6 (3.75)
Complications	ARDS	22 (13.75)
	Acute renal failure	30 (18.75)
	Electrolyte disturbance	48 (30)
	Polyserositis	15 (9.37)
	MODS	22 (13.75)
	Encephalopathy	6 (3.75)
	Death	6 (3.75)

ARDS: Acute respiratory distress syndrome, MODS: Multi-organ dysfunction syndrome, CSF: Cerebrospinal fluid, WBC: White blood cell

et al. reported an increase in seroprevalence during August (48.1%), September (40.7%), and October (11.1%).[14] These findings emphasize the importance of increased clinical suspicion for scrub typhus during these peak seasons.

In our study, rural residents were mostly affected (80% of males and 82.7% of females), and a majority of them were involved in agriculture. The mean age was similar among males and females (40.83±13.79 and 38.77±2.90 years), with no significant difference (P=0.33), and most patients belonged to the 20–60-year age group (80%). Similarly, Jain et al. analyzed 50 patients and reported that the majority belonged to a rural background (92%) and were farmers (86%). Most were 40–60 years old, and females were predominant in their study (60 vs. 40%).[15] Hence, rural occupation and age-related outdoor activity appear to be significant risk factors.

Clinically, all patients in our study had fever with a mean duration of 6.4 days. The most common associated symptoms were vomiting (31.25%), myalgia (30%), abdominal pain (20%), and headache (19.37%). Anemia (36.25%), splenomegaly (31.25%), and hepatomegaly (30%) were frequently observed in the majority of patients. Eschar, a standard diagnostic marker, was observed in only 3.75% of cases, most commonly located on the groin, back, or lower limbs. Aligning with our findings, Jain et al. reported 100% prevalence for fever and myalgia, 82% headache, and 24% eschar mark.[15] Further strengthening our findings, Phukan observed that all patients with scrub typhus had fever (100%), with a mean duration of 6.8±3.9 days. Common symptoms included skin rash (73.3%), body ache (53.3%), and vomiting (53.3%), whereas eschar was found in only two patients.[16] This highlights that the absence of eschar should not exclude the diagnosis in endemic areas.

Laboratory parameters revealed hypoalbuminemia (70%), elevated liver enzymes (68.75%), and thrombocytopenia (67.5%) as the most common abnormalities, followed by hypertriglyceridemia (50%) and elevated LDH (43.75%). Aligning with our study, Jana et al. evaluated 105 patients and reported hypoalbuminemia (23.81%), elevated serum ALT (66.67%), and thrombocytopenia (46.67%) as common abnormalities.[17] Similarly, Sarswat et al. reported that 71% had hypertriglyceridemia, 93% had low HDL, whereas only 4% had elevated LDH levels.[18] Hence, the combination of thrombocytopenia, elevated liver enzymes, and hypoalbuminemia should prompt consideration of scrub typhus in endemic settings.

Among the complications, electrolyte disturbances were the most frequent (30%), followed by acute renal failure (18.75%), ARDS (13.75%), and MODS (13.75%). Encephalopathy and death occurred in 3.75% of patients. These findings are supported by Sharma et al., who also reported that acute kidney injury (32%), ARDS (25%), and MODS (20%) were the most common complications, with a mortality rate of 13.6%.[19] Further strengthening our findings, Goyal et al. reported that hepatic transaminitis (69.7%), renal insufficiency (44.0%), ARDS (37.6%), and

shock (33.9%) were the major and common complications, and they were associated with high mortality.[20] This indicates that the presence of such systemic complications requires early diagnosis and immediate supportive care to reduce mortality.

Scrub typhus is a seasonal, rural disease that often mimics other febrile illnesses. Laboratory abnormalities, such as hypoalbuminemia, elevated liver enzyme levels, and thrombocytopenia, are key diagnostic clues. Increased awareness among healthcare providers and improved diagnostic accessibility are important for reducing complications and preventing mortality. Future research should focus on identifying early biomarkers of severe disease and assessing outcomes in larger multicenter studies.

Limitations of the study

This study was limited by its single-center design and small sample size, which could have affected the generalizability of the results. Furthermore, long-term monitoring of late-onset complications was not performed.

CONCLUSION

Scrub typhus is a significant cause of acute febrile illness in rural populations, particularly during the monsoon and post-monsoon seasons. The disease predominantly affects individuals aged 20–60 years, with non-specific symptoms and a low frequency of eschar, making early diagnosis challenging. Laboratory abnormalities, such as hypoalbuminemia, thrombocytopenia, and elevated liver enzymes, are commonly observed, and delayed presentation and diagnosis lead to complications, such as MODS, ARDS, acute renal failure, and death. Further large-scale multicenter studies are recommended to standardize the diagnostic criteria and treatment protocols for scrub typhus.

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