

Research Article

# From Febrile Illness To Multiorgan Dysfunction: Expanding The Clinical, Biochemical And Epidemiological Spectrum Of Scrub Typhus — A 12-Month Retrospective Study

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## A B S T R A C T

**Background:** Scrub typhus is caused by *Orientia tsutsugamushi* and transmitted to humans through the bite of infected larval trombiculid mites (chiggers). It is an underdiagnosed cause of acute febrile illness in India, as it presents with nonspecific manifestations and resembles other tropical infections. If not recognised early, scrub typhus can progress to severe complications, including multiorgan dysfunction and death.

**Objectives:** To evaluate the demographic profile, clinical manifestations, biochemical abnormalities, complications and outcome of patients suffering from scrub typhus in a tertiary care hospital.

**Methods:** The study was carried out in the Department of Microbiology, Saveetha Medical College, Chennai, from January to December 2025. Patients of all ages presenting with acute febrile illness and positive for scrub typhus by IgM ELISA were enrolled in the study. Serum samples were subjected to IgM ELISA using the Scrub Typhus Detect™ IgM ELISA Kit (InBios).

**Results:** Of 2566 samples, 193 (7.5%) were positive. Males accounted for 52% and females 48%. Most cases were aged 41–60 years (35%) with a statistically significant difference across age groups (Chi-square test,  $p < 0.0001$ ). Seasonal peaks were observed in December (17%) and January (15%). Fever was predominant (94.8%), followed by cough (32.6%), chills and rigour (30.6%), vomiting (28%), myalgia (24.9%), abdominal pain (23.3%) and headache (22.8%). Eschar was observed in 7.3%. Laboratory abnormalities included liver dysfunction (78%), electrolyte imbalance (60%), thrombocytopenia (35%) and renal dysfunction (24.4%). Comorbidities were present in 34%, mainly diabetes and hypertension. Complications included ARDS (9%), septic shock (7%) and AKI (3%). Mortality was 2.6%, and 97.4% recovered after treatment.

**Conclusion:** Scrub typhus remains an important cause of acute febrile illness in endemic areas. Early diagnosis enables timely treatment and reduces complications and mortality.

**Keywords:** ELISA – Enzyme Linked Immunosorbent Assay; ARDS – Acute Respiratory Distress Syndrome; AKI – Acute Kidney Injury

## Introduction

Scrub typhus is an acute febrile illness caused by the intracellular Gram-negative bacterium *Orientia tsutsugamushi*, which belongs to the Rickettsiaceae family.<sup>1</sup> Scrub typhus is transmitted to man through the bite of infected larval trombiculid mites, also called chiggers. After the bite, the infection spreads throughout the body through the lymphatic and circulatory systems, leading to endothelial infection and consequent vasculitis which accounts for the different symptoms exhibited by infected individuals.<sup>2,3</sup>

Scrub typhus is endemic in the “Tsutsugamushi Triangle”, which includes northern Japan and far-eastern Russia in the north, northern Australia in the south and Pakistan and Afghanistan in the west and the Pacific Islands in the east.<sup>3</sup> This region includes the country of India, where scrub typhus is a major contributor to the incidence of acute febrile illness. Though the disease has been prevalent in this region, it has remained largely underdiagnosed due to the nonspecific symptoms of the infection.<sup>4</sup>

In the past few years, scrub typhus has again come to the forefront as a significant cause of public health concern in many Asian countries, including India. Several epidemiological studies have documented the presence of this disease in different states of the country, such as Tamil Nadu, Himachal Pradesh, Rajasthan and Odisha.<sup>5</sup> Scrub typhus accounts for a significant proportion of undifferentiated fever, particularly during the monsoon and post-monsoon seasons, when the vectors are most active.<sup>6</sup>

The clinical presentation of scrub typhus is nonspecific and variable, which may sometimes lead to a delay in the diagnosis of the disease.<sup>7</sup> Patients with scrub typhus present with the acute onset of fever, headache, myalgia, malaise and gastrointestinal symptoms like nausea, vomiting and abdominal pain.<sup>8</sup> An eschar at the site of the chigger bite is a characteristic feature of scrub typhus, although it is absent in a significant percentage of the population, particularly in dark-skinned individuals or if the bite is in a secluded part of the body.<sup>9</sup>

If left untreated, scrub typhus can transform from an uncomplicated febrile illness into a severe systemic illness involving multiple organ systems.<sup>10</sup> This is because of underlying endothelial damage leading to vasculitis,

which can cause complications such as acute respiratory distress syndrome, acute kidney injury, myocarditis, meningoencephalitis and septic shock.<sup>11,12,13</sup>

Besides the various signs and symptoms, various biochemical changes have been reported in patients with scrub typhus including thrombocytopenia, elevated liver enzymes, renal dysfunction and disturbances in electrolyte levels including hyponatremia.<sup>3,4,5</sup> Liver involvement, as indicated by transaminitis, is commonly seen, and renal dysfunction can vary from mildly elevated creatinine levels to acute kidney injury.<sup>5,13,14</sup>

Even though scrub typhus is becoming increasingly recognised, underdiagnosis of the disease still occurs due to the presence of similar manifestations to other tropical febrile illnesses, including dengue, malaria, leptospirosis and enteric fever.<sup>6,7</sup> Therefore, the clinical and biochemical spectrum of scrub typhus is important for the early diagnosis and management of the disease. The aim of the current study is to assess the demographic profile, clinical manifestations, biochemical changes, complications and outcomes of scrub typhus cases diagnosed at the tertiary care facility over the past year.

## Materials And Methods

### Study Design and Setting

The study was conducted as a retrospective observational study in the Department of Microbiology at Saveetha Medical College, Chennai after obtaining approval from the Institutional Scientific Committee (760/03/2026/SRB/SMCH). The study included patients diagnosed with scrub typhus over a 12-month period from January 2025 to December 2025.

### Inclusion Criteria

- Patients of all age groups presenting with acute febrile illness and confirmed cases of scrub typhus infection by IgM ELISA test.
- Patients with complete medical records.

### Exclusion Criteria

- Patients with incomplete medical records.
- Confirmed cases of other febrile illnesses such as dengue, malaria, leptospirosis, and enteric fever.
- Scrub typhus cases negative for the IgM ELISA test.

### Sample Collection And Processing

Approximately 3-5 mL of venous blood was collected aseptically from patients who had acute febrile illness and were suspected to have scrub typhus. The blood samples were collected into plain sterile vacutainer tubes without anticoagulant and left to clot at room temperature. The blood samples were centrifuged at 3000 rpm for 10 minutes to separate the serum. The separated serum was carefully

collected into sterile labelled microcentrifuge tubes and processed on the same day.

### Methodology: IgM ELISA 15,16

The test was performed using the Scrub Typhus Detect™ IgM ELISA kit manufactured by InBios International In., USA.

### Method: Indirect Enzyme-Linked Immunosorbent Assay (ELISA)

- Wells are coated with recombinant *Orientia tsutsugamushi* antigen.
- Patient serum (diluted) is added; specific IgM in serum binds antigen.
- After incubation and washing, an HRP-conjugated polyclonal goat anti-human IgM binds captured IgM.
- After washing, TMB substrate reacts with HRP to produce a color change; the intensity (OD450) is proportional to IgM amount.
- An acidic stop solution halts the reaction and yields a yellow colour measured at 450 nm.

The optical density (OD) was read using an ELISA reader at the appropriate wavelength. The samples were considered positive for scrub typhus IgM antibodies when the OD was greater than the cutoff set by the manufacturer.

### Statistical Analysis

Data were entered in Microsoft Excel and analysed using OpenEpi software version 3.01. Frequency and percentage were used to represent the variable. The chi-square test was used, and a p-value of less than 0.05 was considered statistically significant. Due to the retrospective and observational design of the study, the data analysis was primarily descriptive.

## Result

### Demographic Profile

During the study period, a total of 2566 samples were subjected to scrub typhus testing, of which 193 samples were positive. Among the positive samples, 101 (52%) of scrub typhus cases were found to be male and 92 (48%) of scrub typhus cases were found to be female. The difference between sexes was not statistically significant ( $\chi^2 = 0.42$ , degree of freedom (df) = 1,  $p > 0.5$ ), suggesting almost equal distribution in males and females. The highest percentage of scrub typhus cases was found in the 41–60 years age group (35%), followed by 21–40 years (24%), 0–20 years (22%), 61–80 years (18%) and 81–100 years (1%). The difference among the age groups was statistically significant ( $\chi^2 = 59.57$ ,  $df = 4$ ,  $p < 0.0001$ ), suggesting that middle-aged adults were more prone to the disease. Scrub typhus cases have been reported throughout the year, with a peak in the month of December (17%) followed by January (15%),

October (14%), November (13%), September (13%) and the lowest in May (2%) and April (1%). As the numbers in certain months were less, the chi-square test could not be performed for the distribution of the disease among the months of the year; trends are shown in percentages only.

**Table 1. Sex, Age and Seasonal Distribution of Scrub Typhus**

Demographic Profile	Number of Cases (n)	Percentage (n%)
Sex-Wise Distribution		
Male	101	52%
Female	92	48%
Age-Wise Distribution (years)		
0-20	43	22%
21-40	46	24%
41-60	68	35%
61-80	34	18%
81-100	2	1%
Seasonal Trends		
January	28	15%
February	20	10%
March	8	4%
April	2	1%
May	3	2%
June	5	3%
July	6	3%
August	10	5%
September	25	13%
October	27	14%
November	26	13%
December	33	17%

### Clinical Features

The clinical manifestations of scrub typhus varied among patients. The most common clinical manifestation was fever, seen in 183 (94.8%) cases, followed by cough in 63 (32.6%) cases, chills and rigour in 59 (30.6%) cases, vomiting in 54 (28%) cases, myalgia in 48 (24.9%) cases, abdominal pain in 45 (23.3%) cases and headache in 44 (22.8%) cases. Other symptoms seen in the patients were breathlessness in 37 (19.2%) cases, loose stools in 19 (9.8%) cases, nausea and anorexia in 14 (7.3%) cases each, giddiness in 13 (6.7%) cases and malaise in 3 (1.6%) cases. Eschar was observed in 14 patients (7.3%).

**Table 2. Clinical Features Among Patients With Scrub Typhus**

Clinical Features	Number Of Cases	Percentage (N%)
Fever	183	95%
Cough	63	33%
Chills and rigor	59	31%
Vomiting	54	28%
Myalgia	48	25%
Abdominal pain	45	23%
Headache	44	23%
Breathlessness	37	19%
Loose stools	19	10%
Nausea	14	7%
Anorexia	14	7%
Eschar	14	7%
Giddiness	13	7%
Malaise	3	2%

**Laboratory Abnormalities**

Laboratory abnormalities were commonly seen among the patients. Liver function abnormalities were the most common, seen in 150 cases (77.7%), followed by electrolyte abnormalities in 115 cases (59.6%) and renal function abnormalities in 47 cases (24.4%). Thrombocytopenia was seen in 67 cases (34.7%), while coagulation abnormalities such as prolonged PT and APTT were seen in 10 cases (5.2%) and 6 cases (3.1%), respectively.

**Table 3. Laboratory Abnormalities Among Patients With Scrub Typhus**

Laboratory Parameter	Number Of Cases (N)	Percentage (N%)
Liver function abnormalities	150	78%
Renal function abnormalities	47	24%
Electrolyte abnormalities	115	60%
Thrombocytopenia	67	35%
Prolonged PT	10	5.2%
Prolonged APTT	6	3.1%

- **Liver function abnormalities:** Elevated total bilirubin; Elevated direct bilirubin; Elevated aspartate amino-

transferase (AST); Elevated alanine aminotransferase (ALT); Elevated alkaline phosphatase (ALP); elevated gamma-glutamyl transferase

- **Kidney function abnormalities:** Elevated urea; elevated creatinine; elevated uric acid
- **Electrolyte abnormalities:** Hyponatraemia; Hypokalaemia; Hypochloraemia; low bicarbonate
- **PT:** Prothrombin time
- **APTT:** Activated partial thromboplastin time

**Comorbidities**

Comorbid conditions were identified in the study population. Diabetes mellitus (18%) and hypertension (18%) were the most common comorbid conditions, followed by chronic kidney disease (3%), hypothyroidism (3%), coronary artery disease (2%), bronchial asthma (1%), chronic obstructive pulmonary disease (COPD) (1%) and tuberculosis (1%). Other comorbid conditions such as SLE (systemic lupus erythematosus), RA (rheumatoid arthritis), chemotherapy-related comorbid conditions and dilated cardiomyopathy (DCM) affected 4 patients (2%) in the study. Most of the patients, 128 (66%) in the study population, had no comorbid conditions. Some patients had multiple comorbid conditions.

**Table 4. Distribution of Comorbidities Among Scrub Typhus Patients**

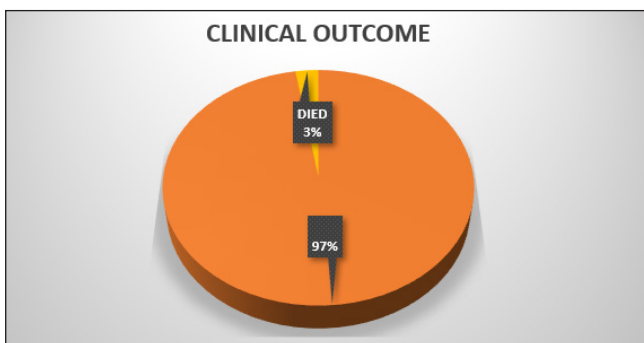
Comorbidity	Number Of Cases (n)	Percentage (n%)
Diabetes mellitus	34	18%
Hypertension	34	18%
Chronic kidney disease	6	3%
Hypothyroidism	5	3%
Coronary artery disease	3	2%
Bronchial asthma	1	1%
COPD	1	1%
Tuberculosis	1	1%
Other comorbidities (SLE, RA, Chemotherapy, DCM)	4	2%
No comorbidity	128	66%

**Complications And Outcome**

Complications were reported in some patients during the course of the disease. Among the reported complications, acute respiratory distress syndrome (ARDS) (9%) was the most common, followed by septic shock/sepsis (7%), acute kidney injury (AKI) (3%), and septic encephalopathy (1%). On the other hand, the mortality rate of the disease has been reported at 2.6% (5 patients), while 188 patients (97.4%) have recovered from the disease following treatment.

**Table 5. Complications Among Scrub Typhus Patients**

Complication	Number Of Cases (n)	Percentage (n%)
Acute respiratory distress syndrome (ARDS)	18	9%
Septic shock/Sepsis	14	7%
Acute kidney injury	5	3%
Septic encephalopathy	2	1%

**Figure 1. Clinical Outcome Among Scrub Typhus Patients**

## Discussion

Scrub typhus is still an important cause of acute fever in various parts of India and other countries in the 'tsutsugamushi triangle'.<sup>17</sup> In the present study, out of the total of 2566 samples, 193 samples were found positive for scrub typhus, resulting in a prevalence rate of 7.5%. The same rate of prevalence has been seen in various studies conducted in the Indian subcontinent and South India showing the endemicity of the disease.<sup>18,19,20</sup> The disease is often underdiagnosed despite the advancement of diagnostic technology, owing to the nonspecific manifestation of the disease.<sup>21</sup>

In the present study, slightly higher numbers of cases were seen in the male population (52%) compared to the female population (48%). The results are in accordance with various studies conducted in South India, where the male population was seen to be slightly higher compared to the female population.<sup>17,22</sup> The male population was seen to be exposed to the disease at work in the outdoor environment, such as agriculture and fieldwork.<sup>20</sup>

Age-wise distribution of the cases in the present study showed that the majority of the cases belonged to the 41-60 years age group, followed by the 21-40 years age group. The pattern of distribution of cases by age group is similar to that reported in other studies conducted in India including South Indian regional studies, where the majority

of the cases belong to the middle-aged adult population [18,19,23]. This may be because this population group would be more likely to be involved in outdoor activities and would have greater exposure to vegetation and mites.<sup>24</sup>

Seasonal variation was observed in the present study, where the majority of the cases presented during the post-monsoon and winter seasons, particularly between September and January, with the highest number of cases presenting in the month of December. The findings of the present study are in concurrence with several studies conducted in various parts of the country, including Tamil Nadu, where a higher incidence of the disease has been observed during the post-monsoon season.<sup>17,20,25</sup>

The most common manifestation in the present study was fever, which accounted for 94.8% of the cases, followed by cough, chills and rigour, vomiting and myalgia. This is in concurrence with the results of the earlier studies from South India, in which the most common manifestation of scrub typhus has been reported as fever, which accounts for more than 90% of the cases.<sup>17,22,26</sup> However, the manifestation of scrub typhus is non-specific and can be similar to that of other tropical fevers like dengue, malaria and leptospirosis.<sup>24</sup> Overlapping signs and symptoms are common in acute febrile diseases in tropical areas, and this often poses difficulties in arriving at a diagnosis. Co-infections due to the simultaneous presence of several pathogens may also happen in endemic areas, affecting the course of the illness and its treatment. Nevertheless, due to the design of the study being retrospective and relying on medical records, it was not possible to perform a comprehensive assessment for all possible pathogens.

The presence of eschar, which is considered a characteristic feature of scrub typhus, was observed in only 7.3% of the patients in the present study. This has been reported in various studies conducted in the Indian population, including regional South Indian studies where eschar detection ranges between 5–15%.<sup>2,21</sup> This low rate of manifestation of eschar in the patients might be due to the fact that the eschar is usually located in hidden areas such as the axilla, groin and inframammary areas, which might not be included in the routine examination.<sup>18</sup>

Laboratory abnormalities were commonly observed in the present study. Among these, liver function abnormalities were the most common, observed in 78% of the patients. This was followed by electrolyte abnormalities in 60% of the patients. Thrombocytopenia was observed in 35% of the patients. Various studies conducted in scrub typhus-infected patients from South India and other endemic regions have observed similar laboratory abnormalities.<sup>17,22,27</sup> Elevated liver enzymes and thrombocytopenia are commonly observed in scrub typhus-infected patients. This may be due to endothelial damage caused by the infection.

Comorbid diseases like diabetes mellitus and hypertension were observed in the present study. These have also been observed in the past, where chronic diseases were commonly observed in the affected patients in South Indian hospital-based studies.<sup>19, 22</sup>

In the present study, complications have been observed in a certain percentage of patients. The commonly observed complication in patients was acute respiratory distress syndrome (9%), followed by septic shock/sepsis (7%) and acute kidney injury (3%). This is in line with other studies from South India and endemic regions of India that have noted respiratory failure, shock and acute kidney injury as serious complications in patients infected with severe scrub typhus.<sup>18,19,25</sup>

The mortality rate in this study was found to be low at only 2.6%, as most patients recovered from the infection after appropriate treatment. The mortality rate in this study was found to be similar to, or even lower than, that found in other studies conducted in hospitals in India, including South Indian tertiary care centres, with a mortality rate of 3 to 7%.<sup>19,22</sup> The low mortality rate in this study could be due to the early diagnosis, appropriate antibiotics and supportive treatment.

Overall, the findings of this study point to the importance of maintaining a high index of suspicion for scrub typhus in patients presenting with acute febrile illness in endemic regions. Early diagnosis of the disease can lead to timely treatment and reduction in complications and mortality.

## Conclusion

Scrub typhus is still a significant cause of acute febrile illness in endemic areas of India. It is very important to recognise clinical features of scrub typhus, even in the absence of classical signs of illness such as eschar formation. Laboratory evidence of increased liver enzymes and thrombocytopenia may also aid in early suspicion of illness and diagnosis of scrub typhus. Seasonal variations, demographic features and co-morbid illnesses may also be useful in improving patient outcomes and reducing mortality in patients suffering from scrub typhus. Referral centres and medical colleges located within endemic areas need to improve their screening protocol for scrub typhus cases among acute febrile illness cases. Early empirical treatment with doxycycline and training clinicians can also be helpful in minimising morbidity and mortality associated with scrub typhus.

## Limitations

The study was conducted in a single centre, which is a tertiary care centre and this could limit the generalisation of the study. In the retrospective study, some demographic information was not available for the patients. The analysis was mainly descriptive and did not assess statistical

associations between clinical variables, risk factors and patient outcomes. Comprehensive evaluation for co-infections and other acute febrile illnesses could not be performed in all cases. The diagnosis was based on routine tests, and the tests were not supplemented with molecular tests to confirm the diagnosis. In addition, there was no follow-up information after discharge, which could limit the assessment of the outcome and complications.

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**Conflict of Interest:** None

## Author Contribution

The author solely contributed to the conceptualization, data collection, analysis, interpretation of results and manuscript preparation.

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