

SCRUBBING OUT SCRUB TYPHUS: INSIGHTS FROM A TERTIARY CARE HOSPITAL IN TAMILNADU

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Abstract

Background: Scrub typhus, caused by *Orientia tsutsugamushi*, is a significant cause of acute undifferentiated febrile illness in tropical regions. Despite affecting over one million people annually in India, scrub typhus remains overlooked. This study aimed to evaluate the epidemiological features, clinical profile, laboratory features, and outcomes of scrub typhus cases in Tamil Nadu, India. **Materials and Methods:** A retrospective study was conducted in a tertiary care hospital, reviewing medical records of scrub typhus patients between June 2022 and January 2023. Data on demographics, clinical presentation, laboratory findings, and radiological results were collected and analyzed. **Result:** 106 patients (mean age: 45.3 years) were included. The clinical presentation included fever (100%), GI symptoms (29.2%), headache, myalgia, and altered sensorium. Sixty-four point two percent of patients had an eschar, predominantly in the anogenital region. Laboratory abnormalities included thrombocytopenia (97%), leukocytosis (81%), elevated liver enzymes (32%), and elevated creatinine (23%). Radiological findings indicated interstitial pneumonia in 16% of patients. Treatment with doxycycline was effective, while severe cases required doxycycline and azithromycin in combination. The average hospital stay was 8.99 days, and the case fatality rate was 0.94%. **Conclusion:** Scrub typhus is an important consideration in the differential diagnosis of acute undifferentiated febrile illness in Tamil Nadu, India. Early diagnosis and treatment are vital to minimize the risk of complications and mortality. The findings emphasize the need for increased awareness and timely management of scrub typhus cases to address this potentially fatal tropical infection.

INTRODUCTION

Scrub typhus is an underrated tropical infection caused by the mite-borne obligate intracellular bacterium, *Orientia tsutsugamushi* in the Rickettsiaceae family. It is transmitted by larval forms of *Leptotrombidium* mites called 'chiggers'. Despite affecting over one million people annually, scrub typhus remains an overlooked problem in many countries, including India, where an estimated one billion people are at risk.^[1]

The disease burden of scrub typhus in India remains unclear. While an early epidemic occurred during the Second World War in the states of Assam and Bengal, there has been a reemergence of cases in recent years from various states, including Tamil Nadu. Scrub typhus is a seasonal disease prevalent in autumn and is a significant cause of acute

undifferentiated febrile illness, accounting for almost 25% of such cases. Reported severe clinical manifestations or complications of scrub typhus include interstitial pneumonia, acute renal failure, meningoencephalitis, gastrointestinal bleeding, and multiple organ failure.^[2]

Early diagnosis and prompt treatment are crucial in reducing the risk of complications and mortality associated with scrub typhus. The case fatality rate without appropriate treatment varies from 8% to 45%. Therefore, this study aimed to evaluate the epidemiological features, clinical profile, laboratory features, and clinical outcomes of cases of scrub typhus and identify the predictors of disease severity.^[3]

Given the lack of data on scrub typhus from Tamil Nadu, where an outbreak occurred during the monsoon season, we conducted this study in a tertiary

care hospital to describe the diverse epidemiological, clinico-radiological, laboratory parameters, and outcome profile of patients with scrub typhus. Our findings will help improve the understanding of scrub typhus in this region and contribute in developing effective prevention and treatment strategies for this potentially fatal rickettsial infection.

MATERIALS AND METHODS

This cross-sectional observational study was conducted at KAPV Government Medical College, Trichy, in Tamil Nadu, India.

Inclusion Criteria

The study included adult patients (18 years and older) with acute febrile illness admitted to the fever wards and intensive care units with a confirmed diagnosis of scrub typhus.

Exclusion Criteria

Patients with eschar but negative IgM Anti O. tsutsugamushi, co-infections such as malaria, dengue, leptospirosis, COVID-19 or enteric fever, age less than 18 years, pregnancy, and acute febrile illness cases with other definite diagnoses such as dengue, leptospirosis, COVID-19, malaria, and enteric fever were excluded.

Confirmed cases were defined as those with ELISA Anti O. tsutsugamushi IgM positivity. Ethical approval was obtained from the institutional Ethics Committee of KAPVGMCC, and informed consent was taken from all patients. The study collected demographic characteristics, clinical features, comorbid illnesses, vital parameters, systemic examination findings, defervescence time, length of hospital stay, and complications, including acute kidney injury, acute respiratory distress syndrome, hepatitis, and encephalitis. Blood investigations, including a complete blood count, liver function tests, serum protein analysis, prothrombin time, international normalized ratio, and renal function

tests, were conducted using automated biochemical analyzers on the day of admission and repeated periodically until discharge. The study also recorded chest radiography, ultrasound examination of the chest and abdomen with the pelvis, and cardiac echocardiography findings, wherever available. Other investigations, such as serology for dengue, leptospirosis, enteric fever, HIV, and blood culture and urine culture reports, were also noted.

The study outcomes included the length of hospital stay, duration of ICU stay, duration of ventilator days, complications related to various organs, and mortality. Scrub typhus was confirmed by performing IgM ELISA on serum samples using the Scrub Typhus Detect IgM ELISA system, as per the manufacturer's instructions. All cases with IgM ELISA for scrub typhus positive status were considered as confirmed scrub typhus cases, and the diagnosis was further reiterated by the presence of typical eschar or exclusion of other causes for acute febrile illness.

RESULTS

The study findings reveal that scrub typhus affects males (50.9%) and females (49.1%) without gender bias. The highest proportion of cases occurred among individuals aged 31-49 (45.2%) and 50-69 (34.9%), while those under 30 accounted for 16.9%. Rural areas reported a higher prevalence (66.3%) than urban areas (33.6%), suggesting a rural predominance. Agriculture-related occupations showed a higher risk (51%) of scrub typhus. Fever was universally present (100%), while gastrointestinal symptoms (29.2%), headache (16.9%), cough (12.2%), myalgia (8.49%), and altered sensorium (7.5%) varied in frequency. These findings highlight scrub typhus's demographic and symptomatic patterns [Table 1].

Table 1: Demographic data of the study

Variable		Number of cases	Percentage
Sex	Male	54	50.9 %
	Female	52	49.1 %
Age	<30 years	18	16.9 %
	31-49 years	48	45.2 %
	50-69 years	37	34.9 %
	>70 years	3	2.8 %
Location	Rural	70	66.3 %
	Urban	36	33.6 %
Occupation	Agriculture related	54	51 %
	Others	52	49 %
Symptoms	Fever	106	100%
	GI symptoms	31	29.2%
	Headache	18	16.9%
	Cough	13	12.2%
	Myalgia	9	8.49 %
Altered Sensorium	8	7.5 %	

Table 2: Distribution of eschar and eschar site

Variable		Number of cases	Percentage
Eschar	Present	68	64.2%
	Absent	38	35.8%

Eschar site	Anogenital region	32	47%
	Upper limb including axilla	11	16.17%
	Abdomen	8	11.76%
	Neck	6	8.82%
	Chest wall/ Inframammary	4	5.9%
	Umbilicus	3	4.4 %
	Legs	2	2.9 %
Back	2	2.9%	

Table 3: Distribution of laboratory findings and USG findings

Variable		Number of cases	Percentage
Laboratory Findings	Leucopenia	3	2.8%
	Leukocytosis	86	81.13%
	Normal WBC count	17	16%
	Thrombocytopenia – Total	103	97%
	Platelet 1-1.5Lakh	14	13.2%
	Platelet 50K-1Lakh	19	17.9%
	Platelet <50000	70	66.0%
	Normal Platelet count	3	2.83%
	Platelet Aggregation	23	22%
	AKI (Creatinine>1.2mg%)	24	22.6%
	Elevated SGOT/SGPT	34	32%
	Hyponatremia	19	17.9%
	Hyperbilirubinemia	9	8.5%
	Hypokalemia	7	6.6%
Hypoalbuminemia	31	29.2%	
USG abdomen findings	Splenomegaly	29	27.35%
	Hepatomegaly	11	10.3 %
	GB wall oedema	6	5.7 %
	Ascites	3	2.8 %

Table 4: Distribution of complications, antibiotics, platelet transfusion, and dialysis

Variable		Number of cases	Percentage
Complications	Hepatitis	32	30.2 %
	AKI	25	23.58%
	Meningoencephalitis	18	16.98%
	ARDS	17	16 %
	Gastritis	12	11 %
	Acalculous Cholecystitis	6	5.5 %
	Ascites	3	2.8 %
	Pleural effusion	4	3.8 %
	Myocarditis	1	0.92%
Antibiotic	Cardiogenic Shock	1	0.92%
	Doxycycline alone	46	43.3%
	Azithromycin alone	0	0
Platelet transfusion	Doxycycline + Azithromycin	60	0.56%
	Total patients who required platelet transfusion	18	16.98%
	1-4 units transfused	13	
	5-8 units transfused	3	
Other blood products transfusion (PRBC / WB)	> 8 units transfused	2	
	Yes	4	3.77%
Dialysis	Yes	6	5.6 %
Respiratory support	Nasal Oxygen	17	16.03%
	Mechanical Ventilation	9	8.49%

Table 5: Duration of hospital stay and outcome

Variable		Number of cases	Percentage
Duration of hospital stay	≤5 days	20	18.86%
	6-10 days	54	50.94%
	>10 days	32	30.18
Outcome	Recovered	104	98.11%
	Death	1	0.94%
	AMA Discharge	1	0.94%

A significant proportion of scrub typhus cases exhibit the presence of eschar (64.2%), a characteristic skin lesion. The most common site of eschar formation is the anogenital region (47%), followed by the upper limb, including the axilla (16.17%). Other sites

include the abdomen (11.76%), neck (8.82%), chest wall/inframammary (5.9%), umbilicus (4.4%), legs (2.9%), and back (2.9%). These findings emphasize the importance of recognizing and examining eschars, particularly in the anogenital region, as they

can serve as a valuable diagnostic clue for identifying scrub typhus cases [Table 2].

Most cases exhibited leukocytosis (81.13%) and thrombocytopenia (97%). Platelet counts below 50,000 was observed in a significant proportion of cases (66.0%). Other notable laboratory findings included elevated levels of SGOT/SGPT (32%), hypoalbuminemia (29.2%), and AKI (creatinine >1.2mg%) in 22.6% of cases. USG abdomen findings indicated the presence of splenomegaly (27.35%) and hepatomegaly (10.3%), along with gallbladder (GB) wall oedema (5.7%) and ascites (2.8%). These findings suggest the involvement of various organ systems and highlight the importance of comprehensive laboratory investigations and USG abdomen in evaluating and managing the studied cases [Table 3].

The most prevalent complications were hepatitis (30.2%), acute kidney injury (AKI) (23.58%), and meningoencephalitis (16.98%). Other complications included acute respiratory distress syndrome (ARDS) (16%), gastritis (11%), acalculous cholecystitis (5.5%), and pleural effusion (3.8%). A small proportion of cases exhibited myocarditis (0.92%) and cardiogenic shock (0.92%). Regarding treatment, most cases received doxycycline alone (43.3%) or a combination of doxycycline and azithromycin (0.56%) as antibiotics. Platelet transfusion was required in 16.98% of cases, with varying units transfused. Additionally, some cases received other blood product transfusion (3.77%) and required dialysis (5.6%). Respiratory support was provided via nasal oxygen (16.03%) and mechanical ventilation (8.49%). These findings emphasize the range of complications observed and the importance of appropriate treatment interventions to manage the studied cases effectively [Table 4].

Most patients had a hospital stay between 6-10 days, with a smaller proportion staying for > 10 days or < 5 days. Most cases resulted in recovery, while a very small percentage resulted in either death or discharge against medical advice [Table 5].

DISCUSSION

Our study on scrub typhus provided valuable insights into various aspects of the disease, including gender distribution, urbanization trends, sleeping habits, age distribution, and the presence of eschars.^[4-8] The results of our study supported previous research findings and contributed to a better understanding of scrub typhus.

One important finding from our study was that males and females showed equal susceptibility to scrub typhus, suggesting that gender does not play a significant role in disease occurrence. However, we observed that women involved in agriculture-related activities may have an increased risk of exposure to the disease. This finding highlights the importance of targeted prevention strategies for this specific population. Additionally, the increasing incidence of

scrub typhus in urban areas was noted, which can be attributed to factors such as rapid urbanization, poor sanitation, and changes in human behaviour. This emphasizes the need for heightened awareness and surveillance in urban settings.

Sleeping on the ground emerged as a significant risk factor for scrub typhus in our study, indicating the need for targeted prevention strategies to address this issue. We also found that scrub typhus can affect individuals across different age groups, and eschars, especially in hidden body parts, further supports the diagnosis of scrub typhus.

Regarding the clinical presentation of scrub typhus, our study confirmed fever as the most common symptom, consistent with all 106 cases examined. Gastrointestinal symptoms, including vomiting, diarrhoea, and abdominal pain, were prevalent in 27% of patients, aligning with a Korean study's findings.^[9] Early recognition of these symptoms is crucial for timely diagnosis and treatment.

Dehydration was observed in 28% of patients upon admission, consistent with a study by Rajapakse et al.^[10] Epigastric tenderness was identified in 11% of patients, suggesting possible gastritis, which aligns with previous reports.^[11] The underlying mechanism of gastric involvement in scrub typhus remains unclear but may be associated with the systemic inflammatory response induced by the infection.

Our study revealed a high incidence of liver involvement in scrub typhus patients, with elevated liver enzymes, bilirubinemia, and hypoalbuminemia observed in many cases. This contrasts with previous research reporting lower rates of liver involvement.^[12,13] Monitoring liver function tests in scrub typhus patients is crucial, as liver involvement may be more prevalent than previously recognized and can lead to severe complications such as liver failure. Hepato-splenomegaly was also a common finding, consistent with previous studies.^[14]

Our study on scrub typhus revealed significant multi-organ involvement, including abdominal, kidney, and lung manifestations. Ascites, acalculous cholecystitis, acute kidney injury (AKI), and respiratory complications such as acute respiratory distress syndrome (ARDS) and bronchopneumonia were observed.^[15] Acute encephalitic syndrome (AES) was also identified in scrub typhus patients.^[16] These findings highlight the systemic nature of the disease and the potential for severe complications.

Multi-organ dysfunction syndrome (MODS) was identified as the most common cause of death in scrub typhus patients, resulting from severe systemic inflammation and organ damage.^[10,16] Other causes of death included respiratory failure, septic shock, and complications of central nervous system involvement.^[17] These findings underscore the importance of early recognition and management of scrub typhus to prevent life-threatening complications.

Regarding laboratory findings, elevated leukocyte counts were significantly correlated with the severity of scrub typhus [Kim et al., 2010; Chung et al.,

2008].^[12,18] However, the correlation between white blood cell (WBC) count and scrub typhus severity is not always straightforward, as severe cases can sometimes present with normal or low WBC counts, especially in patients with a longer duration of illness. Thrombocytopenia, a low platelet count, was prevalent and correlated with disease severity [Everson GT et al., 2006; Winer ES et al., 2017].^[19,20] Monitoring leukocyte and platelet counts can aid in diagnosing and managing scrub typhus, but their interpretation should consider the overall clinical context.

CONCLUSION

In conclusion, our study of 106 scrub typhus patients yielded significant findings. Scrub typhus can affect individuals of all ages and genders, regardless of location. The peak occurrence was noted in November and December, emphasizing the need for enhanced preventive measures. Common symptoms included fever, gastrointestinal issues, headache, and myalgia, along with the presence of anogenital eschars. Laboratory abnormalities, such as leukocytosis and thrombocytopenia, were frequently observed. Complications included hepatitis, encephalitis-like syndrome, and other organ-related disorders. Early recognition and treatment are crucial for improved outcomes.

REFERENCES

1. Vincent G. Scrub Typhus and Its Causative Agent, *Orientia tsutsugamushi*. Rickettsiales, Cham: Springer International Publishing; 2016, p. 329–72.
2. Devasagayam E, Dayanand D, Kundu D, Kamath MS, Kirubakaran R, Varghese GM. The burden of scrub typhus in India: A systematic review. *PLoS Negl Trop Dis*. 2021;15:e0009619.
3. Xu G, Walker DH, Jupiter D, Melby PC, Arcari CM. A review of the global epidemiology of scrub typhus. *PLoS Negl Trop Dis* 2017;11:e0006062.
4. Sivarajan S, Shivalli S. Trends in the epidemiology of scrub typhus in south India: a review of the literature. *J Glob Infect Dis*. 2014;6:149-54.
5. Varghese GM, Trowbridge P, Janardhanan J, Thomas K, Peter JV, Mathews P, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis* 2014;23:39–43.
6. Premaratna R, Chandrasena TG, Dassayake AS, et al. Clinical and laboratory features of spotted fever and murine typhus in hospitalized patients, Sri Lanka. *Emerg Infect Dis*. 2016;22(7): 1217-22.
7. Traub R, Wisseman CL Jr. The ecology of chigger-borne disease (scrub typhus). *J Med Entomol*. 1974;11:237-303.
8. Strickman D, Tanskul P, Eamsila C, Kelly DJ. Prevalence of antibodies to rickettsiae in the human population of suburban Bangkok. *Am J Trop Med Hyg*. 1994;51:149-53.
9. Park H. Functional gastrointestinal disorders and overlap syndrome in Korea: Functional gastrointestinal disorders and overlap syndrome. *J Gastroenterol Hepatol* 2011;26 Suppl 3:12–4.
10. Rajapakse S, Rodrigo C, Fernando D. Scrub typhus: pathophysiology, clinical manifestations and prognosis. *Asian Pac J Trop Med*. 2012;5:261-4.
11. Blacksell SD, Bryant NJ, Paris DH, Doust JA, Sakoda Y, Day NP. Scrub typhus serologic testing with the indirect immunofluorescence method as a diagnostic gold standard: a lack of consensus leads to a lot of confusion. *Clinical infectious diseases*. 2007;44:391-401..
12. Kim DM, Kim SW, Choi SH, Yun NR. Clinical and laboratory findings associated with severe scrub typhus. *BMC Infect Dis*. 2010 Nov 9;10:108.
13. Mahajan SK, Rolain J-M, Kashyap R, Bakshi D, Sharma V, Prasher BS, et al. Scrub typhus in the Himalayas. *Emerg Infect Dis* 2006;12:1590–2.
14. Suputtamongkol Y, Suttinont C, Niwatayakul K, Hoontrakul S, Limpai boon R, Chierakul W, et al. Epidemiology and clinical aspects of rickettsioses in Thailand. *Ann N Y Acad Sci* 2009;1166:172–9.
15. Kim DM. Clinical features and diagnosis of scrub typhus. *Infect Chemother*. 2009;41:315-22.
16. Peter JV, Sudarsan TI, Prakash JAJ, Varghese GM. Severe scrub typhus infection: Clinical features, diagnostic challenges and management. *World J Crit Care Med* 2015;4:244–50.
17. Mahajan SK. Scrub typhus. *J Assoc Physicians India*. 2005;53:954-8.
18. Chung DR, Lee YS, Lee SS. Kinetics of inflammatory cytokines in patients with scrub typhus receiving doxycycline treatment. *J Infect* 2008;56:44–50.
19. Everson GT, Hoefs JC, Seeff LB, Bonkovsky HL, Naishadham D, Shiffman ML, et al. Impact of disease severity on outcome of antiviral therapy for chronic hepatitis C: Lessons from the HALT-C trial. *Hepatology* 2006;44:1675–84.
20. Winer ES, Safran H, Karaszewska B, Bauer S, Khan D, Doerfel S, et al. Eltrombopag for thrombocytopenia in patients with advanced solid tumors receiving gemcitabine-based chemotherapy: a randomized, placebo-controlled phase 2 study. *Int J Hematol* 2017;106:765–76.