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Original Research Article

Unveiling the spectrum of manifestations of scrub typhus: A study from a tertiary care teaching hospital of Kolkata, West Bengal

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Abstract

Introduction: Scrub typhus presents with features of acute undifferentiated febrile illness (AUFI), like fever with chills, malaise, and headache, making differentiation difficult from other causes of AUFI. This remains one of the underdiagnosed and underreported cause of febrile illness in tropical countries.
Aims and Objectives: The study was conducted to assess the socio-demographic profile of scrub typhus admitted patients and to assess the spectrum of clinical manifestations and laboratory parameters in these patients
Materials and Methods: This observational cross-sectional study was conducted between February 2021 to January 2024 in the Department of Microbiology at NRS Medical College and Hospital, among patients admitted with AUFI who were scrub typhus IgM reactive
Results: During our study period**,** among 10,547 AUFI patients, 10% (n=1024) were scrub typhus IgM reactive. Most patients belonged to the 0-20 year's age group. There was a distinctive surge of cases in the rainy season. The hallmark sign, "eschar," was absent in the majority of cases. Among the pediatric patients, central nervous system involvement was marked, but among the adult's respiratory system was mainly affected. In our study adverse outcome was observed in 2.55% (n=26) patients.
Conclusion: Scrub typhus presents significant diagnostic challenges due to its diverse and nonspecific clinical manifestations. High case fatality was observed among cases with multi-organ dysfunction, among whom the diagnosis was delayed. Hence, early initiation of appropriate antibiotic therapy is critical, as it can significantly reduce disease duration, prevent complications, and ultimately decrease morbidity and mortality.

Keywords: Scrub typhus, Meningoencephalitis, Multiple organ failure, Respiratory distress syndrome.

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1. Introduction

Scrub typhus is a zoonosis caused by *Orientia tsutsugamushi*, transmitted by the bite of the trombiculid mite. It is endemic in South-Eastern and far Eastern countries of Asia, often termed as the Tsutsugamushi triangle,[1] which extends from Japan in the east to Afghanistan in the west, up to Northern Australia in the South. This disease has re-emerged in many parts of India, Sri Lanka, Japan, Korea, and Thailand. The trombiculid mite like *Leptotrombidium deliense* and *Leptotrombidium palladium* are the natural host of the organism and humans acquire the infection through the bite of chiggers i.e. infected larval stage of the mite. Eschar formed at the site of the bite of the mite is the pathognomonic[2] feature of scrub typhus. Scrub typhus-infected patients present with features of acute undifferentiated febrile illness (AUFI), like fever with chills, malaise, and headache, making it difficult to differentiate it from other causes of AUFI.[3] Due to diverse presentations and limited laboratory resources,

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scrub typhus remains one of the under-reported and underdiagnosed illnesses in the regions where it has re-emerged in recent times.[3] Due to the paucity of studies conducted in this region and the lack of awareness of the disease in the general population, the magnitude of scrub typhus remains underestimated. With this background, the study is conducted with the following objectives,

1. To assess the socio-demographic profile of patients diagnosed with scrub typhus admitted to our hospital
2. To ascertain the spectrum of clinical manifestations and laboratory findings in scrub typhus patients

2. Materials and Methods

2.1. Study site

Department of Microbiology, NRS Medical College and Hospital

2.2. Study duration

1st February 2021 to 31st January 2024

2.3. Study design

The study was an observational cross-sectional study

2.4. Study population

AUFI cases who were scrub typhus IgM reactive by ELISA in the departments of Medicine and Pediatrics

2.5. Sample size

During the study duration, all the AUFI patients who were scrub typhus IgM reactive by ELISA were included in the study

2.6. Sampling method

Consecutive sampling

2.7. Institutional ethical clearance

Institutional ethical clearance was obtained vide memo No/NMC/540 dt. 06-02-2021

2.8. Case definitions

2.8.1. Confirmed case of scrub typhus

A case is classified as confirmed when either of the following criteria is met:

Detection of Rickettsial DNA in eschar tissue or whole blood samples using polymerase chain reaction (PCR) or Demonstration of a rise in antibody titres between acute and convalescent-phase serum samples, as determined by indirect immunofluorescence assay (IFA).[4]

2.8.2. Acute undifferentiated febrile illness

Acute onset of fever and other symptoms such as headache, diarrhoea, chills, and cough without any obvious focus of infection for less than 14 days duration.[4]

2.8.3. Serological diagnosis

Scrub typhus IgM antibody ELISA reactive with other serologies non-reactive, and blood culture‑negative.

2.8.4. Data collection

Clinical, epidemiological data, and laboratory parameters from patients were recorded in a pretested structured questionnaire study tool.

2.8.5. Data analysis

Collected data was compiled in a Microsoft Excel data sheet and was analyzed with the help of different charts and tables.

3. Results

During the study period, among 10,547 AUFI cases, 1024 cases were Scrub typhus reactive (10%). Among the reactive cases majority belonged to the age group of 0-20 years (50.31%, n=515), followed by 21-30 years (27%, n=276). There was a male preponderance with a male: female ratio of 1.28:1, and 88.54% (n=907) of patients were from rural areas (**Table 1**).

Table 1: Distribution of age, sex, and geographic location in scrub typhus

Age means (SD)	24.22 (18.84)
Male n (%)	574 (56.05)
Female n (%)	450 (43.95)
Urban n (%)	117 (11.46)
Rural n (%)	907 (88.54)

There was a notable increase in scrub typhus cases during the monsoon and post-monsoon period of July to September (**Figure 1**).

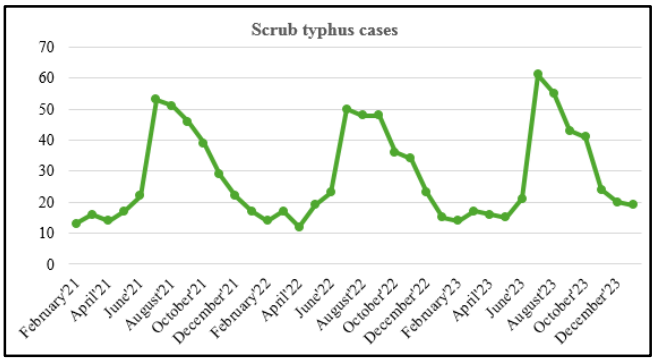

Figure 1: Seasonal distribution of scrub typhus cases

In clinical manifestation majority of patients presented with fever in the first week of illness, with a mean duration of presentation was 7.62 days (SD=2.71).

In organ involvement, based on clinical manifestations and laboratory parameters it was found, hepatomegaly was seen in 26%(n=266), splenomegaly in 16%(n=164) cases,

ascites was observed in 3%(n=31) patients, and pancreatitis was seen in 7 patients and mesenteric lymph node involvement was noted in 3.8%(n=39) cases.

In the respiratory system, pneumonia was observed in 5.66% (n=58) cases, pleural effusion developed in 12% (n=123) cases, and among these patients, 9% (n=92) developed ARDS.

Central nervous system involvement in the form of meningoencephalitis was seen in 12.69% (n=130) cases.

Renal involvement in the form of acute kidney injury, which was assessed based on KDIGO criteria[5], was observed in 5% (n=51) patients.

Cardiac involvement was seen in 2% (n=20) cases in the form of myocarditis (**Figure 2**).

Among the pediatric population, there was a preponderance of central nervous system involvement, e.g., meningoencephalitis, as compared to the adult population, where respiratory system involvement was markedly noted in the form of ARDS.

Adverse outcome was recorded in patients with meningoencephalitis, ARDS, and in patients where multiple organ system involvement (MODS) was recognized. In our study fatal outcome was seen in 2.55% (n=26) patients.

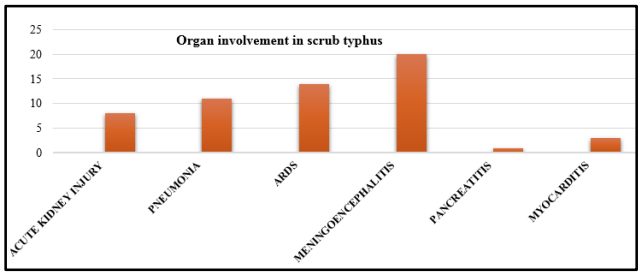

Figure 2: Organ involvement in scrub typhus

In our study, we also recorded co-infections with other causes of AUFI e.g., leptospirosis, dengue, malaria (**Table 2**).

Table 2: Co-infection in scrub typhus patients

Co-infection	Number	Percentage
Scrub typhus & leptospirosis	102	10.2%
Scrub typhus & malaria	33	3.2%
Scrub typhus & dengue	26	2.5%

4. Discussion

Our study contributes to the limited literature from Eastern India emphasizing the wide clinical spectrum of scrub typhus in hospitalized patients at a tertiary care teaching hospital. The diagnosis of scrub typhus remains challenging due to its non-specific symptoms, low index of clinical suspicion, and limited availability of confirmatory diagnostics. Serological tests like ELISA, ICT are easy to perform and have a rapid turnaround time.

In our cohort, the predominant age group affected was 1–20 years, with a male preponderance. Children and adolescents in rural areas are often exposed to infected chiggers through activities such as farming and harvesting, increasing their susceptibility. This pattern aligns with findings from Bajracharya L. *et al*.,[6] Bhat *et al*.,[7] and Basu *et al*.,[8] who reported a mean age of presentation was six years. Gupta N. *et al*.[9] also demonstrated high seropositivity in children and adolescents. In contrast, Mandal R. *et al*.[10] reported a higher prevalence in the 14–20 age group with female predominance, while Malik S. *et al*.[12] found most cases in the 21–50 age group with female preponderance. Kundu S. *et al*.[13] and Malik *et al*.[12] both reported a largely rural patient population population, though occasional urban cases suggest potential chigger migration via working populations or poorly maintained urban gardens.

The seasonal distribution in our study showed increased in cases from July to November, aligning with findings by Gupta N. *et al*.,[9] Gurung *et al*.,[14] and Kundu S. *et al*.,[13] reflecting a monsoon and post-monsoon surge in scrub typhus incidence.

Fever was universal among patients, consistent with observations by Venkategowda P. M. *et al*.,[15] Peesapati N. *et al*,[16] and Rajapakse S. *et al*.[17] Eschar and rash, though pathognomonic, were infrequent in our series, as also observed by Kamath S. D. *et al*.,[18] who reported eschar in 38.1% and rash in 19.1% of cases. Mandal R. *et al*.[10] observed eschar in 34.3% and rash in 42.9%. Variability in eschar detection may stem from factors such as skin pigmentation, anatomical site, or strain variation.[4]

Gastrointestinal and hepatobiliary manifestations were prominent. Manjunath V.G. *et al*.[19] reported hepatomegaly in 96.3%, splenomegaly in 81.5%, and ascites in 29.3% of patients. Hepatitis was noted in 87% and 95.2% of patients in studies by Varghese *et al*.[20] and Chrispal *et al*.,[21] respectively. Mondal R. *et al*.[10] observed ascites in 8.6%, edema in 25.7%, and jaundice in 8.6%.

Pulmonary involvement was significant, with cases of pneumonia, pleural effusion, and ARDS consistent with reports by Rajapakse *et al*.,[17] Jeong *et al*.,[22] and Chaeroneak *et al*.[23] Jeong *et al*. noted pneumonia in 51%, pleural effusion in 15–20%, and radiological abnormalities in 65%. Im JH *et al*.[26] emphasized the diagnostic role of radiological consolidation, showing reversibility with doxycycline. Pleural effusions were common in older males with cardiac involvement or hypoalbuminemia.

Renal involvement in our study included oliguria, pedal edema, proteinuria, and AKI. Kumar V. *et al*.[27] documented renal abnormalities in 82%, with AKI in 53%. Other studies confirm AKI as a frequent and often underestimated

complication.[20,28] We found AKI in 5.1% and hematuria in 1.9% of patients. Mechanisms include vasculitis, renal hypoperfusion, and direct invasion of renal tissue, leading to tubular necrosis.[29]

CNS manifestations, particularly in the pediatric population, included meningoencephalitis. Kamath S.D. *et al*.[18] reported CNS involvement in 28.1% of pediatric cases. Mahajan S.K. *et al*.[30] observed encephalopathy in 24%, encephalitis in 16%, and meningoencephalitis in 35%. Viswanathan S. *et al*.[31] found meningitis in 26%, emphasizing the need for high clinical suspicion, especially in febrile children with minimal respiratory symptoms.

In our study hematological abnormalities were common. Manjunath V.G. *et al*.[19] found thrombocytopenia in 66.7%, anemia in 48.1%, and elevated AST in 85.2%. Peesapati N. *et al*.[16] observed hemoglobin <11 g/dL in 46.6%, leukocytosis in 43.3%, and thrombocytopenia in 33.3%. These findings highlight frequent hematological and hepatic dysfunction.

Our study reported severe complications in the form of MODS, meningoencephalitis, and ARDS. Peesapati N. *et al*.[16] noted MODS in 8.3%, ARDS in 6.6%, and CNS involvement in 3.3%. Malik S. *et al*.[12] reported shock in 16.7%, requiring vasopressors in 60% of those cases.

Co-infections were another challenge in our study. Mehta V. *et al*.[32] and Mahajan S.K. *et al*.[30] reported concurrent leptospirosis. Sapkota S. *et al*.[33] and Subedi P. *et al*.[34] documented co-infection with dengue. Barkotoky B. *et al*.[35] found 25% of PUO cases had scrub typhus leptospirosis co-infection.

The case fatality rate in our study was 2.54%, comparable to study done by Pathak S. *et al*.[36] (3.9%), but lower than that reported by Yogendra V. *et al*.[37] (17.2%) and Subbalaxmi M. *et al*.[28] (6.25%). Kumar V. *et al*.[27] described ICU stays with ventilator support lasting up to 26 days.

5. Limitations of the Study

In our study, only hospitalized patients were included. However, a considerable number of scrub typhus IgM-reactive patients were managed on an outpatient basis, as their infections were self-limiting and did not require admission. Additionally, part of the study period coincided with the COVID-19 pandemic, which posed challenges to patient follow-up and data completeness. Furthermore, since our hospital does not serve a defined catchment area, the patient population is heterogeneous, limiting the ability to draw precise epidemiological conclusions from this study.

A small proportion of patients required life support interventions, including mechanical ventilation and hemodialysis, primarily due to complications such as acute respiratory distress syndrome (ARDS) and acute kidney injury (AKI). The overall mortality rate in our study was 2.54%.

6. Conclusion

Diverse manifestations in the early phase of illness, under-diagnosis due to less clinical suspicion and challenges in sero-diagnosis are contributing factors for delay of initiation of appropriate treatment of scrub typhus. Due to high occurrence of co-infections in our country, the provision of molecular diagnostics will also aid in appropriate management. Although scrub typhus typically responds well to timely treatment with doxycycline or azithromycin, delays in initiation of therapy can lead to severe complications and increased morbidity and mortality contributing to socio-economic burden to the family and the community. Therefore, heightened clinical vigilance is essential, particularly in endemic regions. Strengthening diagnostic laboratory capabilities and increasing awareness among healthcare providers are critical steps in reducing the burden of scrub typhus, which still remains a under-diagnosed and under reported entity.

7. Source of Funding

None.

8. Conflict of Interest

None.

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