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Clinical Profile and Outcome of Scrub Typhus: A Hospital-Based Observational Study

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ABSTRACT

Introduction: Scrub typhus is a re-emerging infectious disease in India caused by *Orientia tsutsugamushi*. It is a vector-borne, zoonotic disease in which humans are accidental host.Scrub typhus is most commonly reported from Southeast Asia and Japan and represents the most frequently documented rickettsial infection in India. Globally, more than one billion individuals are at risk with estimated one million new cases occurring annually.

It commonly presents with fever, maculopapular rash, eschar and regional lymphadenopathy. Severity of illness ranges from a mild, self- limiting disease to a fatal outcome.

Aims and Objective: To assess the clinical profile, laboratory parameters and outcomes of scrub typhus patients during hospital stay.

Material and Method: This hospital-based study was conducted in tertiary care hospital in Assam. Diagnosis was confirmed by thorough clinical examination, relevant laboratory investigations, and a positive IgM ELISA test for *Orientia tsutsugamushi*.

Results and Observation: A total of 49 cases were enrolled in the study. The predominant age group was 21-30 years (34.69%), with a majority of cases reported during rainy season among farmers from rural areas. Fever (100%) was present in all patients followed by headache (65.31%) and gastrointestinal and respiratory symptoms. Acute kidney injury (24.49%) was the most frequent observed complication. Multiple organ dysfunction syndrome was observed in 8.16%. The overall mortality rate was 4.08%.

Conclusion: Scrub typhus should be evaluated in all cases of undifferentiated acute febrile illness, particularly during monsoon season. Due to its varied clinical presentation, a strong degree of clinical suspicion is very important for early diagnosis and appropriate management to minimize complications and reduce mortality.

Keywords*: Orientia tsutsugamushi; Eschar; Acute febrile illness; Meningoencephalitis; Rickettsia; Upper Assam.*

INTRODUCTION

Scrub typhus remains a significant causes of undifferentiated acute febrile illness due to *Orientia tsutsugamushi* infection. Among the rickettsial infections, scrub typhus is the most common and widely reported across several states in India including Jammu and Kashmir, Uttarakhand ,Himachal Pradesh, Bihar, West Bengal, Rajasthan ,Meghalaya, Kerala, Maharashtra, Tamil Nadu and Karnataka .[1] Globally, scrub typhus is most commonly reported from Southeast Asia and Japan and more than one billion individuals are at risk with estimated one million new cases occurring annually.[2] It is also referred to as tsutsugamushi disease. The term '*tsutsugamushi*' originates from Japanese words: 'tsutsuga', meaning small and potentially dangerous, and 'mushi', meaning creature.**[2]**

Scrub typhus is a vectore-borne, zoonotic disease in which humans are accidental host. The infection is vector-borne, transmitted by the chiggers (larval stage) of trombiculid mites, which are parasites of rodents.The larval stage or the

chiggers becomes infected either through transovarian route or by feeding on infected rodents. these larvae act as a vector and can transmit infection to human [3]

Clinically, scrub typhus commonly presents with fever, maculopapular rash, eschar at the mite attachment site, and regional lymphadenopathy. Disease severity ranges from benign, self-limiting illness to a life-threatening and fatal outcome, depending on organism virulence and host immune response.

Based on clinical presentation, there are few distinguishing features to differentiate scrub typhus from other co-endemic diseases such as typhoid fever, dengue and leptospirosis. Therefore, diagnosis of the disease depends on high degree of suspicion along with appropriate laboratory investigations. Serology remains the mainstay for accurate diagnosis of scrub typhus.[4]

Scrub typhus is a re-emerging disease in India and is now widely distributed in forested and rural areas of many parts of the country, where endemic pockets have been established and seasonal outbreaks occur regularly.[3]

An increasing number of scrub typhus cases are also being reported from North Eastern India including Assam and Arunachal Pradesh and Nagaland. Despite this re-emergence, there remains a paucity of systematic data or evidences from this region. Many cases remain undiagnosed, largely due to non- specific clinical presentation, lack of high degree of suspicion and limited availability of specific diagnostic test for the disease. Our hospital is a tertiary care centre in Assam that serves a vast area of upper Assam, Arunachal Pradesh and Nagaland.

Through this study we attempted to elucidate the various presentations observed in this part of the country and to provide a better clinical profile and laboratory parameters of this re-emerging disease, thereby aiding clinicians in routine clinical practice.

AIM AND OBJECTIVES:

To evaluate the clinical profile, laboratory parameters, complications, and disease outcomes during hospital stay among patients with scrub typhus presenting to a tertiary care centre in Assam .

MATERIAL AND METHOD

Study Design and Setting

This was a hospital-based cross-sectional observational study conducted in the Department of Medicine at a tertiary care centre in Assam, over a one-year period, from June 1, 2020 to May 31, 2021.

Study Population and Sample Size

A total of 49 consecutive patients who met the inclusion criteria were enrolled in the study.

Inclusion criteria

Patients aged ≥12 years who were admitted with confirmed scrub typhus, diagnosis by positive IgM antibody (ELISA) against *O. tsutsugamushi* (optical density >0.5) were included.

Exclusion criteria

Patients with concurrent infections such as leptospirosis, dengue, malaria, enteric fever, those patients with known comorbidities (chronic renal failure, chronic liver disease, neoplastic disease), or those who declined consent were excluded from the study.

Ethics

The study received approval from Institutional Ethics Committee. Informed written consent was secured from all patients or legal guardians prior to enrollment.

Data collection

History

A through clinical history was obtained including presence of fever, headache, respiratory symptoms (cough, breathing difficulty), gastrointestinal symptoms (pain abdomen, vomiting), altered sensorium, decreased urine output, and skin rash. Socio-demographic details such as occupation, place of residence (rural or urban) and educational status were also recorded.

Clinical examination

A thorough general physical examination and comprehensive systemic examination of all organ systems were carried out to assess multisystem involvement. A meticulous examination of the skin was performed to identify the presence or absence of an eschar. In the early course of eschar evolution, there is a central vesicle associated with surrounding erythematous lesion. Later, in the central part, a typical necrotic black crust or eschar with surrounding erythema appears and it increases in size to produce typical eschar after 6 to 8 days.[5]

Investigation

The necessary investigations included complete blood count, renal function tests (serum creatinine and urea), liver function tests (bilirubin, SGOT, SGPT, and albumin), serum electrolytes, blood glucose, and cerebrospinal fluid analysis (when indicated). Imaging studies such as ultrasonography of abdomen, chest x-ray, and Computed tomography of the brain were performed as indicated.

Scrub typhus diagnosis was confirmed serologically by IgM ELISA, using Scrub Typhus Detect™ kit (InBios International, Inc., USA), a qualitative immunoassay detecting IgM antibodies to *O. tsutsugamushi* using recombinant antigen-coated wells.

Other possible diagnoses were excluded by history, clinical examination along with appropriate laboratory investigations, including malaria (rapid antigen detection), leptospirosis (IgM ELISA), dengue (IgM/NS1 ELISA), typhoid fever (rapid IgM/IgG and Widal test), and hepatitis A (Anti HAV IgM), hepatitis B (HBsAg), hepatitis C (Anti- HCV) and hepatitis E (Anti-HEV IgM)
All patients confirmed with scrub typhus received doxycycline 100 mg twice daily for 7days, administered either orally or intravenously depending on the clinical condition of the patient. Azithromycin was preferred in children and pregnant women.[5] Other supportive measures including, mechanical ventilation, hemodialysis were provided as per indication. Outcomes were recorded as either recovery or death during the hospital stay.
Complications were defined using standard criteria-

Multiple Organ Dysfunction Syndrome (MODS): Defined as dysfunction of more than one organ requiring intervention to maintain homoeostasis.[6,7]
Acute Kidney Injury (AKI): Defined as a rise in serum creatinine >1.6 mg/dl or urine output less than 400 ml/24 hour and failing to improve after adequate rehydration.[6,7]
Acute Respiratory Distress Syndrome (ARDS): Defined by the presence of bilateral alveolar or interstitial infiltrates on chest radiograph and PaO2/FiO2 less than or equal to 200 mmHg.[6,7]
Hepatitis: Defined as an elevation of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) of more than three times the upper normal limit and/or elevation of serum bilirubin >3 times upper limit of normal value.[6,7]
Meningitis/meningoencephalitis: Defined by presence of headache, altered sensorium with features of meningeal irritation like neck rigidity, positive Kernig sign with elevated protein and/or polymorphic leukocytosis with normal or low sugar level on cerebrospinal fluid (CSF) analysis.[6,7]
Pneumonia: Pneumonia was identified in patients presenting with an acute onset of cough and breathlessness along with unilateral or bilateral alveolar or interstitial infiltrates on chest X-ray.[8]

Statistical Analysis
Data were analyzed using SPSS version 21.0 (IBM Chicago, Illinois). Continuous data were expressed as mean ± standard deviation, while categorical data were presented as frequencies and percentage. Descriptive statistical analysis was used to describe patient characteristics.

RESULTS AND OBSERVATION

Patient Demographics
Among 49 scrub typhus patients, 30 (61.22%) were male and 19 (38.78%) were female, with a male-to-female ratio of 1.58 :1. The patients had mean age of 35.28 ± 14.54 years. The predominant age group was 21-30 years (34.69%), followed by 31-40 years (22.45%) and 41-50 years (16.33%). Most patients resided in rural areas (85.71%) (Table–1)

Table–1: Socio-demographic Profile

Variables	Number *(n = 49)*	Percentage *(%)*
Age group *(in years)*		
▪ 13–20	6	12.24
▪ 21–30	17	34.69
▪ 31–40	11	22.45
▪ 41–50	8	16.33
▪ 51–60	3	6.12
▪ 61–70	2	4.08
▪ >70	2	4.08
Gender		
▪ Male	30	61.22
▪ Female	19	38.78
Locality		
▪ Rural	42	85.71
▪ Urban	7	14.29

Table–2: Month wise distribution of the cases

Month Year	Number *(n = 49)*	Percentage *(%)*
June	7	14.29
July	8	16.33
August	9	18.37
September	4	8.16
October	4	8.16
November	2	4.08
December	3	6.12
January	2	4.08
February	3	6.12
March	2	4.08
April	3	6.12
May	2	4.08

Cases were reported throughout the year and the maximum numbers were seen during the period of June to August. (Table–2)

Table–3: Occupation profile

Occupation	Number *(n = 49)*	Percentage *(%)*
Farmer	20	40.82
Housewife	11	22.45
Student	7	14.29
Tea Garden Laborer	4	8.16
Businessman	3	6.12
Government employee	2	4.08
Fisherman	1	2.04
Daily Wage Earner	1	2.04

Among all patients, 40.82% were farmers followed by housewives (22.45%), students (14.29%), tea garden laborer (8.16%), businessman (6.12%), government employee (4.08%), fisherman (2.04%) and daily wage earner (2.04%). (Table–3)

Table–4: Clinical features

Clinical Features	Number *(n = 49)*	Percentage *(%)*
Fever	49	100
Headache	32	65.31
Cough	17	34.69
Vomiting	17	34.69
Abdominal Pain	14	28.57
Myalgia	12	24.49
Eschar	10	20.41
Lymphadenopathy	9	18.37
Breathlessness	9	18.37
Hepatomegaly	9	18.37
Jaundice	8	16.33
Decreased Urine Output	8	16.33
Splenomegaly	7	14.29
Diarrhea	5	10.20
Altered Sensorium	4	8.16
Rash	2	4.08
Neck rigidity	2	4.08
Seizure	1	2.04

Fever was observed in all 49 patients (100%). Headache (65.31%), cough and vomiting (34.69% each), abdominal pain (28.57%), myalgia (24.49%) and eschar (20.41%) were common presenting clinical features. (Table–4)

Distribution of ESCHAR:

Eschar was observed in 10 patients (20.41%). Among these, the predominant site of eschar was inguinal region, seen in 4 patients (40%). This was followed by the abdomen in 2 patients (20%) and the axillary region in 2 patients (20%). Eschar was noted on the chest in 1 patient (10%) and on the thigh in 1 patient (10%).

Figure-1: ESCHAR

Anemia (hemoglobin level <11 gm/dl) was noted in 23 patients (46.94%). Leukocytosis was observed in 18 (36.73%) patients, whereas leucopenia was noted in only 2 patients (4.08%). Thrombocytopenia was recorded in 21(42.86%) patients, while thrombocytosis was present in 1 patient (2.04%).

Hyperbilirubinemia was noted in 27 (55.10%) patients. Serum bilirubin levels >3 times the upper limit of normal were noted in 10 (20.4%) patients. Deranged/elevated SGOT and SGPT were observed in 44 (89.79%) and 36 (73.46%) cases respectively. Marked transaminase elevation (more than threefold above the upper limit of normal) was noted in 15 (30.61%) patients for SGOT and 8 (16.33%) patients for SGPT. Hypoalbuminemia (85.71%) was also frequently observed indicating systemic involvement.

Among all patients, elevated serum creatinine level (>1.6 mg/dl) were observed in 12 patients (24.49%). Among them, 5(10.20%) had values between 1.7-2.9 mg/dl, 3 (6.12%) had creatinine levels between 3.0- 4.9 mg/dl, and 4 (8.16%) had creatinine values > 5 mg/dl. The mean serum creatinine value was 1.87 ±2.16 mg/dl. (Table–5)

Table–5: Serum creatinine values

Serum Creatinine values *(mg/dl)*	Number *(n = 49)*	Percentage *(%)*
≤1.6	37	75.51
1.7–2.9	5	10.20
3.0–4.9	3	6.12
>5.0	4	8.16

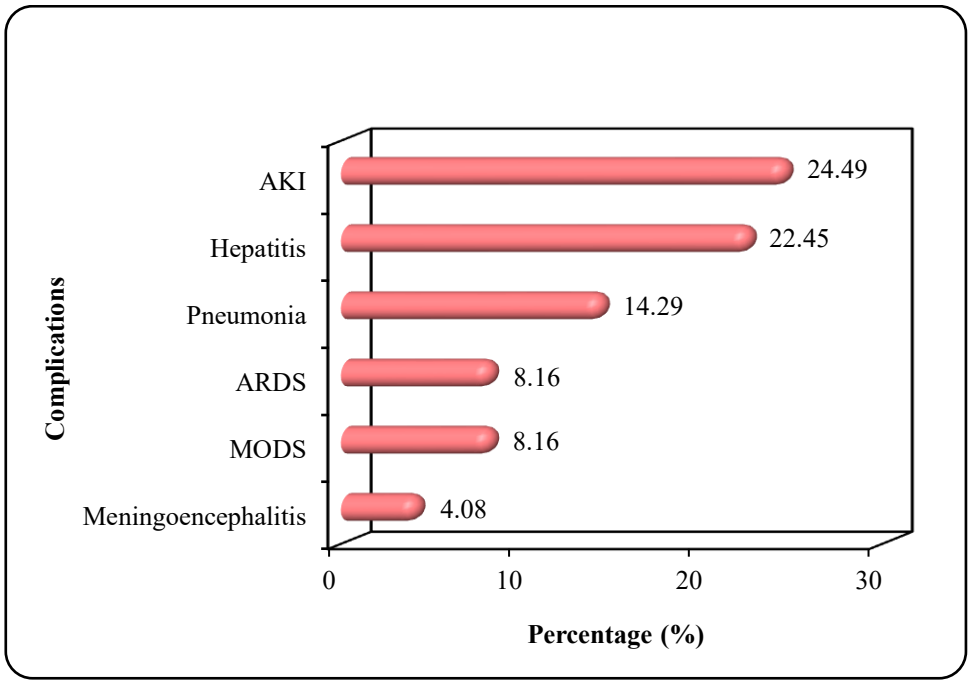

Figure-2: Complications during hospital stay

Among 49 patients, most common complication, observed in scrub typhus patients, was AKI (24.49%) followed by Hepatitis (22.45%), pneumonia (14.29%), ARDS (8.16%) and meningoencephalitis (4.08%) and 4 (8.16%) patients developed MODS. (Figure–2)
Overall, 47 (95.92%) recovered and while 2 patients died resulting in a mortality rate of 4.08%.

DISCUSSION

The present study highlights that the majority of affected patients were young adults with a clear male predominance and a substantial representation from rural areas. These findings aligns with previous studies conducted in India, suggesting a consistent demographic pattern [6,9]. The higher involvement of younger males may be explained by greater participation in outdoor and agricultural activities, which increases exposure to relevant environmental risk factors.

However, other similar studies have observed nearly equal gender distribution from Tamil Nadu or a female predominance from Southern Rajasthan (55.2%).[10,8] In this region, males tend to be more engaged in certain occupations such as farming and outdoor activities that increase their exposure to mites, leading to more number of cases. A predominance of rural patients (85.71%) was observed in this study, consistent with findings from other Indian studies reporting similar trends.[11,12]

Exposure to environmental risk factors such as piles of wood, bushes, rodents and domestic animals, is a well-established risk factor for infection of scrub typhus.[13] Individuals residing in rural areas are more commonly associated with agricultural activities and are therefore more exposed to these environmental risk factors contributing to more number of cases.

Scrub typhus cases were reported throughout the year, with a distinct peak observed between June and August (48.97%). The majority of cases was observed during August .

This corresponds to the rainy season in Assam, where maximum rainfall occurs in July and August (29% of Southwest monsoon rainfall) followed by September (24% of Southwest monsoon rainfall). Approximately, 66% of annual rainfall is received during southwest monsoon rainfall (June-September).[14] In this region, farmers are mostly involved in agricultural activities during the period of May to August, during which they are frequently exposed to bites of larval mites.

Similar seasonal clustering of cases during monsoon and post-monsoon months has been documented in studies from Meghalaya and Southern Rajasthan with peak incidence observed between august and October.[6,8]
Farmers constituted the largest occupational group (40.82%) followed by housewives and students in our study. Similar occupational patterns have been observed from South India where a substantial proportion of patients (42%) occurred among agricultural laborers and 36% were housewives.[15] A study from Odisha has shown that 76.92% of study participants were identified as being associated with agricultural works, exceeding the proportion reported in the study.[16]

The higher incidence observed in agricultural workers could be explained by frequent exposure to chiggers during daily life and farming activities.
Fever was observed in all patients (100%) followed by headache in this study. These findings align with previous Indian studies, conducted in Vellore, Rajasthan and West Bengal where fever was observed in nearly all cases.[8,10,17]
Respiratory and gastrointestinal system involvement including cough, vomiting, abdominal pain was observed in approximately one-third of cases highlighting the multisystem involvement in scrub typhus infection .

In this study, hepatomegaly, splenomegaly and lymphadenopathy were observed in 18.37%,14.29% and 18.37 % of patients, respectively. These findings are largely consistent with previous Indian data from Vellore, which reported comparable frequencies of hepatomegaly(24%) and splenomegaly(18%).[10] Similar observations were reported in studies from Rajasthan and Goa documenting lymphadenopathy in 18.2% and 13.3% of cases respectively.[11,7] However, a study from Meghalaya, reported marked higher prevalence of lymphadenopathy(52.5%), which differs from the observations in the our study.[6] such variations may be explained by differences in study population, geographic distribution, disease severity or sample size.

Eschar is a key diagnostic sign for febrile illness resulting from scrub typhus infection. The relatively low prevalence of eschar (20.41%) was observed in this study and inguinal region was the predominant site , which differs significantly from higher rates (43.5-58%) reported in south Indian studies, possibly reflecting strain heterogeneity across geographic regions.[9,12] Preexisting cellular immunity due to repeated exposures may also reduce the likelihood of eschar manifestation in endemic populations.

In the current analysis, nearly half of the patients were anemic, with mean hemoglobin levels 10.88 ±2.76 gm/dl. These findings aligns with previous Indian studies by Peesapati N *et al.* and Sarkar k *et al.* who reported anemia in 46.66% and 52% of cases respectively. [17,9]

Leukocytosis was observed in 36.73% of cases, whereas leukopenia was noted in 4.08% of cases, reflecting heterogenous/varied hematological response during acute illness. Similar results were reported by Sarkar K *et al.* demonstrating leukocytosis in 37% patients and leukopenia in 5%, and by Peesapati N *et al.* who reported leukocytosis in 43.3% patients. [17,9]

Thrombocytopenia (<1.5 lac/mcl)) was observed in 42.86% patients, which is consistent with a study from Uttarakhand, where thrombocytopenia was reported in 46.8%.[18] Thrombocytosis was found in only one patient in our study. However, a study from North Western India reported a significantly higher prevalance of thrombocytopenia and thrombocytosis ,observed in 85.7% and 14.2% cases respectively.[19] These findings highlight the relevance of thrombocytopenia as an important laboratory indicator and underscores the utility of routine blood investigations in early diagnosis and clinical assessment of acute febrile illnesses.

Hepatic involvement was common in this study, with more than half of the patients (55.1%) showing hyperbilirubinemia. Serum bilirubin levels exceeding > 3 times the upper limit of normal were noted in 20.4% of patients. A large number of cases exhibited deranged transaminases, with elevated SGPT and SGOT levels noted in 89.79% and 73.46% of patients respectively. Marked transaminases elevation exceeding >3 times the upper limit of normal, observed in 30.61% and 16.33% of patients, respectively. Hypoalbuminemia was also frequently encountered (85.71%) indicating significant hepatic dysfunction and systemic involvement.

Elevated SGPT or SGOT levels were reported in 80% cases and low serum albumin levels observed in 60% of the patients in a study from Goa.[7]

Similarly, Gaba S *et al.*, reported SGPT elevation (>40IU/ml) in 90.3% of patients and SGOT elevation (>40IU/ml) in 88.6% of cases, findings that are consistent with those of the present study.[20] Overall, these findings align with previously published literature and underscore the importance of routine liver function assessment in patients presenting with undifferentiated acute febrile illness to facilitate early diagnosis and appropriate management.[12,20]

AKI emerged as the commonest complication in the present study (24.49%) followed by hepatitis (22.45%), pneumonia (14.29%), ARDS (8.16%) and meningoencephalitis (4.08%). In similar studies by Philomena J *et al.* elevated serum creatinine levels(> 1.6 mg/ dl) were reported in 22%, finding that is similar to those observed in our study.[10]

The prevalence of AKI in the current study is comparable to reports from multiple region in India, including the North-East Region, South India Southern Rajasthan, and Southern India, where AKI was reported ranging between 13.16% to 32% of cases .[6,8,15,21] However, an another study from Rajasthan conducted by Takhar RP *et al.* reported higher prevalence of AKI (51.5%) which contrasts with our findings. [11]

Similar observations were noted in studies from south India and Meghalaya, in which hepatitis was present in 34% and 15.25% cases respectively, consistent with the present study.[15,6] In contrast , Sharma N et al, noted higher prevalence of hepatic dysfunction in 61% of cases.[22]

A study was conducted Bhowmik KK et al, observed pneumonia in 11.7% cases which is consistent with our findings.[23] In contrast, the prevalence observed in our study was markedly lower than the 39.55% reported from Rajasthan, potentially reflecting regional variations.[8]

Overall, the consistency of complications across geographically diverse regions highlights the multisystem natures of the disease and underscores the need of vigilant monitoring for renal, hepatic and respiratory involvement to enable early detection and timely management.

In this study, meningoencephalitis was observed at lower frequency compared with reports from Meghalaya, Odisha, North Western India and west Bengal, where prevalence rates ranged from 8.47% to 10.4%.[6,16,20,23].

MODS and ARDS were each observed in 8.16% of cases which is comparable to earlier Indian studies, indicating consistency in severe disease manifestations across different geographic regions. [9,10,19]

ARDS was reported at higher frequencies in studies from Uttarakhand and North Western India**,** with prevalence rate of 19.2% and 11.59% cases respectively, exceeding those observed in present study.[19,20]

Similarly, Takhar *et al*. noted significantly higher rates of MODS and ARDS (51.5% and 48.5% ,respectively) which are not consistent with findings of the present study.[11]

In the present cohort of 49 patients, five required intensive care unit (ICU) admission and three (6.12%) patients had undergone hemodialysis for renal failure. The observed mortality rate of 4.08% was substantially lower than that reported in earlier studies (8-13.6%) from India, likely reflecting early recognition, prompt antibiotic therapy, and timely supportive care including mechanical ventilation and dialysis.[9,6,22]

Among the fatal cases, both patients presented late in the course of illness and developed rapidly progressive multiple organ dysfunction.one patient, a 45-year-old female who had presented with fever and headache, followed by altered sensorium and decreased urine output along with signs of meningeal irritation; despite intensive care management, she succumbed to MODS. The second fatal case, a 38-year-old female who presented with fever, cough, breathlessness, and reduced urine output. Subsequently developed ARDS with AKI and eventually resulting in death due to MODS. These findings underscore that delayed presentation is strongly associated with severe complications such as ARDS, AKI, and MODS, highlighting the critical importance of early diagnosis and timely intervention to improve clinical outcomes.

Strength and Limitation

The study provides valuable regional insights into scrub typhus from the North East region, where it remains a frequently underdiagnosed cause of acute febrile illness. Comprehensive assessment of clinical features, laboratory investigations and complications enhances understanding of the disease spectrum and facilitates early diagnosis and appropriate management in endemic areas.

This was a single center study with a relatively smaller sample size; therefore, the findings may not be generalizable. In addition, strain specific variations could not be assessed.

CONCLUSION

Scrub typhus remains a significant cause of undifferentiated acute febrile illness in North Eastern India, occurring throughout the year with a surge in the rainy seasons particularly among agricultural workers.

Low prevalence of eschar observed in this study highlights the need for a strong clinical suspicion for early diagnosis in scrub typhus rather than pathognomonic sign.

Early clinical recognition, prompt serological confirmation, and timely doxycycline initiation are paramount for favorable outcomes.

Educational initiatives targeting high-risk populations, particularly agricultural workers with emphasis on personal protection measures are critically needed.

This study concludes that scrub typhus must be considered in the list of differential diagnosis of undifferentiated acute febrile illness, especially during monsoon seasons, to reduce diagnostic delays and mortality.

Further epidemiological surveillance and research in this region will help better characterize strain-specific manifestations and optimize management strategies**.**

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