

Original Article

Clinico-demographic Profile and Outcome of Scrub Typhus in North Eastern State of India

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Scrub typhus is a form of bacterial Zoonosis caused by *Orientia tsutsugamushi* usually presents as Acute febrile illness with multiorgan involvement as a complication and is associated with significant mortality. This study aims to document the clinico-demographic profile, laboratory parameters and complication of Scrub Typhus in North Eastern Hilly State of Tripura with background of tropical climate.

This retrospective study was conducted at Tripura Medical College, including 42 patients admitted with acute febrile illness between June, 2020 to December, 2021 during the era of COVID-19 Pandemic. The diagnosis was established by Rapid card test, Lateral Flow Metry Assay (LFA) followed by confirmation through IgM, ELISA test and pathognomic Eschar where feasible. The clinical, demographic and laboratory profile were documented and analysed.

Post rainy season and people from rural area with farming background were mostly affected population. Apart from Fever and Flu like symptom, respiratory and Gastrointestinal (GI) symptoms were more prominent feature. Pathognomic skin lesion eschar was found in maximum cases followed by shortness of breath, GI involvement and Renal failure. Acute Respiratory Distress Syndrome (ARDS), Acute Kidney Injury (AKI), Hepatic encephalopathy and meningitis were the serious complications.

While evaluating cases of acute febrile illness with multiorgan involvement clinician should have high index of suspicion for Scrub typhus specially resource poor areas of North Eastern (NE) state of India so that early detection and time bound intervention may help to reduce the mortality.

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Key words : Febrile illness, Scrub Typhus, Zoonosis.

Scrub typhus is a public health problem causing severe morbidity and mortality. It is caused by *Orientia tsutsugamushi* (*O. tsutsugamushi*) can result in severe multiorgan failure with a case fatality rate up to 70% without appropriate treatment¹. It is the oldest vector born Zoonotic disease now re emerging with new trends worldwide specially in the endemic areas². Antigenic heterogeneity of *O. tsutsugamushi* may be the reason behind the generic immunity which causes re-infection. Clinical picture consist of high grade fever, severe headache, apathy, myalgia and generalised lymphadenopathy. A maculopapular rash may appear first on the trunk and then on extremities. Eyelid edema and facial edema are also prominent feature. Black Eschar may be seen at the site of inoculation. Patients may develop complication like interstitial pneumonia, ARDS, HE, AKI, meningoencephalitis, and myocarditis³⁻⁵. Diagnostic approaches for Scrub Typhus are based on detection of antibody in the serum

Editor's Comment :

- Scrub typhus is a bacterial zoonosis caused by *Orientia tsutsugamushi* presents as an acute febrile illness with multiorgan involvement and is associated with high mortality.
- A simple Rapid diagnostic test Lateral flow assay can assist in the early diagnosis of the disease especially in the resource-poor difficult areas of Northeastern states so that early initiation of treatment can prevent life-threatening complications and reduce mortality.

of patient suspected suffering from Scrub typhus. The mainstay in Scrub-Typhus diagnostics remains serology. The gold standard of diagnostic test is Indirect Immunofluorescent Antibody (IFA) test. Indirect immunoperoxidase (IIP) reduces cost of a fluorescent microscope by substituting peroxidase for fluorescein⁶. Weil-Felix OX-K agglutination reaction are the oldest test which lacks of specificity or sensitivity. Lateral flow assay, SD – Biolin rapid card test and detection of IgM antibody to Scrub Typhus by ELISA are also used in resource poor settings of difficult areas of India with high specificity and low sensitivity¹⁸. Early detection and treatment can reduce the burden of the disease. It is the general conception that in the state of Tripura Scrub Typhus is not seen, though the geotopology, climate, humidity and vegetations are favorable for the growth of tick, the vector of the O

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tsugtsugamushi. As in the recent past we are encountering considerable number of patients being diagnosed as Scrub Typhus, we feel, it is relevant to study scientifically the characteristics of the patients. It will help to generate awareness among the health service providers hence forth of interest for the people of the beautiful state of Tripura.

MATERIALS AND METHOD

This is a retrospective observational study carried out in 2021 in the Department of General Medicine Tripura Medical College and Dr BRAM Teaching Hospital, Tripura. The case records of 42 Scrub Typhus antibody positive by rapid diagnostic test Lateral Flow Assay (LFA) subsequently confirmed by detection of IgM by ELISA admitted in the Department of General Medicine of TMC & Dr BRAM Hospital, in one and half year (1st June, 2020 to 31st December, 2021) were collected and analyzed. The demographic profile, Age, Sex, Gender, occupation and clinical features, examination findings, laboratory results, complications and outcome in the form of discharged or death were documented in pre-designed proforma.

Inclusion Criteria :

- (1) Fever more than 3 days.
- (2) Age more than 18 years.
- (3) Positive serology for Scrub Typhus.
- (4) With or without complication.

Exclusion criteria :

- (1) Patient with other established causes of fever (Infectious or Non infectious)
- (2) Negative serology for Scrub Typhus.

The study was conducted with due permission from the appropriate authority of Hospital and after Clearance from the Institutional Ethical Committee.

RESULT

Socio-demographic Profile :

The middle aged group of people between 31 to 50 years 60.05% (n=29) were mostly affected population in our study followed by young people below the age of 30, 21.43% (n=9) and older age group 9.52% (N=4). Male were affected more 61% compared to female population 31% (Table 1). The minimum and maximum age of the patient were 21 years and 78 years respectively with a mean age of 43.6±12.2 years. The Male to female ratio was 2.23 : 1. Most of the affected people were from rural and hilly areas of Tripura with farming as occupation in the background. Maximum no cases were reported from South district of Tripura followed by Sepahijala

and Gomti District the main harvesting areas of Tripura. Most of the cases were observed in Rainy season that is July to October (Table 1).

Clinical Profile :

All the study population (n=42) presented with fever with average duration of 5.52±2.07 days (Table 2). Maximum temperature noted was 104°F 23.08% (n=10)(Table 2). The most common symptom in our study were headache (81%) and respiratory symptom in the form of Cough (73.8%) and Breathlessness 16.7% followed by Body ache (64%), Arthralgia (64%) and GI symptom (64%). Only six (14.29%) patient had Central Nervous System (CNS) involvement in the form of altered sensorium of which two (33.33%) of them had seizure during their hospital stay (Fig 1). Among the six (14.3%) patient presented with Icterus two (33.33%) of them developed Hepatic Encephalopathy.

The most common clinical examination findings Eschar was observed in 26 (61.9%) patients in our study followed by Hepatomegaly 42.9% (n=18), Anemia 28.6% (n=12), Skin rash 19.5% (n=8), Eyelid edema 14.3% (n=6) and Jaundice 14.3% (n=6). Four patient (66.67%) developed acute hepatitis, Two (33.33%) of them developed hepatic encephalopathy

Table 1 — Showing Demographic profile (n = 42)

Parameters	Number	Percentage (%)
Age group (in Years) :		
Group I (20-30 years)	4	9.52%
Group II (31-50 years)	29	69.05%
Group III (>50 years)	9	21.43%
Gender :		
Male	29	69.0%
Female	13	31.0%
Area of Distribution (District wise) :		
South District	13	31.0%
West District	10	23.8%
North District	0	-
Gomati	6	14.3%
Dhalai	1	2.4%
Sipahijala	5	11.9%
Khowai	6	14.3%
Unokoti	1	2.4%

Table 2 — Showing pattern of fever (n = 42)

Parameters	Number	Percentage (%)
Fever	Present	42
	Absent	0
Temperature (in °F)	Average temperature – 102.57 ± 0.99 °F	
	101 °F	5
	102 °F	18
	103 °F	9
	104 °F	10
Duration of fever (in days)	Average duration of fever – 5.52±2.07	
	3-4 days	13
	5-6 days	18
	≥7 days	11

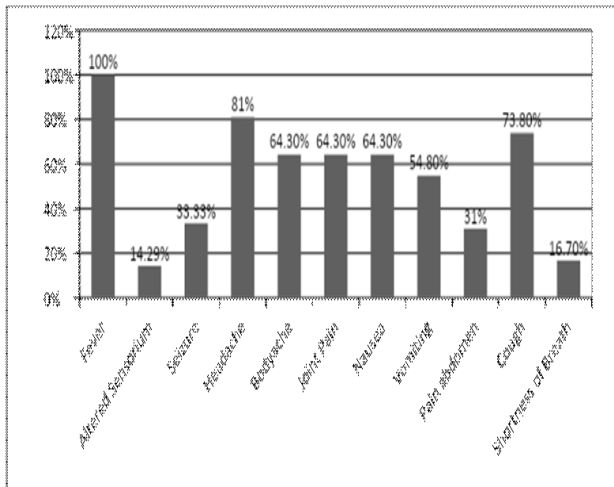


Fig 1 — Symptomatology of Scrub typhus

(Fig 2). Abdominal Ultrasonography(USG) showed hepatomegaly in 23.81% (n=10), splenomegaly in 4.8% (n=2). There was no alteration of hepatic echotexture or obstructive features in USG except in two patients who showed periportal cuffing and increased echogenicity of liver. Chest radiography that is chest X-Ray postero anterior view done in all the cases (n=42), showed radio opacities in 64.41% (n=20), peribronchial thickening in 25.81% (n= 8) ARDS in 6.45% (n=2), pleural effusion in 3.22% (n=1) Lumbar puncture were done in six patient who presented with altered sensorium. Amongst them only one (42.8%) had shown high protein and lymphocytic predominance in Cerebrospinal Fluid (CSF) examination. Computed Tomography with contrast were performed in six cases of suspected CNS involvement and was essentially normal study. Apart from sinus tachycardia no other significant abnormality

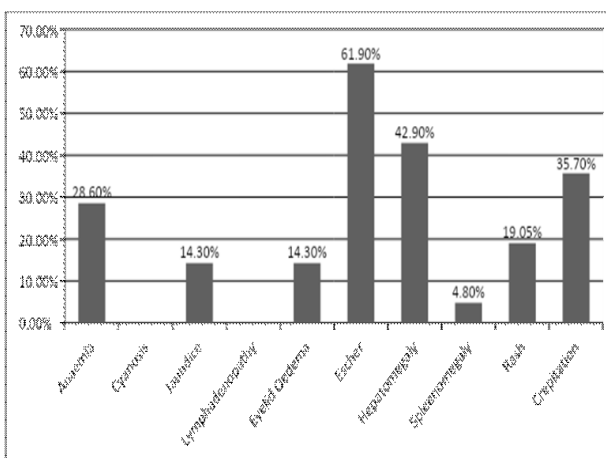


Fig 2 — Clinical signs of Scrub typhus

was found in Electrocardiography done in twenty patients. Urine routine and microscopic examination showed increased protein and Red blood cells in one case (2.38%)(Table 3).

Laboratory Parameter :

In laboratory parameter Anaemia was observed with mean of 10.83±1.54 followed by raised hepatic transaminases 99.996±8.96 for AST(Aspartate Aminotransferase) and 82.864±9.69 for ALT (Alanin aminotransferase). Total count ranges from 4100 to 18000 with mean of 8764.29±3095.85, with neutrophil predominance mean of 76.05±11.79. Alteration in kidney function also observed for urea mean 35.76±32.89 and creatinine 1.06±0.30. Electrolytes abnormality in the form of Hyponatremia (n=4) 9.52% and hypokalemia also noted in our study (Table 3).

DISCUSSION

Scrub Typhus is a Zoonotic disease caused by Orientia tsutsugamushi, has wide range of serotypal variability due to the antigenic protein -56Da, TSA in the genus Orienta⁵. The various type of clinical presentation, multiple organ involvement and case fatality may be duo to antigenic variability. The middle aged male were most affected group in our study like Varghese, *et al*, may be duo to outdoor activity in day time with an occupation of farming from the hilly areas of Tripura⁶. Maximum no of cases were observed in Rainy or extended Rainy season in the month of July to October due to the tropical climate of Tripura where rains continues even to November⁷. This is the main

Parameters	Minimum	Maximum	Mean ± SD
Hemoglobin	5.80	13.00	10.83 ± 1.54
Total count	4100	18000	8764.29 ± 3095.85
Neutrofil	45	90	76.05 ± 11.79
Lymphocytes	10	50	19.79 ± 8.464
Eosinophil	0	5	1.07 ± 1.50
ESR	22	68	44.62 ± 10.92
CRP	0.0	58	21.68 ± 15.27
Billirubin	0.06	2.10	1.09 ± 0.43
SGPT	26	246	99.98 ± 68.69
SGOT	28	235	82.86 ± 49.69
ALP	130	242	175.26 ± 35.4
TP	5.6	7.7	6.86 ± 0.45
Albumin	2.1	6.8	3.54 ± 0.68
Urea	21	232	35.76 ± 32.89
Creatinine	0.70	2.00	1.06 ± 0.30
Urinary protein	0	1	0.31 ± 0.47
Urinary RBC	0	1	0.12 ± 0.32
Na ⁺	129	149	134.60 ± 4.41
K ⁺	2.9	4.8	3.6 ± 0.38
Mg ⁺	1.5	2.1	1.84 ± 0.15

[SD = Standard Deviation]

cultivating time for JOOM cultivations in the hills of Tripura. There are very few cases from the North Tripura probably due to lack of communication and difficult transport duo to the period of Lock down and Government regulation.

Eschar which is the pathognomic lesion for Scrub Typhus were found in 26 cases in our study corresponds with other Asian and Indian study⁸. The most commonest site of Eschar in the Inguinal, peri inguinal area followed by axilla and below the breast. It is very difficult to demonstrate Eschar in highly pigmented people because of its non itchy nature, so thorough clinical examination is required in suspected individuals in the endemic areas⁹.

Almost all the cases presented with fever followed by headache, arthralgia, and myalgia which mimicked with other viral illness specially when the study was conducted during COVID-19 Pandemic period. Most prominent symptom was breathlessness in our study though less documented in other Asian study except in few North Indian study^{5,11}. In the background of Pandemic it was difficult to differentiate the pulmonary involvement of Scrub Typhus from COVID 19. All the patient were admitted after screening through RT PCR and those developed respiratory complications were retested through RT PCR for COVID-19 on fifth day according to ICMR protocol. Interstitial pneumonia, bronchopneumonia and pleural effusion were the prominent respiratory findings which are similar to the other studies done in the sub Himalayan region¹⁴. Initial low oxygen saturation (SpO₂) may be due to mild pleural effusion and Pneumonia which resolved with treatment. Severe form of respiratory complication ARDS also found in our study which correlates with other North Indian studies¹¹.

Second commonest involvement is GI system in our observation in the form of elevated Liver enzymes and anicteric hepatitis, though jaundice was not a prominent feature but different study described Scrub typhus as a commonest cause for acute febrile jaundice in the sub Himalayan region¹³.

Facial oedema and periorbital oedema were observed in few cases in our study is not very uncommon rather sizeable number of cases reported in other studies¹⁰. This oedema may be due to accumulation of fluid in the interstitial space after breaching of endothelial lining with perivasculitis¹⁰. Very few cases of Central Nervous System (CNS) involvement in the form of altered sensorium and seizure were noted, with a complication of meningitis in our study which is similar to other studies as well¹⁵.

The important complications noted in our study were

AKI (Acute Kidney Injury), ARDS, hepatic encephalopathy and Meningitis. Most of the complications were due to delayed presentation or treatment initiation. one patient developed AKI which resolved with treatment in the second week though some studies in adult showed AKI in 12% to 22%¹⁶. Two of our patient who developed hepatic encephalopathy during hospital stay had a history of chronic alcohol intake so may be preexisting liver disease worsen with acute injury, though hepatic complication mentioned in studies by Vikrant, *et al*¹⁶.

Leucocytosis with neutrophilic preponderance observed in our study though different Indian studies showed lymphocytic preponderance with thrombocytopenia¹⁷. Some studies from China showed lower rates of Thrombocytopenia 4.6% to 48.9%¹⁷. Elevated CRP in our study may be attributed to systemic inflammation. Low albumin in few patient may be duo to acute on chronic Liver failure.

Dyselctrolytemia may be duo to Fever and Dehydration which is mentioned in other studies also.

The limitation of our study is that the study was based on first detection of Scrub Typhus by Lateral flow assay which has got high specificity and low sensitivity in the absence of Standard diagnostic test like Indirect immunofluorescence assay. All the cases subsequently confirmed by IgM positivity by ELISA. However, a positive correlation of 97% between IgM ELISA and SD BIOLINE rapid test was reported in India¹⁸.

In conclusion Scrub Typhus should be one of the important differential diagnosis while evaluating a patient with Acute Febrile Illness and multiorgan involvement specially in the North Eastern Region of India where Malaria is endemic. Tropical rain forest is one of the main source of vector larval mite for Rickettsial disease. Varied clinical presentation and low case fatality of Scrub Typhus in NE Region may be due to antigenic variability of *O tsutsugamushi* and recurrent exposure to the organism. Primary care physician should have a high index of suspicion for Scrub Typhus especially in resource poor setting of difficult areas of NE States so that early diagnosis and treatment can prevent severe complications and also will help in reduction of mortality due to Scrub Typhus.

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